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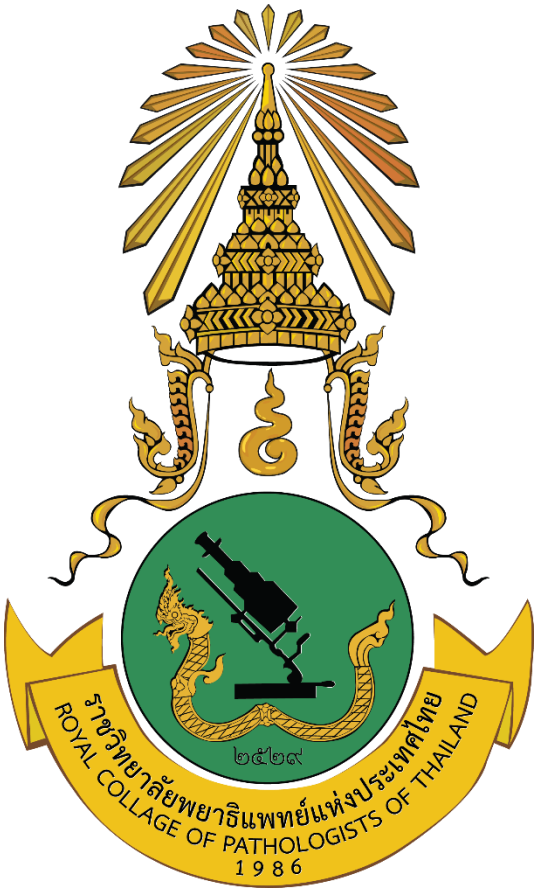

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ABOUT THE JOURNAL

Aims and Scope

Asian Archives of Pathology (AAP) is an open access, peer-reviewed journal. The journal was first published in 2002 under the Thai name "วารสารราชวิทยาลัยพยาธิแพทย์แห่งประเทศไทย" and English name "Journal of the Royal College of Pathologists of Thailand". The journal is a publication for workers in all disciplines of pathology and forensic medicine. In the first 3 years (volumes), the journal was published every 4 months. Until 2005, the journal has changed its name to be "Asian Archives of Pathology: The Official Journal of the Royal College of Pathologists of Thailand", published quarterly to expand the collaboration among people in the fields of pathology and forensic medicine in the Asia-Pacific regions and the Western countries.

The full articles of the journal are appeared in either Thai or English. However, the abstracts of all Thai articles are published in both Thai and English languages. The journal features letters to the editor, original articles, review articles, case reports, case illustrations, and technical notes. Diagnostic and research areas covered consist of (1) **Anatomical Pathology** (including cellular pathology, cytopathology, haematopathology, histopathology, immunopathology, and surgical pathology); (2) **Clinical Pathology (Laboratory Medicine)** [including blood banking and transfusion medicine, clinical chemistry (chemical pathology or clinical biochemistry), clinical immunology, clinical microbiology, clinical toxicology, cytogenetics, parasitology, and point-of-care testing]; (3) **Forensic Medicine (Legal Medicine or Medical Jurisprudence)** (including forensic science and forensic pathology); (4) **Molecular Medicine** (including molecular genetics, molecular oncology, and molecular pathology); (5) **Pathobiology**; and (6) **Pathophysiology**.

All issues of our journal have been printed in hard copy since the beginning. Around the late 2014, we developed our website (www.asianarchpath.com) in order to increase our visibility. We would like to acknowledge that our journal has been sponsored by the Royal College of Pathologists of Thailand. We have the policy to disseminate the verified scientific knowledge to the public on a non-profit basis. Hence, we have not charged the authors whose manuscripts have been submitted or accepted for publication in our journal.

On the other hand, if any authors request a printed copy of the journal issue containing the articles, each of the copied journals costs 450 bahts for Thai authors and 30 United States dollars (USD) for international authors.

Publication Frequency

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ORIGINAL ARTICLE

[OA-01] A study of type VII collagen expression in oral squamous cell carcinoma using immunohistochemical staining

Abdulshukor Kariya[1], Thirayost Nimmanon[2], Sopee Poomsawat[3] and Sirima Sanguansin[3]

1. *Division of Anatomical Pathology, Army Institute of Pathology, Bangkok, Thailand*
2. *Department of Pathology, Phramongkutklao College of Medicine, Bangkok, Thailand*
3. *Department of Oral and Maxillofacial Pathology, Faculty of Dentistry, Mahidol University, Bangkok, Thailand*

Type VII collagen is a main component of anchoring fibrils, providing stability to the dermal-epidermal adhesion. Its reduction or absence has been associated with an increased risk of squamous cell carcinoma (SCC). This study aimed to evaluate type VII collagen expression in oral SCC compared to normal oral mucosa and its relationship with cancer stages. The immunohistochemical study for type VII collagen was performed in 60 cases of oral SCC and 10 cases of normal oral mucosa. The staining intensity and extension were evaluated by two pathologists. Total scores were calculated. The statistical analysis was performed using a Mann-Whitney U test. Oral SCC had a median total score of 0, compared to 7.5 in normal oral mucosa (p = 0.001). Amongst the oral SCC cases, the expression was shown to be decreased in cases at the advanced stages (WHO stages 3 – 4) when compared to those at earlier stages (WHO stages 1 – 2) (p = 0.030). In conclusion, type VII collagen has a high potential for becoming a useful immunohistochemical marker that helps to distinguish oral SCC from its normal tissue counterpart and predict aggressiveness of the tumour.

Keywords: immunohistochemical staining; oral squamous cell carcinoma; type VII collagen

ORIGINAL ARTICLE

[OA-02] Concordance rate of HER2 immunohistochemistry compared to dual-colour in situ hybridisation (DISH) for detecting *HER2* amplification in breast cancer

Adiluck Pisutpunya and Kroonpong Iampenkhae

Department of Pathology, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand

Gold standard of *HER2* amplification detection is fluorescence in situ hybridisation (FISH), but it has several limitations. Many centres use dual-colour in situ hybridisation (DISH) assays to detect *HER2* gene amplification, which is cost less and can be done in a general laboratory. The aim of this study was to determine concordance between immunohistochemistry (IHC) and DISH testing for *HER2* status in breast cancer. A total of 1,307 formalin-fixed paraffin-embedded breast cancer tissues obtained from 2014 to 2021 were evaluated for HER2 score and *HER2* gene status using IHC and DISH, respectively. Breast cancer tissues revealed 481 cases of HER2 score 2+ and 826 cases of HER2 score 3+. *HER2* gene amplification was detected in 173 (36%) cases of HER2 score 2+ and 760 (92%) cases of HER2 score 3+. There were no amplification of *HER2* gene in 308 (64%) cases of HER2 score 2+ and 66 (8%) cases of HER2 score 3+. In conclusion, DISH can be substituted for FISH in the determination of *HER2* gene amplification because there is no difference of consistency with HER2 immunohistochemistry.

Keywords: dual-colour in situ hybridisation; gene amplification; *HER2* status; immunohistochemistry

ORIGINAL ARTICLE

[OA-03] A comparison of placental pathology in pregnant women developing severe pre-eclampsia with and without intrauterine growth restriction

Ananya Trongpisutsak[1] and Patou Tantbirojn[2]

1. *Department of Pathology, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand*
2. *Division of Gynaecologic Pathology, Department of Obstetrics and Gynaecology, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand*

Intrauterine growth restriction (IUGR) is commonly found in women with severe pre-eclampsia. However, the placental pathologic findings are varied reported between cases with and without IUGR. The aim of this study was to compare the placental pathology between pregnant women complicated by severe pre-eclampsia with and without IUGR. Microscopic slides and medical records of severe pre-eclamptic women who delivered during 2009 and 2020 were reviewed. Patients' clinical characteristics and pathologic features were evaluated and analysed. A total of 671 patients were included. IUGR was detected in 26.1%. Cases with IUGR had significantly small-sized placenta (45.7% vs 9.3%, $p < 0.010$), abnormal cord insertion (26.3% vs 13.3%, $p < 0.010$), hypercoiled cord (47.4% vs 33.7%, $p < 0.010$), placental infarct (67.4% vs 43.3%, $p < 0.010$), decidual vasculopathy (46.3% vs 22.2%, $p < 0.010$), foetal thrombotic vasculopathy (14.9% vs 8.1%, $p < 0.010$), distal villous hypoplasia (4.6% vs 0.6%, $p < 0.010$) and accelerated villous maturation (12.6% vs 1.8%, $p < 0.010$). Severe vasculopathy was also significantly increased in IUGR cases (32.6 vs 12.7%, $p < 0.010$). In conclusion, comparing to non-IUGR cases, placentas of cases with IUGR show higher rates of gross and histological features that associated with uteroplacental hypoperfusion.

Keywords: intrauterine growth restriction; placenta; pre-eclampsia

ORIGINAL ARTICLE

[OA-04] Detection of a HIV false elite controller in Thai blood donors

Aphisit Thongthaisin[1], Duangnapa Intharasongkroh[2], Pokrath Hansasuta[3], Jettawan Siriaksorn[1] and Sasitorn Bejrachandra[2]

1. *Department of Laboratory Medicine, Faculty of Medicine, Chulalongkorn University and King Chulalongkorn Memorial Hospital, Bangkok, Thailand*
2. *National Blood Centre, Thai Red Cross Society, Bangkok, Thailand*
3. *Department of Microbiology, Faculty of Medicine, Chulalongkorn University and King Chulalongkorn Memorial Hospital, Bangkok, Thailand*

National Blood Centre, Thai Red Cross Society screens blood samples from every donor for HIV with both serology and nucleic acid testing (NAT). Potential elite controllers (EC) are donors who tested reactive by serology, but non-reactive by NAT. There is no study in Thailand to date to find the cause of this group's test results whether they are due to genetics (true EC) or antiretroviral therapy (ART) drugs (false EC). The aim of this study was to assess the prevalence of HIV false EC in HIV serology reactive Thai blood donors. Stored frozen plasma samples from potential EC collected during July to December 2021 were tested for nucleoside reverse transcriptase inhibitors (NRTIs). Positive sample was further tested for non-nucleoside reverse transcriptase inhibitors (NNRTIs) and protease inhibitors (PIs). In addition, Geenius HIV-1/2 confirmatory assay was also performed for reactive sample. Of 70 potential ECs from total of 315,170 donors (0.02%) during that period, there was one sample (1.43%) that tested positive for NRTIs (tenofovir and emtricitabine). Efavirenz was also found on further testing for NNRTIs. Geenius assay was positive for HIV-1. In conclusion, the prevalence of false EC due to NRTIs was 1.43% in HIV serology reactive only Thai blood donors.

Keywords: antiretroviral therapy; elite controller; HIV

ORIGINAL ARTICLE

[OA-05] Pancreatic islets of Langerhans and insulin secreting cells in haemoglobin Bart's hydrops foetalis

Bunyarit Srisamut and Mana Taweevisit

Department of Pathology, Faculty of Medicine, Chulalongkorn University and King Chulalongkorn Memorial Hospital, Bangkok, Thailand

A finding of islet cell hyperplasia has been reported in infants of diabetic mothers and hydrops foetalis (HF), but no any report in haemoglobin (Hb) Bart's HF. The aim of this study was to analyse the morphometry of beta cells in Hb Bart. Pancreas from 10 Hb Bart cases and 9 controls were retrieved. To detect morphology and nuclear proliferation rate of beta cells, insulin and Ki-67 were immunostained, followed by image analysis measurement. Fifty islets of each case were assessed. Beta cell hyperplasia was assessed by number of nuclei/immunopositive area beta cell hypertrophy assessed by dividing the total immunopositive area by the number of nuclei. Surface areas of islet and beta cells in Hb Bart were not significantly different from controls. In addition, number of beta cell nuclei and cell size in Hb Bart were not significantly different from controls. Since the amount of beta cells was not increased in Hb Bart, the conclusion cannot be substantiated from morphology alone. The insulin in blood and urine should be studied further to measure the secretory activity in Hb Bart disease.

