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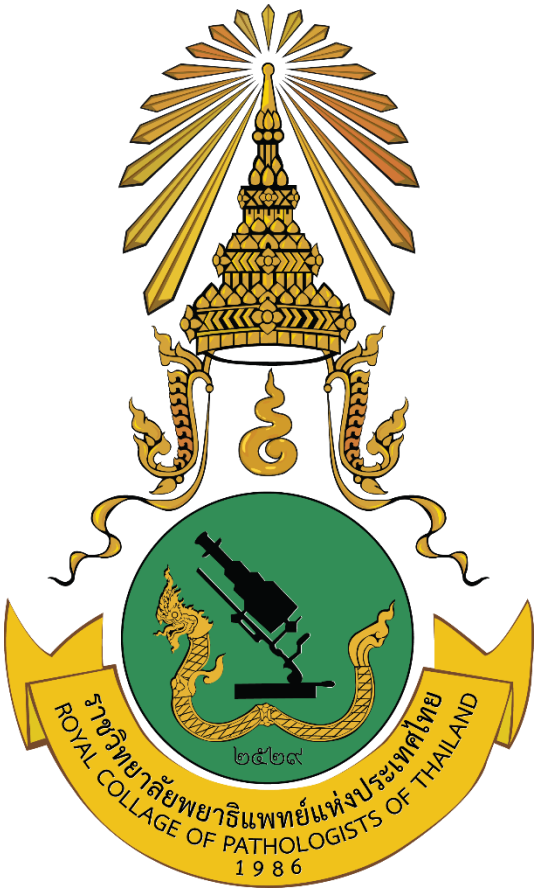

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ABOUT THE JOURNAL

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.

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ความหลากหลายที่เกิดในแต่ละเซลล์ของเนื้อเยื่อมะเร็ง (Tumour heterogeneity)

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จากการศึกษาทางอณูพยาธิวิทยา (Molecular pathology) ของมะเร็งแสดงให้เห็นว่า ภายในเนื้อเยื่อมะเร็งจะปรากฏความหลากหลายของลักษณะทางจุลกายพยาธิสภาพ (Histopathological appearances) และลักษณะการแสดงออกทางโมเลกุล (Molecular expression profile) ของเซลล์มะเร็ง ทั้งนี้สิ่งที่ปรากฏในเนื้อเยื่อมะเร็งดังกล่าวนั้นเรียกว่า "***Tumour heterogeneity***" ซึ่งความหลากหลายเหล่านี้สามารถเกิดขึ้นได้ใน 4 รูปแบบ[(1)] ดังนี้คือ

<u>รูปแบบที่ 1</u> เป็นความหลากหลายที่เกิดในแต่ละเซลล์ของเนื้อเยื่อมะเร็งปฐมภูมิ (Primary cancer) ของผู้ป่วยแต่ละรายที่มีมะเร็งเกิดขึ้นในอวัยวะเดียวกันและมีลักษณะทางจุลกายพยาธิสภาพชนิดเดียวกันอีกด้วย ซึ่งเรียกความหลากหลายของเนื้อเยื่อมะเร็งแบบนี้ว่า "***Interpatient tumour heterogeneity***"

<u>รูปแบบที่ 2</u> เป็นความหลากหลายที่เกิดในแต่ละเซลล์ของเนื้อเยื่อมะเร็งปฐมภูมิของผู้ป่วย ซึ่งเรียกความหลากหลายของเนื้อเยื่อมะเร็งแบบนี้ว่า "***Intratumour heterogeneity***"

<u>รูปแบบที่ 3</u> เป็นความหลากหลายที่เกิดในแต่ละเซลล์ของเนื้อเยื่อมะเร็งทุติยภูมิ [Secondary (metastatic) cancer] ที่กระจายไปยังอวัยวะต่างๆของผู้ป่วย ซึ่งเรียกความหลากหลายของเนื้อเยื่อมะเร็งแบบนี้ว่า "***Intermetastatic heterogeneity***"

<u>รูปแบบที่ 4</u> เป็นความหลากหลายที่เกิดในแต่ละเซลล์ของเนื้อเยื่อมะเร็งทุติยภูมิที่อยู่ในอวัยวะนั้น ซึ่งเรียกความหลากหลายของเนื้อเยื่อมะเร็งแบบนี้ว่า "***Intrametastatic heterogeneity***"

เนื่องจากความหลากหลายในลักษณะการแสดงออกทางโมเลกุลของเซลล์มะเร็งเต้านมแต่ละเซลล์ที่ปรากฏอยู่ในเนื้อเยื่อมะเร็งนั้น ทำให้เกิดสมมติฐานว่าการแพร่กระจายของเซลล์มะเร็งไปยังตำแหน่งต่างๆของร่างกายนั้น เกิดจากการคัดเลือกเซลล์มะเร็งบางตัวในตำแหน่งปฐมภูมิ (Primary cancer cells) ซึ่งเซลล์นั้นถูกแบ่งตัวจากเซลล์มะเร็งเริ่มแรกโดยกระบวนการที่เรียกว่า "***Clonal selection***" โดยเซลล์ที่ถูกคัดเลือกดังกล่าวจะมีคุณสมบัติทางโมเลกุลซึ่งเอื้อต่อคุณสมบัติของการแพร่กระจาย ดังนั้นมิใช่เซลล์มะเร็งทั้งหมดใน