Keywords: haemoglobin Bart; hydrops foetalis; islets of Langerhans; pancreas

ORIGINAL ARTICLE

[OA-06] Immunophenotypic analysis of CD5, CD30 and p53 in diffuse large B-cell lymphoma, not otherwise specified

Burana Khiankaew[1], Paisarn Boonsakan[1] and Pimjai Niparuck[2]

1. *Department of Pathology, Faculty of Medicine Ramathibodi Hospital, Mahidol University, Bangkok, Thailand*
2. *Division of Haematology, Department of Internal Medicine, Faculty of Medicine Ramathibodi Hospital, Mahidol University, Bangkok, Thailand*

Diffuse large B-cell lymphoma, not otherwise specified (DLBCL, NOS), is a common aggressive lymphoma in both developing and developed countries. DLBCL, NOS can express a wide range of immunohistochemical markers that may be used for prognostic evaluation. This study aimed to investigate the immunoexpression of CD5, CD30, and p53 in DLBCL, NOS and its impact to survival. A retrospective study of 111 patients diagnosed with DLBCL, NOS in the Department of Pathology, Ramathibodi Hospital, between the years 2017 to 2019 was conducted. Clinical data, histomorphology, immunophenotypic features and molecular findings were evaluated. Immunostains of CD5, CD30 and p53 were performed. All cases were reviewed by an experienced haematopathologist and a pathology trainee. Of all patients studied, CD5 and CD30 immunostains demonstrated positivity in less than 10% of all cases. Statistical analysis revealed no significant overall survival difference between CD5-, CD30- and p53-positive and negative groups. In conclusion, CD5 and CD30 expression were infrequently identified in DLBCL, NOS patients diagnosed in the Department of Pathology, Ramathibodi Hospital. A study with a larger sample size may be required to represent the population better.

Keywords: CD5; CD30; diffuse large B-cell lymphoma; p53; survival

ORIGINAL ARTICLE

[OA-07] Completeness of the pathological reporting on colorectal cancer specimens: current practice among Thai pathologists

Chanitti Tivitmahaisoon and Somruetai Shuangshoti

Institute of Pathology, Department of Medical Services, Ministry of Public Health, Bangkok, Thailand

Pathological reports play an important role in the treatment of cancer, and the College of American Pathologists (CAP) cancer protocol template is widely used. This study has the purpose to evaluate the completeness of the pathological report and factors that might contribute to it. The aim of this study was to evaluate the completion of pathological reports on colorectal cancer (CRC), according to the CAP guideline, and determine factors that might contribute to it. CRC pathological reports, submitted from various laboratories for molecular testing at the Institute of Pathology, Department of Medical Service, Ministry of Public Health during 2019 – 2020, were reviewed. Factors that might contribute to the practice (pathologist's workplace, expertise and service years) were analysed using Fisher's exact test and Chi-square test. Of the 87 reports, only 3 were complete. The lacking data included treatment effect (84), pathological staging (72), tumour deposit (69), macroscopic tumour perforation (58), perineural invasion (32), lymphovascular invasion (10), tumour site (9), tumour size (5), margin (3), procedure (2), lymph node (1) and tumour extension (1). No correlation was found between the completeness of reports and previously mentioned pathologist's factors. In conclusion, increasing awareness of pathologists is needed.

Keywords: College of American Pathologists; colorectal cancer; pathological report

ORIGINAL ARTICLE

[OA-08] Accuracy of whole slide imaging for frozen section diagnosis of lymph node metastasis: a retrospective study from a tertiary care hospital in Thailand

Charinee Kantasiripitak[1], Thiyaphat Laohawetwanit[1,2] and Sompon Apornvirat[1,2]

1. *Department of Pathology, Thammasat University Hospital, Pathumthani, Thailand*
2. *Chulabhorn International College of Medicine, Thammasat University, Pathumthani, Thailand*

The use of whole slide imaging (WSI) for frozen section (FS) diagnosis is helpful, particularly in the setting of a shortage of pathologists. However, data on such an adoption is minimal in resource-limited settings. The aim of this study was to evaluate the accuracy of WSI for FS diagnosis of lymph node metastasis using a low-cost scanner. FS slides in which the clinical query was to evaluate lymph node metastasis were retrieved. They were digitised by a virtual microscope scanner (MoticEasyScan, Hong Kong) using 40X optical magnification. Three observers with different levels of experience in pathology provided the diagnosis for each slide. Each observer reviewed glass slides (GS) followed by digital slides (DS) after two weeks of washing period. Permanent section (PS) diagnoses were used as a gold standard. A total of 295 FS slides from 63 cases were retrieved and digitised. The agreement between GS and DS diagnosis with PS diagnosis and intra- and interobserver agreements were high. GS and DS diagnoses provided by all observers yielded more than 90% sensitivity, specificity and accuracy. Regardless of a variety of experience in pathology, hence, pathologists could provide accurate FS diagnoses of lymph node metastasis using WSI.

Keywords: accuracy; frozen section; lymph node metastasis; whole slide imaging

ORIGINAL ARTICLE

[OA-09] Assessment of different cut-offs of equivocal HER2 IHC in breast cancer for HER2 ISH to reach appropriate sensitivity, AUC and reduction of ISH assay

Chayanan Puriwat[1], Natthawadee Laokulrat[1], Panitta Sitthinamsuwan[1], Malee Warnnissorn[1], Naree Warnnissorn[2] and Norasate Samarnthai[1]

1. *Department of Pathology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand*
2. *Department of Pathology and Forensic Medicine, Faculty of Medicine, Thammasat University, Pathumthani, Thailand*

The equivocal range of HER2 immunohistochemistry (IHC) is complete weak to moderate staining > 10% of breast cancer cells. This range has increased the numbers of HER2 in situ hybridisation (ISH) testing compared to the previous recommendations. The aim of this study was to assess different cut-offs of equivocal HER2 IHC to reach > 95% sensitivity, improved area under the ROC curve (AUC) and > 15% case reduction of ISH testing. We retrospectively recruited consecutive cases of equivocal IHC from Siriraj Hospital, diagnosed from July 2018 to June 2020. Breast pathologist reviewed the HER2 IHC staining intensity level and percentage. Statistical analysis compared IHC (index test) to dual-colour ISH (DISH) (reference standard). The cohort of 306 equivocal HER2 IHC cases were 56 DISH-positive and 250 DISH-negative. Cut-off at > 10% had 100% sensitivity, AUC of 0.5020 and DISH testing reduction 0%. Cut-offs with > 95% sensitivity were at > 20%, > 30%, > 40% and > 50%. Those with significantly improved AUC were >30%, >40% and >50%. Case reduction > 15% was at cut-offs > 40% and > 50%. In conclusion, weak to moderate > 40% or > 50% HER2 IHC could be a new cut-off for HER2 DISH testing.

Keywords: breast cancer; dual-colour in situ hybridisation; HER2; immunohistochemistry; percentage cut-off

ORIGINAL ARTICLE

[OA-10] The thyroid Bethesda AUS/FLUS category subgroup and the risk of malignancy in Thammasat University Hospital

Chutima Jiragawasan and Wanwisa Himakhun

Department of Pathology, Thammasat University Hospital, Pathumthani, Thailand

The atypia of undetermined significance / follicular lesion of undetermined significance (AUS/FLUS) is one of the categories in the Bethesda System for Reporting Thyroid Cytopathology. The rate of reporting and risk of malignancy (ROM) varies among intuitions. The aim of this study was to determine the reporting rate and risk of malignancy for AUS/FLUS and subgroups in Thammasat University Hospital. A retrospective study collected the data of patients who underwent thyroid FNAs from January 2016 to December 2019. All slides were re-evaluated and subcategorised as cytological atypia, architectural atypia, cytological and architectural atypia, Hurthle cell aspirates and atypia of non-specific (NOS). The ROM was calculated as the lower and upper limits. There were 258 out of 2,995 FNAs (8.6%) diagnosed as AUS/FLUS (mean age, 54.1 years). Of 81 (38.9%) patients had histological correlations. The ROM of the AUS/FLUS was 9.1% – 23.5%. The subgroups of cytological atypia and atypia, NOS risks, were 11.4% – 28.1% and 16.7% – 50%, respectively. No malignancy was present in the other subgroups. Features of pseudonuclear-inclusions had the highest ROM (33.3% – 42.9%). In conclusion, AUS/FLUS interpretation rate of less than 10% is in the practice agreement. The subclassification and histology correlation enhance diagnostic criteria and proper managements.

Keywords: AUS/FLUS; FNA; ROM; subclassification; thyroid

ORIGINAL ARTICLE

[OA-11] Appropriate use of thrombophilia panels testing

Jirakit Sattayapornpipat, Preechaya Wongkrajang and Panutsaya Tientadakul

Department of Clinical Pathology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand

Thrombophilia can be hereditary or acquired. Thrombophilia testing may help making decisions in prevention and treatment in thrombophilia patients. The aim of this study was to evaluate the inappropriate use of the thrombophilia testing both hereditary [protein S (PS), protein C (PC) and antithrombin activity (AT)] and acquired [antiphospholipid syndrome — lupus anticoagulant (LA), anti-beta-2 glycoprotein 1 antibody (aB2GP1 Ab) and anti-cardiolipin antibody (aCL Ab)]. A total of 4,768 tests of PS, PC, AT, LA, aB2GP1 Ab, aCL Ab from Siriraj hospital were retrospectively reviewed using the indication for ordering the tests. The inappropriate rate of the hereditary thrombophilia test orders were 75.81% (188/248), 77.78% (182/234) and 76.97% (137/178) for PS, PC and AT, respectively. On the contrary, acquired thrombophilia test orders were less than 50%, 43.23% (287/664), 42.75% (282/660) and 8.58% (29/338) for aB2GP1 Ab, aCL Ab and LA, respectively. The most common cause of inappropriateness for hereditary thrombophilia test orders was age more than 50 years old (38.37%) and the second most common was testing during acute thrombosis (37.66%). In conclusion, there are many factors influencing the thrombophilia testing orders, so education is the key to utilise the tests.

Keywords: anti-phospholipid antibody; lupus anticoagulant; protein C; protein S; thrombophilia

ORIGINAL ARTICLE

[OA-12] The prevalence of bone marrow involvement in lymphoma patients from Northern Thailand

Kanokkan Saipattranusorn, Charin Yain, Wiyada Dankai and Teerada Daroontum

Department of Pathology, Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand

Several studies on the pattern of bone marrow involvement (BMI) by lymphoma show different results. Multiple factors affect the results including the prevalence. Some lymphomas have a pattern preference. This study aimed to evaluate the prevalence of lymphoma with BMI, including the percentage, the patterns and the discordance in cases with BMI. A total of 1,083 patients newly diagnosed with lymphoma in Maharaj Nakorn Chiang Mai between January 2013 and December 2020 were evaluated for the BMI. Patients with BMI were 267. The available slides for evaluation were 260. The prevalence of BMI for non-Hodgkin lymphoma and Hodgkin lymphoma (HL) was 255/1014 (25.1%) and 12/69 (17.4%), respectively. The prevalence of BMI was highest in lymphoplasmacytic lymphoma (92.3%). The most common pattern was interstitial. A diffuse pattern was common in Burkitt lymphoma and diffuse large B-cell lymphoma (DLBCL). A paratrabecular pattern was most common in follicular lymphoma. HL with BMI showed Reed-Sternberg cells with a characteristic background. Patients with discordant DLBCL tended to have a superior survival. In conclusions, some subtypes of lymphoma have a pattern preference. This can provide the differential diagnosis. The discordant lymphoma tends to have a better prognosis.

Keywords: bone marrow involvement; discordance; lymphoma; pattern

ORIGINAL ARTICLE

[OA-13] Inappropriate use of dilute prolactin testing

Krit Achaloetvaranon[1], Paweena Chunharojrith[2] and Busadee Pratumvinit[1]

1. *Department of Clinical Pathology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand*
2. *Division of Endocrinology and Metabolism, Department of Medicine, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand*

Prolactinoma is the most common cause of pathologic hyperprolactinaemia. The tumour size usually correlates with the prolactin level. Extremely high prolactin levels might cause the hook effect, resulting in erroneously low readings. In patients with pituitary adenomas (≥ 3 cm) and normal to modestly elevated prolactin levels, a 100-fold sample dilution is required to eliminate the hook effect. The aim of this study was to evaluate inappropriate requests of dilution prolactin test (dPRL) at Siriraj hospital, to compare the rate before and after dPRL ordering was formally separated, and to estimate the prevalence of the hook effect. We defined the appropriate ordering criteria for dPRL. We conducted a retrospective review of dPRL ordering between May 2010 and April 2020. Of 440 patients, 20.2% had prolactinoma. From 864 specimens, the inappropriate requests were 81.1% (95% CI: 78.3 – 83.7). After separating dPRL ordering, the number of dilute prolactin requests increased from 1.8 to 5.7% and the rate of appropriateness declined dramatically from 20.5 to 14.0%. Throughout the 10-year study period, no evidence of the hook effect was observed. In conclusion, the inappropriate rate of dPRL test ordering is substantial. Communication between laboratory staff and physicians is critical to the appropriate laboratory use.

Keywords: appropriate use; dilute prolactin; hook effect; hyperprolactinaemia; prolactinoma

ORIGINAL ARTICLE

[OA-14] Clinico-radio-pathological characters of intracranial germ cell tumours and the cut-off values of tumour markers

Napiya Angkarn[1], Kamon Phuakpet[2], Siriwan Piyapittayanan[3] and Pornsuk Cheunsuchon[1]

1. *Department of Pathology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand*
2. *Department of Paediatrics, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand*
3. *Department of Radiology, Faculty of Medicine, Siriraj Hospital, Mahidol University, Bangkok, Thailand*

Intracranial germ cell tumours (ICGCTs) are rare; current treatment depends on tumour secreting status. ICGCTs with beta-hCG > 50 U/L or/and AFP > 10 ng/dL do not need histopathology before treatment initiation. Correlation of clinical, pathological diagnosis and reliability of tumour marker cut-off values are unknown. The aim of this study was to describe clinico-radio-pathological characters of ICGCTs, study the correlation between clinical, pathological diagnosis and the optimal cut-off values of ICGCTs tumour markers. ICGCTs patients diagnosed between 2006 and 2020 were included. Clinical, imaging data, pathologic diagnosis and tumour markers were reviewed. Kappa statistic and ROC curves were used to analyse the correlation and cut-off values. In 128 cases, male to female ratio was 4.5: 1. Pineal region predominated (54.1%). Approximately 68% of ICGCTs were non-secreting. Correlation between clinical and pathological diagnosis was 82.9%. Agreement between serum tumour markers and histopathology were moderate (0.599). Sensitivity and specificity of the current cut-off beta-hCG and AFP ranged from 88.9 – 92.9%. In conclusion, the correlation between clinical and pathological diagnosis is high. Current cut-off values of tumor markers are highly reliable in ICGCTs diagnosis.

Keywords: cut-off value; intracranial germ cell tumours; histopathology; tumour markers

ORIGINAL ARTICLE

[OA-15] Effect of quantity and quality of biopsy specimen on the success of oral cancer diagnosis: a case-control study

Narawich Meemongkol[1], Kitti Jantharapattana[2] and Paramee Thongsuksai[1]

1. *Department of Pathology, Faculty of Medicine, Prince of Songkla University, Songkhla, Thailand*
2. *Department of Otolaryngology Head and Neck Surgery, Faculty of Medicine, Prince of Songkla University, Songkhla, Thailand*

Pathological diagnosis of oral cancer through tissue biopsy is needed before treatment. However, cancer diagnosis is not achieved at first attempt and the repeat biopsy has to be taken. There are limited studies investigating tissue quality and quantity associated with successful biopsy. This study aimed to evaluate the association of quantity and quality of biopsy specimen with the successful diagnosis of oral cancer. This case-control study included patients diagnosed of oral cancer at Songklanagarind Hospital during 2009 – 2019. First biopsy with cancer diagnosis was defined as "successful biopsy" and those with non-cancer diagnosis were "failed biopsy". Number and size of tissue and various histologic features were evaluated on H&E slides. The study included 65 failed biopsies and a random selected 252 successful biopsies. Multivariate logistic analysis showed that biopsy with more than 2 fragments [odd ratio (OR) = 2.36], largest fragment of ≥ 2.6 mm (OR = 4.25), total tissue size ≥ 13.9 mm^2 were significantly associated with successful biopsy. Superficial biopsy is strongly factor associated with failed biopsy (OR = 0.07). In conclusion, a deep biopsy or a biopsy of at least 2.6 mm or biopsy more than two pieces are recommended for successful oral biopsy at first attempt.

Keywords: biopsy; diagnosis; oral cancer; tissue quality; tissue quantity

ORIGINAL ARTICLE

[OA-16] *IDH*, *TERT* and *MGMT* status in Thai patients with high-grade diffuse astrocytomas

Natthapol Kritsana[1], Sakun Santisukwongchote[1],
Chinnachote Teerapakpinyo[2] and Shanop Shuangshoti[1,2]

1. *Department of Pathology, Faculty of Medicine, Chulalongkorn University and Chulalongkorn Memorial Hospital, Bangkok, Thailand*
2. *Chulalongkorn GenePRO Centre, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand*

IDH, *TERT* and *MGMT* status play role in the diagnosis, treatment and outcome of patients with adult gliomas. Since molecular testing is not routinely performed in Thai patients with gliomas, data are limited. A total of 58 high-grade diffuse astrocytomas in Thai adults underwent molecular studies at Chulalongkorn GenePRO Centre, from 2017 to 2018, were included. Demographic data and correlation of the 3 molecular markers were analysed. For the 58 cases, there were 32 men and 26 women, with an average age of 54.9 years (range from 26 – 82 years old). *IDH* and *TERT* promoter mutation were found in 7 cases (14.28%) and 32 cases (56.14%), respectively. There were 22 cases (44%) carrying methylated *MGMT* promoter. *IDH*-mutant gliomas were significantly associated with methylated *MGMT* (p = 0.032, Fisher-exact test) whereas the *IDH*-wild type tumours were significantly correlated with *TERT* mutation (p = 0.017, Fisher-exact test). In conclusion, the prevalence of *IDH*, *TERT* and *MGMT* in our patients with high-grade diffuse gliomas and their associations are in keeping with those described in the literature. Our data enables the clinicians to select the tests more efficiently when the resources are limited.

Keywords: astrocytoma; glioma; *IDH*; *MGMT*; *TERT*

ORIGINAL ARTICLE

[OA-17] The expression of CD15 in placental vessels belonging haemoglobin Bart's hydrops foetalis

Nawaluk Atiroj and Mana Taweevisit

Department of Pathology, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand

Haemoglobin Bart can lead to hydrops foetalis (HF). Its placental findings include abnormally increased intermediate villi with immature endothelium. CD15 assists in diagnosis of delayed villous maturation by identification of foetoplacental endothelial immaturity. Thus, investigation of CD15 expression has benefit for understand pathophysiology of Hb Bart's HF. This study aimed to evaluate CD15 immunoreactivity in placental endothelium of Hb Bart's HF in comparison to that in other causes of HF. CD15 was performed in 14 cases of Hb Bart and 9 cases of HF by other causes (4 cases from anaemia of non-Hb Bart and 5 cases from causes other than anaemia). Twenty-seven cases of control group being gestational age-matched were compared. CD15 was measured by counting stained placental vessels per 100 proximal and distal vessels. The immunoreactivity was recorded as positive, and graded as continuous or discontinuous intense expression. Compared to the control, mean number of distal vasculature that expresses CD15 in continuous pattern was significantly higher in Hb Bart, anaemic HF other than Hb Bart and non-anaemic HF. In conclusion, the significant CD15 expression in distal vasculature proves that Hb Bart's disease is caused by delayed villous maturation, leading to ineffective oxygen transport with later HF.

Keywords: CD15; endothelium; haemoglobin Bart; placenta

ORIGINAL ARTICLE

[OA-18] Histone 3 and histone 4 acetylation pattern in well-differentiated thyroid neoplasms and nodular goitre

Nishal Chhetri and Somboon Keelawat

Department of Pathology, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand

Several epigenetic mechanisms of oncogenesis such as histone acetylation and DNA methylation are now known to play a key role in developing cancers. So far, these molecular events have rarely been evaluated in thyroid neoplasms. The aim of this study was to estimate the histone acetylation level in benign and malignant thyroid lesions and compare it to the normal counterpart. A total of 147 formalin-fixed, paraffin-embedded tissue sections composed of 50 papillary thyroid carcinoma (PTC), 28 follicular adenoma (FA), 19 follicular thyroid carcinoma (FTC) and 50 nodular goitre samples from the archives of the Department of Pathology, Faculty of Medicine, Chulalongkorn University from the year 2016 – 2018, were stained with anti-acetyl histone 3 antibodies (H3K9/K14ac) and anti-acetyl histone 4 antibodies (H4K5,8,12 and 16ac) and scored by Aperio Imagescope software. Deacetylation of both anti-acetyl histone 3 antibody (H3K9/K14ac) and anti-acetyl histone 4 antibody (H4K5,8,12 and 16ac) was detected in nodular goitre ($p = 0.0016$ and $p < 0.0001$ respectively) compared to their normal counterpart. However, the difference in acetylation status for FTC, PTC, and FA compared to their normal counterpart were not statistically significant ($p > 0.0500$). In conclusion, deacetylation is present in nodular goitre.

Keywords: epigenetics; histone acetylation; immunohistochemistry; nodular goitre; well-differentiated thyroid neoplasms

ORIGINAL ARTICLE

[OA-19] Comparing performance of two point-of-care testing (POCT) devices for haemoglobin measurement

Orakan Limpornpugdee, Chitnuphong Saengnil, Panatda Sohab,
Sithee Sodmanee and Narisorn Kongruttachok

Department of Laboratory Medicine, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand

Haemoglobin point-of-care test (POCT-Hb) devices can provide rapid evaluation for blood transfusion decisions in patients with critical bleeding at emergency, intensive care unit, and operating unit. The aim of this study was to compare the performance of two haemoglobin POC devices (HemoCue 201 DM and StatStrip Hb/Hct) in different specimen types. The first step, capillary, venous EDTA, and heparin blood samples were collected from healthy non-anaemic volunteers and anaemic patients. Next step, we evaluated the analytical performance of POCT-Hb devices and a central laboratory analyser was used for reference method. The final step, SPSS version 22.0 was used for statistical analysis. The total allowable error was used to determine the agreement. We found that HemoCue 201 DM performance was better than StatStrip Hb/Hct including heparin and capillary samples. Besides, HemoCue 201 DM has a good performance by using EDTA samples when compared with the central laboratory analyser. In conclusion, POCT-Hb devices are suitable instruments for haemoglobin level evaluation. However, capillary-finger prick blood might yield biased results concerning the individual technique of specimen collection and pre-analytical errors.