ตำแหน่งปฐมภูมิที่สามารถแพร่กระจายได้ ทั้งนี้เซลล์มะเร็งซึ่งแพร่กระจายไปยังตำแหน่งต่างๆของร่างกาย (Metastatic cancer cells) จะปรากฏการแสดงออกทางโมเลกุลที่แตกต่างไปจากเซลล์มะเร็งส่วนใหญ่ในตำแหน่งปฐมภูมิด้วย อันเป็นผลให้การเจริญเติบโตของเซลล์มะเร็งทั้งสองแห่งนั้นมีความแตกต่างกันด้วยเช่นกัน[2]

<u>เอกสารอ้างอิง</u>

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CASE REPORT

Effect of healthy lifestyle on lipid profile in a young woman with overweight

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Abstract

In the past decades, the prevalence of overweight and obesity have increased substantially worldwide, especially in South-East Asia countries including Thailand. Recent data from prospective studies have indicated that overweight and obesity in children and adolescents are predictors of adult obesity. There is also substantial evidence that the association between obesity and cardiovascular disease is explained by the adverse cardiovascular risk factor profile including hypertension, type 2 diabetes mellitus and dyslipidaemia. Since the occurrence of overweight and obesity is mainly attributed to an unhealthy lifestyle (unhealthy diet and sedentary behaviour), we demonstrated in a case study that adopting a lifestyle of consuming a healthy diet and performing regular physical activity can reverse the adverse abnormal lipid profile seen in our overweight patient.

Keywords: healthy lifestyle; lipid profile; overweight

Introduction

Increased serum concentrations of total cholesterol (TC) and low-density lipoprotein cholesterol (LDL-C) represent established major cardiovascular disease (CVD) risk factors, and LDL-C levels have long been used as the target for lipid-lowering therapy. The role of triglycerides (TG) in predicting cardiovascular risk, on the other hand, is the topic of debate for several decades. Recent data from prospective epidemiological and genetic studies have, however, indicated that TG and TG-rich lipoprotein including remnant cholesterol (RN-C) have a causal association with the development of atherosclerotic cardiovascular disease (ASCVD)[1,2]. We report herein a case of a young women with overweight, in whom adoption of a healthy lifestyle alone, without the use of lipid-lowering medication, resulted in a significant improvement in serum lipid profile.

Case Report

A 27-year-old woman came to the hospital because she was concerned about her abnormal lipid profile detected at the routine laboratory check-up in the year 2017. She reported to have no family history of hypercholesterolaemia or dyslipidaemia associated with type 2 diabetes mellitus. Her calculated body mass index (BMI) was high at 25.6 kg/m^2, indicating an overweight[3], and her waist circumference was normal at 78 cm. Laboratory investigations of liver and renal function as well as plasma glucose were all in the normal ranges.

Serum concentrations of lipid and lipoprotein were determined on a fully-automated analyzer Cobas 602 (Roche Diagnostics) using standard enzymatic methods. As shown in *Table*, serum TG (reference value < 150 mg/dL) and high-density lipoprotein cholesterol (HDL-C, reference value > 50 mg/dL) level was high and low at 304 mg/dL and 41 mg/dL, respectively, resulting in a high TG to HDL-C ratio of 7.41. The calculated RN-C (TC minus LDL-C minus HDL-C, reference value < 30 mg/dL) level was also high at 61 mg/dL. Her TC, LDL-C (calculated by Friedewald formula: LDL-C = TC – HDL-C – TG/5), and non-HDL-C (TC minus HDL-C, reference value < 200, 130 and 160 mg/dL, respectively) levels in 2017 were all above the reference ranges. A retrospective analysis of the data between the year 2014 and 2017 has revealed a rising trend in serum levels of TG and RN-C, and a decreasing trend in concentrations of HDL-C. A rising trend in levels of TC, LDL-C and non-HDL-C was also observed (*Table*).

Table: Serum lipid and lipoprotein concentrations serially determined between the year 2014 and 2019.