Keywords: analytical performance; haemoglobin; point-of-care test

ORIGINAL ARTICLE

[OA-20] High-risk histopathologic features of retinoblastoma: correlation with prognosis

Panuwat Kongtrakun[1], Rangsima Aroonroch[1], Duangnate Rojanaporn[2], Nattawat Asawaworarit[2] and Suradej Hongeng[3]

1. *Department of Pathology, Faculty of Medicine Ramathibodi Hospital, Mahidol University, Bangkok, Thailand*
2. *Department of Ophthalmology, Faculty of Medicine Ramathibodi Hospital, Mahidol University, Bangkok, Thailand*
3. *Department of Paediatrics, Faculty of Medicine Ramathibodi Hospital, Mahidol University, Bangkok, Thailand*

Retinoblastoma is the most common malignant intraocular tumour in children. It has been shown that adjuvant therapy following enucleation in patient with high-risk histopathologic features significantly decrease the mortality. We described the association of histopathologic features with prognostic factors. The aim of this study was to determine the correlation between histopathologic features and prognosis of retinoblastoma. Based on retrospective case series, we evaluated the clinical data, histopathologic features and prognostic factors of 57 retinoblastoma patients who were treated by enucleation at Ramathibodi Hospital, between 2009 and 2019. Twenty-eight of 57 patient (49%) had high-risk histopathologic features. Extraocular extension ($p < 0.001$) and marginal invasion ($p < 0.001$) were associated with all prognostic factors. Post-laminar optic nerve invasion ($p = 0.001$) was associated with survival, death and metastasis. Massive choroidal invasion ($p = 0.005$) was associated with survival and death. Scleral invasion ($p < 0.001$) was associated with survival. Another histopathologic feature; tumour size including basal diameter ($p = 0.002$) and thickness ($p < 0.001$) were associated with prognostic factors. In conclusion, high-risk histopathologic features and tumour size are associated with prognosis of retinoblastoma.

Keywords: high-risk histopathologic features; prognosis; retinoblastoma

ORIGINAL ARTICLE

[OA-21] HPV-related oropharyngeal squamous cell carcinoma: temporal trend and its association with survival

Phatcharipha Saiya[1], Kitti Jantharapattana[2], Arunee Dechaphunkul[3] and Paramee Thongsuksai[1]

1. *Department of Pathology, Faculty of Medicine, Prince of Songkhla University, Songkhla, Thailand*
2. *Department of Otolaryngology Head and Neck surgery, Faculty of Medicine, Prince of Songkhla University, Songkhla, Thailand*
3. *Department of Medicine, Faculty of Medicine, Prince of Songkhla University, Songkhla, Thailand*

Human papillomavirus (HPV) – related oropharyngeal squamous cell carcinoma (OPSCC) is rising in Western countries. In Thailand, proportion of HPV-related OPSCC and its temporal trend are limited data on its temporal trend. This study aimed to determine the proportion and temporal trend of HPV-related OPSCC as well as prognostic significance of HPV status in OPSCC in Southern Thai population. Patients with OPSCC who had available tissue blocks in Songkhlanagarind Hospital between 2009 and 2020 were included. HPV status of the tumour was screened by p16 immunohistochemistry and then confirmed by real-time PCR. Cox regression analysis was used to evaluate prognostic significance. A total of 494 formalin-fixed, paraffin-embedded tissues of OPSCC patients was evaluated. HPV-related OPSCC was found in 56/494 (11.3%) which showed single HPV infection 73.2% and multiple HPV infections 26.8%. During 12 years, the proportion of HPV-related OPSCC showed a trend of increasing but no statistically significance. The p16-positive and HPV-positive OPSCC had significant better overall survival than p16-negative and HPV-negative status. In conclusion, southern Thai patients had a low prevalence of HPV-related OPSCC with a trend of increasing. Both p16 and HPV DNA status are strong independent prognostic factors in OPSCC.

Keywords: human papillomavirus; oropharyngeal squamous cell carcinoma; p16

ORIGINAL ARTICLE

[OA-22] The adjusted protocol in cryosection of axillary sentinel lymph node reduces the overall diagnostic discordance

Phongamorn Rattanasiriphibun, Wiyada Dankai, Surapan Khunamornpong and Suree Lekawanvijit

Department of Pathology, Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand

The cryosection of axillary sentinel lymph node is useful for intraoperative decision in breast cancer patients. However, the consequence from cryosection-permanent section discordance, mainly from sampling error, still occurs. The aim of this study was to evaluate discordant rate, as well as its cause, of the adjusted protocol for cryosection in axillary sentinel lymph node compared to the traditional protocol. The lymph nodes ≥ 9 mm in size were sectioned in 3 mm intervals perpendicular, the smaller nodes were bisected or submitted entirely. The traditional protocol bisected all lymph nodes. The adjusted protocol had been implemented since July 2020. Data were collected until July 2021 to compare with data from 2017 to June 2020 for traditional protocol. For the adjusted protocol, 3 out of 114 (2.63%) were diagnosed as discordance, compared to 16 out of 270 (5.86%) in traditional protocol. Regarding the lymph nodes ≥ 9 mm in size, discordant rate was 5% (12/240) in traditional protocol, compared to 1% (1/100) in adjusted protocol. Sampling error was found in 9 and 1 cases in traditional and adjusted protocols, respectively. In conclusion, the adjusted protocol substantially reduces the overall discordant rate by five times compared to traditional protocol.

Keywords: axillary sentinel lymph node; cryosection; discordance; sampling error

ORIGINAL ARTICLE

[OA-23] Tropomyosin receptor kinase protein expression in Thai cholangiocarcinoma: clinicopathological correlation, pattern expression and prognosis

Pimpika Leepisuth, Sasithorn Watcharadetwittaya and
Prakasit Sa-ngiamwibool
Department of Pathology, Faculty of Medicine, Khon Kaen University, Khon Kaen, Thailand

Tropomyosin receptor kinase (TRK) gene fusion has been found in associated with many tumours and could be targeted treatment. Immunohistochemistry (IHC) expression of TRK is widely used to screening this alternation. The aim of this study was to investigate the expression of TRK protein detected by IHC in Thai cholangiocarcinoma (CCA) and to correlate with clinicopathological and survival data. Retrospective study of CCA patients who diagnosed from January 2011 to December 2015. A total of 85 CCA patients were enrolled. The TRK IHC was expressed in 26 cases (31%) and most of them (25 cases, 96.2%) showed cytoplasmic expression with focal and weak intensity. No clinicopathological correlation with TRK IHC expression was observed. The median survival time of the positive and negative TRK IHC groups were 1.88-year and 1.30-year, respectively (p = 0.041) with hazard ratio 0.564 (p = 0.039, 95% CI = 0.328 – 0.971). In conclusion, the TRK IHC is wildly available, rapid, and high sensitivity but the confirmatory testing is necessary in tumours with low incidence of *NTRK* gene fusion.

Keywords: cholangiocarcinoma; immunohistochemistry; prognosis; tropomyosin receptor kinase

ORIGINAL ARTICLE

[OA-24] The risk of non-standardised clinical chemistry assay in method verification

Piyapat Limprapassorn[1,2], Lawan Piyasuwanying[1,2] and
Narisorn Kongruttanachok[1,2]

1. *Department of Laboratory Medicine, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand*
2. *King Chulalongkorn Memorial Hospital and Thai Red Cross Society, Bangkok, Thailand*

Before implementing Alinity c (Alinity) system, the verification procedure recommended by Clinical and Laboratory Standards Institute (CLSI) was followed on each assays. All parameters passed acceptable criteria of method verification except fructosamine assay. The objective of this study is to investigate the causes of unsuccessful method verification. The principle of fructosamine detection was similar between old and new reagent kits. Therefore, different calibrators and different analyser models might be the causes of unsuccessful verification. We compared fructosamine results by using different calibrators and different analyser models including Architect and Alinity. Fructosamine data were not different between two analyser models. In contrast with different calibrators, we found the poor correlation and positive bias. In conclusion, the effect of calibrator is greater than the analyser model in fructosamine analysis. The assigned value of calibrator plays an important role on clinical chemistry measurement. Since this assay lacks commutable calibrator, this leads to different fructosamine results among fructosamine assay providers.

Keywords: commutable calibrator; diabetes mellitus; fructosamine; glycaemic marker

ORIGINAL ARTICLE

[OA-25] Diagnostic concordance of low-grade endometrial carcinoma between preoperative endometrial biopsy compared to hysterectomy specimen

Pongdanai Damyod[1], Suchanan Hanamornroongruang[1], Malee Warnnissorn[1], Nida Jareemit[2] and Natthawadee Laokulrath[1]

1. *Department of Pathology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand*
2. *Department of Obstetrics and Gynaecology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand*

The discordant histologic grade and subtype of endometrial carcinoma (EC) between the diagnosis of endometrial biopsy and hysterectomy specimen has an impact on patient management. This study aimed to compare the diagnosis of endometrial biopsy with hysterectomy specimen and to determine the histologic factors leading to the discordant grade and subtype. A retrospective study was conducted in 187 cases of low-grade EC diagnosed from endometrial biopsy with subsequent hysterectomy, during 2018 to 2020 in Siriraj Hospital. The blinded review was performed in all discordant cases by three gynaecologic pathologists. The diagnostic accuracy of endometrial biopsy in low-grade endometrial carcinoma was 91.44%. Only 16 cases (8.56%) had discordant histologic grade and subtype. In resection specimen of these cases; twelve cases showed grade 3 endometrioid carcinoma, four cases showed high-grade components (undifferentiated EC, serous and clear cell carcinoma). In conclusion, the endometrial biopsy has a high diagnostic accuracy. However, rendering the diagnosis of high-grade carcinoma is sometimes limited by small amount of high-grade component or overlapping histomorphology of tumour subtype. The suspicion of high-grade component should be raised when unusual morphology is identified in biopsy specimen.

Keywords: endometrial biopsy; endometrial carcinoma; endometrioid carcinoma; low-grade

ORIGINAL ARTICLE

[OA-26] Prognostic significance of combined histologic factors, tumour budding and tumour-infiltrating lymphocyte, in patients with stage II colonic cancer

Prapatsorn Deelon and Sarawut Kongkanka

Department of Pathology, Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand

Colorectal cancer prognosis is based on conventional histologic factors, i.e. subtype, grade, size, lymphovascular invasion, perineural invasion and margin status. The 5th edition of WHO classification of digestive tumours newly updates histologic factors, i.e. growth pattern, tumour budding (TB), poorly differentiated clusters (PDC), tumour-infiltrating lymphocyte (TIL) and Crohn-like reaction (CLR). This study aimed to assess conventional histologic factors and newly updated histologic factors. Haematoxylin and eosin stained slides of 41 patients with stage II colonic adenocarcinoma at Maharaj Nakorn Chiang Mai hospital during 2014 to 2016 were evaluated. The combined histologic factors were grouped as low TB + high TIL (n = 18); low TB + low TIL (n = 11); high TB + high TIL (n = 2); and high TB + low TIL (n = 10). The combined histologic factors showed significant difference in overall survival (OS). Low TB + high TIL showed the best OS, followed by low TB + low TIL and high TB + high TIL. High TB + low TIL showed the worst OS. In conclusion, high-risk histologic factors are considered for the chosen treatment for stage II colonic cancer patients. The combined histologic factors may be useful as high-risk histologic factors.

Keywords: colon cancer; tumour budding; tumour-infiltrating lymphocyte

ORIGINAL ARTICLE

[OA-27] A study of tumour-infiltrating lymphocyte in distal cholangiocarcinoma

Sirada Sangpaibool, Piyapharom Intarawichian and Chaiwat Aphivatanasiri
Department of Pathology, Faculty of Medicine, Khon Kaen University, Khon Kaen, Thailand

Cholangiocarcinoma (CCA) is one of major cancer in Northeast Thailand. Studies reveal tumours can induce immune response due to their altered protein products recognised as foreign bodies by the immune system. Tumour-infiltrating lymphocytes (TILs) can be assessed to represent the mentioned immune response. Recently, TILs are a potential predictive factor of prognosis in many solid tumours; still, data researched in CCA are limited. This study aimed to assess TILs in distal cholangiocarcinoma according to The International TILs Working Group (ITWG) guideline and to correlate it with clinicopathological characteristics and prognosis. TILs were evaluated on H&E sections from surgically resected specimens. Fifty-two cases of distal cholangiocarcinoma were included retrospectively. Average percentages of TILs in each case were calculated and established into ordinal levels used to correlate with clinicopathologic variables and survival. Following clinicopathologic factors, gender ($p < 0.050$), specific growth pattern ($p = 0.010$) and nuclear pleomorphism ($p = 0.010$) correlated with TILs levels. Furthermore, TILs levels corresponded significantly to the overall survival ($p < 0.010$). In conclusion, TILs are significantly associated with prognosis in distal cholangiocarcinoma, similar to other solid tumours.

Keywords: cholangiocarcinoma; pathology; prognosis; tumour-infiltrating lymphocytes

ORIGINAL ARTICLE

[OA-28] The Milan system for reporting salivary gland cytopathology: a 7-year retrospective institutional study

Sirawich Jessadapattarakul and Sasithorn Watcharadetwittaya

Department of Pathology, Faculty of Medicine, Khon Kaen University, Khon Kaen, Thailand

Fine needle aspiration (FNA) cytology is efficient in guiding salivary gland lesions management. Lack of standardised reporting complicates communication between pathologists and clinicians. The Milan System for Reporting Salivary Gland Cytopathology (MSRSGC) has been proposed to improve reporting uniformity. This study aimed to reclassify salivary gland FNA and evaluate risk of malignancy (ROM) in each diagnostic category. All salivary gland FNA cytology in Srinagarind Hospital from January 2013 to December 2019 were retrospectively reviewed and reclassified according to MSRSGC. The ROMs were calculated using the available concurrent histology. A total of 699 cases were included and reclassified as non-diagnostic 333 (45.9%), non-neoplastic 145 (22.5%), AUS 28 (4.0%), benign 101 (14.5%), SUMP 42 (6.0%), suspicious for malignancy 39 (5.6%) and malignant 11 (1.6%). Histologic follow-up was available in 283 cases. The calculated ROMs were 36.1% for non-diagnostic, 37.1% for non-neoplastic, 33.3% for AUS, 10.2% for benign, 50% for SUMP, 92% for suspicious for malignancy and 100% for malignant. Sensitivity, specificity, positive predictive value, negative predictive value and accuracy were 42.9%, 98.0%, 93.1%, 72.9% and 76.5%, respectively. In conclusion, MSRSGC is a valuable classification system that establishes a standard reporting terminology and quantifies the risk of malignancy for each category.

Keywords: cytopathology; fine needle aspiration; risk of malignancy; salivary gland; Milan System

ORIGINAL ARTICLE

[OA-29] Histopathological characteristics of phyllodes tumour and cellular fibroadenoma in core needle biopsy specimens in Army Institute of Pathology

Supasin Boocha and Kittisak Wongchansom

Division of Anatomical Pathology, Army Institute of Pathology, Bangkok, Thailand

Fibroepithelial lesions of the breast encompass various groups of tumours, including fibroadenoma and phyllodes tumour. Fibroadenoma can be clinically observed or complete excision with low recurrent rate, while phyllodes tumour needs wide local excision with negative margins. The diagnosis requires core biopsy assessment which is challenging especially between cellular fibroadenoma and phyllodes tumour. The objective of this study was to differentiate histopathological features of phyllodes tumour and cellular fibroadenoma on core needle biopsy. The cellular fibroadenoma (n = 12) and phyllodes tumour (n = 24) slides from core needle biopsy and subsequent excision in army institute of pathology had been assessed. Histopathological features, including mitosis, stromal cellularity, stromal overgrowth, nuclear pleomorphism, tumour heterogeneity, stromal fragmentation, fat trapping and subepithelial condensation, were evaluated on core needle biopsy slides. Twenty-four cases (66.7%) were diagnosed as phyllodes tumours. Twelve cases (33.3%) were diagnosed as cellular fibroadenoma. The following three histopathological features were statistically significant differences among the two groups, i.e. mitosis, stromal cellularity and subepithelial condensation. In conclusion, subepithelial condensation, stromal cellularity (moderate or more) and mitosis (more than 1 per 10 HPF) are the most helpful features to distinguish phyllodes tumour from cellular fibroadenoma on core needle biopsy.

Keywords: cellular fibroadenoma; core needle biopsy; fibroepithelial lesions; phyllodes tumour

ORIGINAL ARTICLE

[OA-30] Prevalence of non-diabetic renal diseases in diabetic nephropathy in Srinagarind Hospital

Teera Chuthangkura and Katanyoo Sawangsri

Department of Pathology, Faculty of Medicine, Khon Kaen University, Khon Kaen, Thailand

When diabetic patients are screened for diabetic nephropathy, it is discovered that some of them have both diabetic nephropathy with other superimposed diseases, which could change their management and prognosis. This study aimed to find out the prevalence of non-diabetic renal diseases which had diabetic nephropathy. Renal biopsies report of diabetic nephropathy cases in Srinagarind Hospital from January 2016 to December 2020 were retrospective descriptive study. A total of 268 cases had reported of diabetic nephropathy. There were 129 females and 139 males with mean age 52.1 ± 10.94 years old. Pathological reports were diabetic nephropathy combined with non-diabetic renal diseases, glomerular diseases in 39 cases, tubulointerstitial diseases in 196 cases and vascular diseases in 22 cases. Non-diabetic renal diseases showed IgA nephropathy (6.05%); membranous nephropathy (3.26%); membranoproliferative glomerulonephritis (2.33%); lupus nephritis (1.86%); tubulointerstitial diseases (73.13%) including acute interstitial nephritis (63.26%), acute tubular necrosis, interstitial fibrosis and tubular atrophy; and vascular diseases (8.21%). In conclusion, the most common lesion is acute interstitial nephritis. As a result, it is important to remember that non-diabetic renal diseases can coexist with diabetic nephropathy.

Keywords: acute interstitial nephritis; diabetes mellitus; diabetic nephropathy; non-diabetic renal diseases

ORIGINAL ARTICLE

[OA-31] Uterine sarcoma and carcinosarcoma in Srinagarind hospital: a clinicopathological correlation

Tritraporn Sawantranon[1], Waritta Kunprom[1], Amornrat Temtanakitpaisan[2] and Pilaiwan Kleebkaow[2]

1. *Department of Pathology, Faculty of Medicine, Khon Kaen University, Khon Kaen, Thailand*
2. *Department of Obstetrics and Gynaecology, Faculty of Medicine, Khon Kaen University, Khon Kaen, Thailand*

Uterine sarcomas are heterogeneous group of rare aggressive tumour accounting for 3 – 7% of all uterine malignancy, with generally poor outcome. The aim of this study was to describe subtypes, clinicopathological characteristics and survival rates of uterine sarcoma and carcinosarcoma. Medical records and histological results of uterine sarcoma and carcinosarcoma between 2010 and 2019 at Srinakarind Hospital, Khon Kaen University were reviewed. A total of 56 cases had been reviewed. The first three most common subtypes were 19 leiomyomas (33.9%), 18 carcinosarcomas (32.1%) and 7 endometrial stromal sarcomas (12.5%). Most cases were in FIGO stage I (33 cases, 58.9%). The 5-year overall survival (OS) and 5-year disease-free survival (DFS) were 40% with median of 40 months and 34% with median of 15 months, respectively. Neither histologic subtypes nor FIGO staging was significantly associated with survival. However, adjuvant therapy tended to have significant impacts in prolonged both OS (37.6 ± 8.8 months vs 3.9 ± 1.4 months, p = 0.000) and DFS (30.4 ± 8.7 months vs 2.0 ± 1.3 months, p = 0.013) in late stages of the disease. In conclusion, the most common subtype of uterine sarcomas is leiomyosarcoma.

Keywords: carcinosarcoma; clinicopathological subtypes; survival rates; uterine sarcoma

ORIGINAL ARTICLE

[OA-32] Analysis of tissue zinc levels in breast cancer subtypes

Vasin Chantaraponpun[1], Thirayost Nimmanon[2] and Chetana Ruangpratheep[2]

1. *Division of Anatomical Pathology, Army Institute of Pathology, Bangkok, Thailand*
2. *Department of Pathology, Phramongkutklao College of Medicine, Bangkok, Thailand*

Our previous study has been discovered that the zinc levels were significantly higher in the surrounding normal breast tissue compared to the invasive breast carcinoma (IBC) tissue. The objective of this study was to quantitatively analyse tissue zinc levels in molecular subtypes of IBC. Zinc concentrations were evaluated in 45 formalin-fixed, paraffin-embedded tissue sections of IBC by the inductively coupled plasma optical emission spectrometry (ICP-OES) method. Molecular subtypes of IBC were classified by immunohistochemical reactivities for oestrogen receptor (ER), progesterone receptor (PR), human epidermal growth factor receptor 2 (HER2) and Ki67 proteins. At the 95% confidence interval, the correlation of tissue zinc levels with immunoexpressions and molecular subtypes was assessed. Forty-five IBC cases were categorised into three main subtypes, i.e. luminal (14 cases), HER2-positive (10 cases) and triple-negative (17 cases) breast cancers. Four cases were not classified because they revealed an equivocal HER2 expression (score 2+). Tissue zinc levels had no significant relationship with hormone receptor (ER, PR and HER2) status, KI67 proliferation index and molecular subtypes. In conclusion, intracellular zinc may not alter significantly during the development of breast cancer molecular subtypes.

Keywords: ICP-OES; immunoexpression; invasive breast carcinoma; molecular subtypes; tissue zinc

ORIGINAL ARTICLE

[OA-33] Histopathological and clinical study between primary adnexal carcinoma with pagetoid spreading and extramammary Paget disease

Warit Chongkolwatana[1], Panitta Sittinamsuwan[1], Suchanan Hanamournroongruang[1], Ngoentra Tantranont[1], Kanapon Pradniwat[1], Thitipat Hansomwong[2], Vuthinun Achariyapota[3], Penvadee Pattanaprichakul[4] and Voraparee Suvannarerg[5]

1. *Department of Pathology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand*
2. *Division of Urological Surgery, Department of Surgery, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand*
3. *Department of Obstetrics and Gynaecology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand*
4. *Department of Dermatology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand*
5. *Division of Diagnostic Radiology, Department of Radiology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand*

Extramammary Paget disease (EMPD) is rare. When EMPD with invasive carcinoma is identified, primary adnexal carcinoma (PAC) is a main differential diagnosis. We aimed to compare difference of histopathology and prognosis of EMPD with invasion and PAC. Haematoxylin and eosin – stained sections of EMPD with invasive carcinoma between 2006 and 2021 were classified into PAC with pagetoid spreading and EMPD with invasion. We compared four characteristics between both entities as follows: (1) clinical presentation; (2) lymphovascular invasion; (3) regional lymph node metastasis; and (4) distant metastasis. A total of 33 cases were recruited and classified into 10 cases of PAC with pagetoid spreading and 23 cases of EMPD with invasion. PAC included adenocarcinoma, not otherwise specified in 5/10 cases, apocrine carcinoma in 3/10 cases, hidradenocarcinoma in 1/10 cases and syringocystadenocarcinoma papilliferum in 1/10 cases. Clinical presentation of PAC was mass lesion (p-value < 0.0001). PAC presented higher lymphovascular invasion (p-value = 0.010) and regional lymph node metastasis (p-value = 0.004). In conclusion, PAC shows worse prognosis when compared with EMPD with invasion due to higher lymphovascular invasion and regional metastasis. Clinical history and specific histologic characteristics are needed for differentiating both diseases.

Keywords: adnexal carcinoma; extramammary Paget disease; pagetoid spreading

ORIGINAL ARTICLE

[OA-34] The use of artificial intelligence in diagnosis of papillary thyroid carcinoma

Wuttichai Kimlap[1], Nopporn Tipparawong[1], Nichthida Tangnuntachai[1], Somboon Keelawat[1], Boonserm Kijsirikul[2] and Pittipol Kantavat[2]

1. *Department of Pathology, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand*
2. *Department of Computer Engineering, Faculty of Engineering, Chulalongkorn University, Bangkok, Thailand*

Thyroid cancer is considered the most common endocrine malignancy, with papillary thyroid carcinoma (PTC) being the most predominant form, accounting for 85% of all diagnoses. Due to the diagnostic dilemma that can commonly occur in these neoplasms, artificial intelligence (AI) technology has been attempted to assist the diagnosis of these cancers. The aim of this study was to apply AI technology in diagnosis of PTC. The 1,027 and 1,054 images of benign thyroid tissue and PTC from 60 patients were used for training and validation by three convolutional neural network models, namely VGG16, VGG19 and ResNet50V2, each with added layers. The VGG19 model with added layers of avgpool2D gave the most reliable test values with an accuracy of 0.9763, false-positive of 2.6667 and false-negative rate of 7.1667. The sensitivity and specificity were 0.9659 and 0.9870, respectively. In conclusion, AI technology could provide a high accuracy in diagnosing PTC and has the potential to become a new diagnostic modality of this cancer.

Keywords: artificial intelligence; medical diagnosis; papillary thyroid carcinoma

REVIEW ARTICLE

[RA-01] Forensic medicine towards entrepreneurial institute

Arnon Jumlongkul

School of Medicine, Mae Fah Luang University, Chiang Rai, Thailand

Disruptive technology and the COVID-19 situation have unavoidably impacted all medical fields as well as academic institutions. Many universities around the world have closed their doors, and new institutes are few and far between. The global trend of university expansion typically begins with an academic institute, then moves on to a research institute, and finally to an entrepreneurial institute. Forensic pathologists are currently confronted with a challenging situation that has the potential to usher in a new era in our traditional routine practices. As a result, the goal of this session is to show participants how to apply medical knowledge to create medical inventions that can lead organisations to entrepreneurial institutes. Second, the author's experience teaching and practicing medical innovation devices will be shared. Finally, we will talk about how to train medical students to be innovative physicians or medical innovators in our medical schools. The author hopes that in the future, all pathology disciplines will be able to develop innovative products to help our profession thrive.

Keywords: entrepreneurial institute; forensic medicine; innovative physician; medical innovation

REVIEW ARTICLE

[RA-02] Anion gap: no magic number!

Busadee Pratumvinit

Department of Clinical Pathology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand

Anion gap (AG) is a parameter that indicates the difference or gap between negatively and positively charged electrolytes. It is primarily used in the differential diagnosis of metabolic acidosis and may be used in clinical laboratories to identify analytical errors. The AG was calculated using sodium (Na^+), chloride (Cl^-) and bicarbonate ($HCO3^-$). Some laboratories add potassium. In the 1970s, the mean AG concentration in healthy persons was between 11 and 15 mmol/L. These values were established using an analyser which is no longer used. Nowadays, the majority of clinical laboratories use ion-selective electrodes to measure Na^+, K^+ and Cl^-. The $HCO3^-$ is measured using the rate of pH change determined with a pH electrode or by an enzymatic method. With these methods, Na^+ concentration differs slightly from that measured with previous methods, while Cl^- concentration can be substantially greater. Thus, AG is lower than previously reported levels, averaging 6 mmol/L. In some laboratories, however, AG is comparable to that observed in the 1970s, owing to lower calibration settings for Cl^- measurement. As a result, AG reference intervals may change amongst clinical laboratories. Laboratory practitioners should validate or create their instrument-specific reference interval for AG.

Keywords: anion gap; metabolic acidosis; quality control; reference interval

REVIEW ARTICLE

[RA-03] Lobular neoplasm: how to define and diagnose?

Chaiwat Aphivatanasiri

Department of Pathology, Faculty of Medicine, Khon Kaen University, Khon Kaen, Thailand

The term "lobular neoplasia (LN)" is defined by the WHO Classification of Breast Tumour, 5th edition, 2019 as the entire spectrum of atypical epithelial lesions originating in the terminal duct lobular unit and characterised by a proliferation of generally small, non-cohesive monomorphic cells, with or without pagetoid involvement of terminal ducts. Atypical lobular neoplasia (ALH) and lobular carcinoma in situ (LCIS) are separated by the extension of the disease. LN is usually presented without specific clinical features and a significant proportion of them are incidentally found according to other breast lesions. The LCIS is found in 0.5 – 3.6% of otherwise benign breast biopsies. *CDH1* inactivation, which leads to loss or impaired function of E-cadherin, is an early event and hallmark of lobular lesions. The management of LN found in core biopsy specimens is still controversial and required a multidisciplinary team and also includes the patient for management discussion and decision.

Keywords: atypical lobular hyperplasia; lobular carcinoma in situ; lobular neoplasia

REVIEW ARTICLE

[RA-04] Current concept of membranoproliferative glomerulonephritis

Katanyoo Sawangsri

Department of Pathology, Faculty of Medicine, Khon Kaen University / Srinagarind Hospital, Khon Kaen, Thailand

Membranoproliferative glomerulonephritis (MPGN) is used to be classified as MPGN type I, II and III. The older classification only gave a diagnosis but did not include the aetiology and pathophysiology of the disease. The new classification gives the clinician more detail and leads to proper treatment. The old and new classification of MPGN include aetiology, a little bit of reporting system of renal pathology and how to report MPGN. In conclusion, MPGN is a pattern of disease which may be caused by primary or secondary glomerular disease. Pathologists should be aware and given the clinician the information as much as the tissue could tell us.

Keywords: glomerular disease; membranoproliferative glomerulonephritis; renal pathology

REVIEW ARTICLE

[RA-05] External consultation of lymphoid neoplasms

Naree Warnnissorn

Department of Pathology, Faculty of Medicine, Thammasat University, Pathumthani, Thailand

Diagnosis of lymphomas is complex and requires resource higher than common cancers. In the difficult cases, the general pathologists could request external consultation (EC) for the interpretive judgment from the haematopathologists. The aim of this review is to reveal recent international experiences of external consultation in lymphoid neoplasms (LN). Regarding the EC of LN, the major diagnostic revision ranges from 16% to 55% with non-diagnostic/ambiguous reports to lymphomas (52%), tumour type revisions (23%) and malignant to benign lesions (14%). The concordance rates are Hodgkin lymphoma (57%), B-cell LN (38%) and T cell LN (33%). The easily missed lymphomas are angioimmunoblastic T-cell lymphoma, diffuse large B-cell lymphoma variants, lymphoplasmacytic lymphoma and mucosal associated lymphoid tissue lymphoma. The high discrepancy rate is attributable to limited use of ancillary tests, deferred/multiple diagnoses, diagnostic uncertainty and unfamiliarity with WHO classification. The Lymphopath Network, a national haematopathology expert, reviews every newly diagnosed lymphoma before starting the therapy. A diagnostic change with impact occurs in 17.4% and most frequently as misclassification in lymphoma subtypes is 41.3%. The Network provides data of under reported lymphomas. In conclusion, EC is a quality process to reduce diagnostic error and enhance continuous education of lymphoma classification.

Keywords: external consultation; haematopathology; lymphoma; major discrepancy

REVIEW ARTICLE

[RA-06] Lymphohistiocytic pattern of ALK-positive anaplastic large cell lymphoma in the brain mimicking inflammatory processes

Narittee Sukswai

Department of Pathology, Chulalongkorn University, Bangkok, Thailand

ALK-positive anaplastic large cell lymphoma (ALCL) constitutes 3% of non-Hodgkin lymphoma in adults. Brain involvement is rarely noted. A systematic review of primary ALCL of the central nervous system is found only 36 globally reported cases with noted clinical course, adequate radiological imaging and *ALK* status. Only 28 of the cases show ALK positivity. Regarding microscopic findings, most of the cases of ALCL (> 60%) is harboured common pattern, exhibiting proliferation of large anaplastic cells that tends to evade sinuses and paracortex of the lymph node. Only a small number of cases (approximately 10%) shows lymphohistiocytic pattern. We hereby present a case of ALK-positive ALCL arranged in lymphohistocytic pattern mimicking inflammation involving the brain. Acknowledgment of such cases may help with the diagnosis of the extremely rare case and lead to the correct management of the patient.

Keywords: *ALK* status; anaplastic large cell lymphoma; central nervous system

REVIEW ARTICLE

[RA-07] Ethanol level and hip flask defence

Peerayuht Phuangphung

Department of Forensic Medicine, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand

Driving under influence (DUI) of alcohol is the common issue in forensic toxicology. In Thailand, blood alcohol concentration (BAC) at 50 mg/dL and 20 mg/dL are statutory limits for general people and people under 20 years old, respectively. However, the time of obtaining blood sample is usually delayed from the time of driving. In addition, alleged drivers can claim that they consumed alcohol after traffic accidents. This claim of post-driving consumption is so-called hip flask defence. Thus, back alcohol calculation is used to determine BAC at the time of driving based on Widmark's equation and alcohol elimination rate. There are some challenges in back alcohol calculation. Firstly, alcohol elimination rate follows zero-order kinetics and alcohol elimination rate is averagely accepted as 15 – 20 mg/dL per hour. However, there are some variations in alcohol elimination rates. Secondly, back alcohol calculation requires the calculation for Widmark's factor (r) and r comes out in range. Finally, some factors affect alcohol absorption and lead to variations in maximal blood alcohol concentrations used for calculation. Thus, medical opinions in back alcohol calculation should be carefully provided.

Keywords: blood alcohol concentration; driving under influence; Widmark's equation

REVIEW ARTICLE

[RA-08] A case study in clinical applications of therapeutic plasma exchange

Phandee Watanaboonyongcharoen

Department of Laboratory Medicine, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand

Therapeutic plasma exchange (TPE) relies on removal of whole blood with subsequent separation into components and removal of plasma component. It is capable of removing pathogenic blood components that causes morbidity from patients. Another benefit of TPE is the use of replacement fluid which has normal and functional proteins. Fresh frozen plasma and 5% albumin are mostly used as replacement fluids. The role of TPE for treatment of diseases and indications is shown in guidelines on the use of therapeutic apheresis in clinical practice – Evidence-based approach from the writing committee of the American Society for Apheresis (ASFA). The guidelines are published in the special issue every 3 years with the goal of providing update, practical evidence-based guidance in the performing of therapeutic apheresis. TPE is relatively safe and most of the adverse reactions are mild and easily resolved. Citrate toxicity is the most common reaction.

Keywords: apheresis; citrate toxicity; fresh frozen plasma; therapeutic plasma exchange

REVIEW ARTICLE

[RA-09] Breast duct lesions: an insight into correlations between sonographic ductal changes and cyto-histology

Pichet Sampatanukul, Darunee Boonjunwetvat and Kris Chatamra

Queen Sirikit Centre for Breast Cancer, King Chulalongkorn Memorial Hospital, Thai Red Cross Society, Bangkok, Thailand

Correlations between ductal changes seen in breast ultrasound and cyto-histology can give useful and subtle information of diseased ducts. The authors propose a systematic classification of large, medium and small duct lesions. Intraductal papillary neoplasm and mammary duct ectasia are main entities of the large duct group that is characterised by subareolar location and single long tube-like image. Medium-sized duct lesions are those seen in periareolar to mid zone and usually have a branching appearance. Ductal carcinoma in situ and other intraductal proliferative diseases are lesions considered within the differential diagnoses. Small duct abnormalities would be challenging and not easily visualized as branching tubes. Focally thickened ducts in association with some ill-defined echogenic and cystic features are characteristics. Signs of lobular obstruction and dilatation may be recognised. Both non-invasive and invasive tumours have to be distinguished from fibrocystic diseases and other benign changes.

Keywords: breast duct lesion; breast ultrasound; ductal carcinoma in situ; intraductal proliferative lesion; thickened duct

REVIEW ARTICLE

[RA-10] Podocytopathy: the new diagnostic entity

Sakkarn Sangkhamanon

Department of Pathology, Faculty of Medicine, Khon Kaen University, Khon Kaen, Thailand

Podocytopathy is an entity of kidney diseases that could be from direct or indirect podocyte injury. The common clinical manifestations are proteinuria and nephrotic syndrome with various severity ranging from steroid-responsive to steroid-resistant cases which could affect both children and adults. Some underlying mechanisms responsible for podocyte damage include genetic susceptibility, particularly *APOL1*, and environmental factors such as immune-mediated, infectious agents, exogenous compounds, haemodynamic abnormality and obesity. Associated common pathological changes in kidney biopsy are minimal change lesions and focal segmental glomerulosclerosis lesions. For primary podocytopathy with morphological features of focal segmental glomerulosclerosis lesions, corticosteroids and other immunosuppressants are choices of therapy. The minority of cases who do not respond to both agents might have poor kidney outcomes. Renin-Angiotensin System (RAS) antagonists can be beneficial in reducing proteinuria and the rate of fibrosis progression. Other supportive management may involve diuresis, lipid-lowering drugs and infectious and thrombotic prevention. This review is to communicate to practicing pathologists in Thailand about the shifting of the diagnostics model formerly based on histopathology alone, for instance, minimal change disease (MCD) and focal segmental glomerulosclerosis (FSGS), toward a multiparametric diagnosis based on clinical, morphology and genetic data.

Keywords: focal segmental glomerulosclerosis; minimal change disease; podocytopathy

REVIEW ARTICLE

[RA-11] Next-generation sequencing in pathology: enabling personalised medicine

Takol Chareonsirisuthigul

Department of Pathology, Faculty of Medicine Ramathibodi Hospital, Mahidol University, Bangkok, Thailand

Personalised medicine promises to minimize health care costs by shifting from a standard medical model of treating pathologies to a tailored predictive and preventative one. Next-generation sequencing (NGS) has the potential to speed up the early detection of diseases as well as the identification of pharmacogenetic markers that can be used to personalize treatments. This overview covers the historical events that led to the development of NGS, as well as its strengths and drawbacks, with a focus on the analytical aspects of NGS data processing. All of the stages required for executing NGS in the clinical environment have answers, and most of them are highly efficient, but there are a few critical steps in the process that require quick attention.

Keywords: next-generation sequencing; pathology; personalised medicine

CASE REPORT

[CR-01] Mitochondrial myopathy in a 50-year-old woman mimicking ocular myasthenia: the fifth reported case of Kearns-Sayre syndrome in Thailand

Chayanont Netsawang[1], Montana Pothong[2], Supoch Tunlayadechanont[2], Takol Chareonsirisuthigul[1], Chinnawut Suriyonplengsaeng[3] and Jariya Waisayarat[1]

1. *Department of Pathology, Faculty of Medicine Ramathibodi Hospital, Mahidol University, Bangkok, Thailand*
2. *Department of Medicine, Faculty of Medicine Ramathibodi Hospital, Mahidol University, Bangkok, Thailand*
3. *Department of Anatomy, Faculty of Science, Mahidol University, Bangkok, Thailand*

Mitochondria are intracellular organelles that play important roles in energy-producing and organismal survival via oxidative phosphorylation. The defection of this system leads to mitochondrial dysfunction and mitochondrial myopathies. The usual ocular motor presentation is a chronic, symmetrical, and diffuse weakness of extraocular muscle. We described a 50-year-old woman of Kearns-Sayre syndrome (KSS) presenting with chronic progressive bilateral ptosis and ophthalmoparesis or chronic progressive external ophthalmoplegia (CPEO) and bilateral generalised muscle weakness with fluctuation since 15 years. There was no evidence of cardiac conduction block, cerebellar ataxia or pigmentary retinopathy. Initially, even though the serologic investigation for acetylcholine receptor antibody was negative, the patient responded to symptomatic treatment for myasthenia gravis (pyridostigmine). The muscle biopsy was performed due to worsened weakness. It showed a large amount of cox-deficient/negative fibres on oxidative enzymatic stains under the light microscope. The ultrastructural study showed subsarcolemmal accumulations of abnormal mitochondria, paracrystalline inclusions and cristae linearization with angular features. These findings were compatible with mitochondrial myopathy. In conclusion, KSS mimics ocular myasthenia in clinical presentation and treatment responsiveness. Definite diagnosis is crucial for prognosis, genetic counseling and proper management.

Keywords: chronic progressive external ophthalmoplegia; Kearns-Sayre syndrome; mitochondrial myopathy; ocular myasthenia

CASE REPORT

[CR-02] ALK-positive large B-cell lymphoma

Piti Ungarreevittaya

Department of Pathology, Faculty of Medicine, Khon Kaen University, Khon Kaen, Thailand

ALK-positive large B-cell lymphoma (ALK-positive LBCL) is a rare type of lymphoma. Because of the overlap of morphological and immunophenotypic features with other haematologic and non-haematologic neoplasms, diagnosing ALK-positive LBCL can be challenging. The lymph nodes showed a marked diffuse infiltrate of monomorphic large immunoblast-like cells with round pale nuclei containing a large central nucleolus and abundant amphophilic cytoplasm. Lymphoma cells were strongly positive for the ALK protein. The neoplastic cells strongly expressed EMA and plasma cell markers with positive cytoplasmic immunoglobulin and light chain restriction. In most cases, they were negative or only sometimes positive for B-cell lineage–associated antigens and CD30. In conclusion, a diagnosis of ALK-positive LBCL is based on a combination of histomorphology and immunohistochemical markers, particularly ALK protein.

Keywords: anaplastic lymphoma kinase; immunohistochemistry; large B-cell lymphoma

CASE REPORT

[CR-03] Inflammatory EBV-positive follicular dendritic cell sarcoma

Piti Ungarreevittaya

Department of Pathology, Faculty of Medicine, Khon Kaen University, Khon Kaen, Thailand

Inflammatory EBV-positive follicular dendritic cell sarcoma is a variant of follicular dendritic cell (FDC) sarcoma, which is a rare neoplasm. Inflammatory EBV-positive FDC sarcoma, also known as inflammatory pseudotumour-like FDC sarcoma, is a type of FDC sarcoma. The tumour has distinct clinical characteristics, as in a preponderance in young to middle-aged women, almost exclusively involving the liver or spleen, having neoplastic cells that are Epstein-Barr virus – positive. The neoplastic spindled cells are scattered inside a significant lymphoplasmacytic infiltration on histological examination. Follicular dendritic cell markers such as CD21, CD23 and CD35 are typically positive in neoplastic cells. In conclusion, inflammatory EBV-positive FDC sarcoma morphology challenges are distinguished from inflammatory pseudotumour and inflammatory myofibroblastic tumour, with which it shares many morphologic and immunohistochemical features. EBV-EBER and immunohistochemical markers of FDC play an important role in the diagnosis.

Keywords: Epstein-Barr virus; follicular dendritic cell sarcoma; inflammatory myofibroblastic tumour; inflammatory pseudotumour

APPENDIX 1
INFORMATION FOR AUTHORS

All authors listed in a paper submitted to Asian Archives of Pathology (AAP) must have contributed substantially to the work. It is the corresponding author who takes responsibility for obtaining permission from all co-authors for the submission. When submitting the paper, the corresponding author is encouraged to indicate the specific contributions of all authors (the author statement, with signatures from all authors and percentage of each contribution can be accepted). Examples of contributions include: designed research, performed research, contributed vital new reagents or analytical tools, analysed data, and wrote the paper. An author may list more than one type of contribution, and more than one author may have contributed to the same aspect of the work.

Authors should take care to exclude overlap and duplication in papers dealing with related materials. See also paragraph on Redundant or Duplicate Publication in "Uniform Requirements for Manuscripts Submitted to Biomedical Journals" at http://www.icmje.org/index.html.

The submitted manuscripts will be reviewed by three members of the Editorial Board or three expert reviewers from different institutions. At the discretion of the Editorial Board, the manuscripts may be returned immediately without full review, if deemed not competitive or outside the realm of interests of the majority of the readership of the Journal. The decision (reject, invite revision, and accept) letter will be coming from the Editorial Board who has assumed responsibility for the manuscript's review. The editor's decision is based not just on technical merit of the work, but also on other factors such as the priority for publication and the relevance to the Journal's general readership. All papers are judged in relation to other submissions currently under consideration.

Categories of Manuscripts

1. Letters to the Editor

The letters to the editor are the reactions to any papers published in AAP. These letters will be reviewed by the Editorial Board and sent to the authors of the original paper with an invitation to respond. Letters and eventual responses will be published together, when appropriate.

- *Word Count: 300 – 500 words (excluding references and figure or table legends)*
- *Abstract: Not required*
- *References: Maximum of 10*
- *Figure or Table: Maximum of 1 (if needed)*

2. Original Articles

The original articles are the researches describing the novel understanding of anatomical pathology, clinical pathology (laboratory medicine), forensic medicine (legal medicine or medical jurisprudence), molecular medicine or pathobiology. Systematic reviews, meta-analyses and clinical trials are classified as articles. The articles should be clearly and concisely written in the well-organised form (see ***Organisation of Manuscripts***): abstract; introduction; materials and methods; results; discussion; and conclusions. The manuscripts that have passed an initial screening by the Editorial Board will be reviewed by two or more experts in the field.

- *Word Count: 3,000 – 5,000 words (excluding abstract, references, and figure or table legends)*
- *Structured Abstract (see **Organisation of Manuscripts**): 150 – 200 words*
- *References: Maximum of 150*
- *Figures or Tables: Maximum of 6*

3. Review Articles

The review articles are generally invited by the Editor-in-Chief. They should focus on a topic of broad scientific interest and on recent advances. These articles are peer-reviewed before the final decision to accept or reject the manuscript for publication. Therefore, revisions may be required.

- *Word Count: 3,000 – 5,000 words (excluding abstract, references, and figure or table legends)*
- *Unstructured Abstract: 150 – 200 words*
- *References: Maximum of 150*
- *Figures or Tables: Maximum of 4*

4. Case Reports

AAP limits publication of case reports to those that are truly novel, unexpected or unusual, provide new information about anatomical pathology, clinical pathology (laboratory medicine) or forensic medicine (legal medicine or medical jurisprudence). In addition, they must have educational value for the aforementioned fields. The journal will not consider case reports describing preventive or therapeutic interventions, as these generally require stronger evidence. Case reports that involve a substantial literature review should be submitted as a review article. The submitted case reports will undergo the usual peer-reviewed process.

- *Word Count: 1,200 – 2,000 words (excluding abstract, references, and figure or table legends)*
- *Unstructured Abstract: 150 – 200 words*
- *References: Maximum of 20*
- *Figures or Tables: Maximum of 4*

5. Case Illustrations

Case illustrations are aimed to provide education to readers through multidisciplinary clinicopathological discussions of interesting cases. The manuscript consists of a clinical presentation or description, laboratory investigations, discussion, final diagnosis, and up to 5 take-home messages (learning points). Regarding continuous learning through self-assessment, each of the case illustrations will contain 3 – 5 multiple choice questions (MCQs) with 4 – 5 suggested answers for each question. These MCQs are placed after the final diagnosis and the correct answers should be revealed after the references. The questions and take-home messages (learning points) are included in the total word count. The manuscripts that have passed an initial screening by the Editorial Board will be reviewed by two experts in the field.

- *Word Count: 1,000 – 2,000 words (excluding references and figure or table legends)*
- *Abstract: Not required*
- *References: Maximum of 10*
- *Figures: Maximum of 2*
- *Tables: Maximum of 5*

6. Technical Notes

The technical notes are brief descriptions of scientific techniques used in the anatomical pathology, clinical pathology (laboratory medicine), forensic medicine (legal medicine or medical jurisprudence), molecular medicine or pathobiology. The submitted manuscripts are usually peer-reviewed.

- *Word Count: Maximum of 1,000 words (excluding references and figure or table legends)*
- *Abstract: Not required*
- *References: Maximum of 5*
- *Figures or Tables: Maximum of 2*

Organisation of Manuscripts

1. General Format

The manuscripts written in English language are preferable. However, Thai papers are also acceptable, but their title pages, abstracts, and keywords must contain both Thai and English. These English and Thai manuscripts are prepared in A4-sized Microsoft Word documents with leaving 2.54-cm (1-inch) margins on all sides. All documents are required to be aligned left and double-spaced throughout the entire manuscript. The text should be typed in 12-point regular Times New Roman font for English manuscript and 16-point regular TH SarabunPSK font for Thai manuscript.

The running titles of English and Thai manuscripts are placed in the top left-hand corner of each page. They cannot exceed 50 characters, including spaces between words and punctuation. For the header of English paper, the running title will be typed in all capital letters. The page number goes on the top right-hand corner.

Footnotes are not used in the manuscripts, but parenthetical statements within text are applied instead and sparingly. Abbreviations should be defined at first mention and thereafter used consistently throughout the article. The standard abbreviations for units of measure must be used in conjunction with numbers.

All studies that involve human subjects should not mention subjects' identifying information (e.g. initials) unless the information is essential for scientific purposes and the patients (or parents or guardians) give written informed consent for publication.

2. Title Page

The title page is the first page of the manuscripts and must contain the following:

- The title of the paper (not more than 150 characters, including spaces between words)
- The full names, institutional addresses, and email addresses for all authors (If authors regard it as essential to indicate that two or more co-authors are equal in status, they may be identified by an asterisk symbol with the caption "These authors contributed equally to this work" immediately under the address list.)
- The name, surname, full postal address, telephone number, facsimile number, and email address of the corresponding author who will take primary responsibility for communication with AAP.
- Conflict of interest statement (If there are no conflicts of interest for any author, the following statement should be inserted: "The authors declare that they have no conflicts of interest with the contents of this article.")

3. Abstract

A structured form of abstract is used in all Original Article manuscripts and must include the following separate sections:

- *Background: The main context of the study*
- *Objective: The main purpose of the study*
- *Materials and Methods: How the study was performed*
- *Results: The main findings*
- *Conclusions: Brief summary and potential implications*
- *Keywords: 3 – 5 words or phrases (listed in alphabetical order) representing the main content of the article*

4. Introduction

The Introduction section should clearly explain the background to the study, its aims, a summary of the existing literature and why this study was necessary or its contribution to the field.

5. Materials and Methods

The Materials and Methods section must be described in sufficient detail to allow the experiments or data collection to be reproduced by others. Common routine methods that have been published in detail elsewhere should not be described in detail. They need only be described in outline with an appropriate reference to a full description. Authors should provide the names of the manufacturers and their locations for any specifically named medical equipment and instruments, and all chemicals and drugs should be identified by their systematic and pharmaceutical names, and by their trivial and trade names if relevant, respectively. Calculations and the statistical methods employed must be described in this section.

All studies involving animal or human subjects must abide by the rules of the appropriate Internal Review Board and the tenets of the recently revised Helsinki protocol. Hence, the manuscripts must include the name of the ethics committee that approved the study and the committee's reference number if appropriate.

6. Results

The Results section should concisely describe the findings of the study including, if appropriate, results of statistical analysis which must be presented either in the text or as tables and figures. It should follow a logical sequence. However, the description of results should not simply repeat the data that appear in tables and figures and, likewise, the same data should not be displayed in both tables and figures. Any chemical equations, structural

formulas or mathematical equations should be placed between successive lines of text. The authors do not discuss the results or draw any conclusions in this section.

7. Discussion

The Discussion section should focus on the interpretation and the significance of the findings against the background of existing knowledge. The discussion should not repeat information in the results. The authors will clearly identify any aspects that are novel. In addition, there is the relation between the results and other work in the area.

8. Conclusion

The Conclusion section should state clearly the main summaries and provide an explanation of the importance and relevance of the study reported. The author will also describe some indication of the direction future research should take.

9. Acknowledgements

The Acknowledgements section should be any brief notes of thanks to the following:

- *Funding sources*
- *A person who provided purely technical help or writing assistance*
- *A department chair who provided only general support*
- *Sources of material (e.g. novel drugs) not available commercially*

Thanks to anonymous reviewers are not allowed. If you do not have anyone to acknowledge, please write "Not applicable" in this section.

10. References

The Vancouver system of referencing should be used in the manuscripts. References should be cited numerically in the order they appear in the text. The authors should identify references in text, tables, and legends by Arabic numerals in parentheses or as superscripts. Please give names of all authors and editors. The references should be numbered and listed in order of appearance in the text. The names of all authors are cited when there are six or fewer. When there are seven or more, only the first three followed by "et al." should be given. The names of journals should be abbreviated in the style used in Index Medicus (see examples below). Reference to unpublished data and personal communications should not appear in the list but should be cited in the text only (e.g. A Smith, unpubl. Data, 2000).

- *Journal article*

1. Sibai BM. Magnesium sulfate is the ideal anticonvulsant in preeclampsia – eclampsia. Am J Obstet Gynecol 1990; 162: 1141 – 5.

- *Books*

  2. Remington JS, Swartz MN. Current Topics in Infectious Diseases, Vol 21. Boston: Blackwell Science Publication, 2001.

- *Chapter in a book*

  3. Cunningham FG, Hauth JC, Leveno KJ, Gilstrap L III, Bloom SL, Wenstrom KD. Hypertensive disorders in pregnancy. In: Cunningham FG, Hauth JC, Leveno KJ, Gilstrap L III, Brom SL, Wenstrom KD, eds. Williams Obstetrics, 22nd ed. New York: McGraw-Hill, 2005: 761 – 808.

11. Tables

The tables should be self-contained and complement, but without duplication, information contained in the text. They should be numbered consecutively in Arabic numerals (Table 1, Table 2, etc.). Each table should be presented on a separate page with a comprehensive but concise legend above the table. The tables should be double-spaced and vertical lines should not be used to separate the columns. The column headings should be brief, with units of measurement in parentheses. All abbreviations should be defined in footnotes. The tables and their legends and footnotes should be understandable without reference to the text. The authors should ensure that the data in the tables are consistent with those cited in the relevant places in the text, totals add up correctly, and percentages have been calculated correctly.

12. Figure Legends

The legends should be self-explanatory and typed on a separate page titled "Figure Legends". They should incorporate definitions of any symbols used and all abbreviations and units of measurement should be explained so that the figures and their legends are understandable without reference to the text.

If the tables or figures have been published before, the authors must obtain written permission to reproduce the materials in both print and electronic formats from the copyright owner and submit them with the manuscripts. These also follow for quotes, illustrations, and other materials taken from previously published works not in the public domain. The original resources should be cited in the figure captions or table footnotes.

13. Figures

All illustrations (line drawings and photographs) are classified as figures. The figures should be numbered consecutively in Arabic numerals (Figure 1, Figure 2, etc.). They are submitted electronically along with the manuscripts. These figures should be referred to specifically in the text of the papers but should not be embedded within the text. The following information must be stated to each microscopic image: staining method,

magnification (especially for electron micrograph), and numerical aperture of the objective lens. The authors are encouraged to use digital images (at least 300 d.p.i.) in .jpg or .tif formats. The use of three-dimensional histograms is strongly discouraged when the addition of these histograms gives no extra information.

14. Components

14.1. Letters to the Editor

The Letter to the Editor manuscripts consist of the following order:

- *Title Page*
- *Main Text*
- *References*
- *Table (if needed)*
- *Figure Legend (if needed)*
- *Figure (if needed)*

14.2. Original Articles

The Original Article manuscripts consist of the following order:

- *Title Page*
- *Structured Abstract*
- *Introduction*
- *Materials and Methods*
- *Results*
- *Discussion*
- *Conclusions*
- *Acknowledgements*
- *References*
- *Table (s)*
- *Figure Legend (s)*
- *Figure (s)*

14.3. Review Articles

The Review Article manuscripts consist of the following order:

- *Title Page*
- *Unstructured Abstract*
- *Introduction*
- *Main Text*
- *Conclusions*
- *Acknowledgements*
- *References*
- *Table (s)*

- *Figure Legend (s)*
- *Figure (s)*

14.4. Case Reports

The Case Report manuscripts consist of the following order:

- *Title Page*
- *Unstructured Abstract*
- *Introduction*
- *Case Description*
- *Discussion*
- *Conclusions*
- *Acknowledgements*
- *References*
- *Table (s)*
- *Figure Legend (s)*
- *Figure (s)*

14.5. Case Illustrations

The Case Illustration manuscripts consist of the following order:

- *Title Page*
- *Clinical Presentation or Description*
- *Laboratory Investigations*
- *Discussion*
- *Final Diagnosis*
- *Multiple Choice Questions (MCQs)*
- *Take-Home Messages (Learning Points)*
- *Acknowledgements*
- *References*
- *Correct Answers to MCQs*
- *Table (s)*
- *Figure Legend (s)*
- *Figure (s)*

14.6. Technical Notes

The Technical Note manuscripts consist of the following order:

- *Title Page*
- *Introduction*
- *Main text*
- *Conclusions*
- *Acknowledgements*
- *References*

- *Table (s)*
- *Figure Legend (s)*
- *Figure (s)*

Proofreading

The authors of the accepted manuscripts will receive proofs and are responsible for proofreading and checking the entire article, including tables, figures, and references. These authors should correct only typesetting errors at this stage and may be charged for extensive alterations. Page proofs must be returned within 48 hours to avoid delays in publication.

Revised Manuscripts

In many cases, the authors will be invited to make revisions to their manuscripts. The revised manuscripts must generally be received by the Editorial Board within 3 months of the date on the decision letter or they will be considered a new submission. An extension can sometimes be negotiated with the Editorial Board.

APPENDIX 2
BENEFITS OF PUBLISHING WITH ASIAN ARCHIVES OF PATHOLOGY

Asian Archives of Pathology (AAP) is an open access journal. Open Access makes your works freely available to everyone in the world. It provides a significant boost to the readership of your articles, and has been shown to have an increase in positive influence on citations and reuse. Hence, open-access leads to more recognition for our esteemed authors.

The journal has been sponsored by the Royal College of Pathologists of Thailand. We have the policy to disseminate the verified scientific knowledge to the public on a non-profit basis. Hence, we have not charged the authors whose manuscripts have been submitted or accepted for publication in our journal.

Since AAP is also a peer-reviewed journal, the submitted manuscripts will be reviewed by three members of the Editorial Board or three expert reviewers from different institutions. The decision on these manuscripts is processed very fast without any delay and in shortest possible time. The processing period is 1 – 2 weeks. These decisions of the reviewers are unbiased and the decision (reject, invite revision, and accept) letter coming from the Editorial Board is always conveyed to the authors.

APPENDIX 3
SUBMISSION OF THE MANUSCRIPTS

Step 1: Access www.asianarchpath.com

Step 2: If you did not register before, please create an account first.

Step 3: Login with your username and password.

Step 4: Click the "+ New Submission" button on the upper right-hand side of the page.

Step 5: Proceed to fill up the Submission Form online and follow the directions given therein.

Step 6: Upload your manuscript file (s).

Step 7: Re-check the content of your manuscript (s) and the uploaded file (s) more carefully prior to the submission. If you have submitted your manuscript file (s) incorrectly, you must contact Editor-in-Chief of Asian Archives of Pathology immediately. The Editor-in-Chief can clear the incorrect attempt and allow you another submission.

Step 8: Click the "Submit Manuscript" button under Important Notice.

If you have any further enquiries, please do not hesitate to contact the Journal.

APPENDIX 4
CONTACT THE JOURNAL

The Editorial Office of Asian Archives of Pathology

Department of Pathology, Floor 6, Her Royal Highness Princess Bejaratana Building
Phramongkutklao College of Medicine
317 Rajavithi Road, Rajadevi, Bangkok 10400 Thailand

Telephone: +66 (0) 90 132 2047

Fax: +66 (0) 2 354 7791

Email: editor@asianarchpath.com

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Assistant Professor Dr Chetana Ruangpratheep
The Editorial Office of Asian Archives of Pathology
Department of Pathology, Floor 6, Her Royal Highness Princess Bejaratana Building
Phramongkutklao College of Medicine
317 Rajavithi Road, Rajadevi, Bangkok 10400 Thailand
Telephone: +66 (0) 90 132 2047
Fax: +66 (0) 2 354 7791
Email: editor@asianarchpath.com

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MD, FRCPath (Thailand), MSc, PhD
Editor-in-Chief of Asian Archives of Pathology

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Assistant Professor Dr Chetana Ruangpratheep
The Editorial Office of Asian Archives of Pathology
Department of Pathology, Floor 6, Her Royal Highness Princess Bejaratana Building
Phramongkutklao College of Medicine
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