	2014	2015	2016	2017	2018	2019
TG (mg/dL)	174	286	249	304	146	186
HDL-C (mg/dL)	47	43	42	41	55	46
RN-C (mg/dL)	35	57	50	61	29	37
TG/HDL-C	3.70	6.65	5.93	7.41	2.65	4.40
TC (mg/dL)	228	257	258	241	268	213
LDL-C (mg/dL)	146	157	166	139	184	130
Non-HDL-C (mg/dL)	181	214	216	200	213	167
TC/HDL-C	4.85	5.98	6.14	5.88	4.87	4.63

Note: *HDL-C = High-density lipoprotein cholesterol; LDL-C = Low-density lipoprotein cholesterol; Non-HDL-C = Non-high-density lipoprotein cholesterol; RN-C = Remnant cholesterol; TC = Total cholesterol; and TG = Triglycerides*

Based on these results, the patient was advised to adopting a healthy lifestyle which primarily consists of a healthy diet (increase consumption of fruits, vegetables and fish, and reduce intake of fatty and high sodium foods as well as sugar-sweetened beverages) and regular physical activity (150 minutes/week of moderate-intensity leisure-time activity). As can be seen in *Table*, there was a significant improvement in the dyslipidaemic profile, with a marked decrease in TG level to the reference range, and a significant rise in HDL-C level, resulting in a low TG/HDL-C ratio after one year of intervention. The RN-C level also showed a decline toward the reference range. Although a rising trend in TG and RN-C concentrations, and a decreasing trend in HDL-C levels were seen after 2 years of intervention (in 2019) as compared with those in 2018, they still showed a favourable profile compared to those before intervention in the year 2017. In contrast, an increasing trend in TC, LDL-C and Non-HDL-C levels, measured in 2018, compared to those determined in 2017 was observed. Nevertheless, their concentrations in 2019 exhibited a strong favourable lipid profile compared to all of those determined between the year 2014 and 2018. Of interest is the observation that all of the lipid and lipoprotein levels determined in 2019 were comparable to those measured in 2014 (*Table*). In this context, it is important to note that during the 2-year period of intervention, her BMI and waist circumference have declined from 25.6 to 24.0 kg/m^2 and 78 to 74 cm, respectively.

Discussions

The main findings in the present case study are that adoption of a healthy lifestyle alone, without the need for pharmacologic intervention, results in a significant increase in HDL-C serum concentration and a considerable reduction in TG level and the TG/HDL-C ratio. Since all the lipid parameters mentioned above have been proved to be strong predictors of ASCVD[4,5], their measurements should be routinely used, along with those of TC and LDL-C, in the risk assessment of cardiovascular disease. In addition, calculation of RN-C level should be performed to predict residual cardiovascular risk, especially in patients with overweight or obese, since this novel parameter has recently been shown to be a potent atherogenic lipoprotein similar to that of LDL-C[6,7]. Recently, calculated RN-C has been recommended to be used as an optional parameter in addition to the standard lipid profile (TC, TG, HDL-C, LDL-C and Non-HDL-C) for cardiovascular risk assessment[8]. In this context, it has been reported that a healthy diet alone may not represent a useful tool to significantly reduce serum TC and LDL-C concentrations. According to the US National Cholesterol Education Programme, Step I or Step II diet lead only to a 12% and 16% reduction in LDL-C level[9], respectively, a far less lipid-lowering effect compared to the effect of lipid-lowering drug in the statin group of 30 to 50%. However, it has been recommended that the use of statins in primary prevention should be confined to the patients considered to be at intermediate or high risk of developing cardiovascular disease[10,11]. On the other hand, by considering the young age and the absence of major CVD risk factors (smoking, hypertension and diabetes mellitus), our patient can be classified into the low risk group in which there is no indication for pharmacological treatment. Nonetheless, the data from this case report indicated that the use of the combination of a healthy diet and regular physical activity can result in a significant reduction in atherogenic lipid and lipoprotein levels. Similar observations have been made in several recent studies on children and adolescents[12,13], as well as in adults[14].

Conclusion

It can be concluded that performing a lifelong healthy lifestyle may represent the appropriate treatment modality in this patient.

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TECHNICAL NOTE

ตัวบ่งชี้ทางชีวภาพทั่วไปในมะเร็งเต้านม โดยใช้วิธีทางอิมมูโนฮีสโตเคมีเป็นฐาน (General immunohistochemical-based biomarkers in breast cancer)

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โดยปกติแล้วการพยากรณ์โรคของมะเร็งเต้านมนั้นอาศัยลักษณะทางคลินิกและ ทางพยาธิวิทยา ดังต่อไปนี้คือ ขนาดของก้อนเนื้องอก (Tumour size)[1] ระดับความแตกต่างทางจุลกายวิภาค (Histological grade)[2-7] การแพร่กระจายของมะเร็งไปยังต่อมน้ำเหลืองบริเวณรักแร้ (The status of axillary lymph node)[1,7] และระยะของมะเร็งเต้านม (Breast cancer staging) ร่วมกับการทำนายผลการตอบสนองต่อการรักษามะเร็งเต้านมโดยการใช้ “ตัวบ่งชี้ทางชีวภาพ (Biomarker)” โดยตัวบ่งชี้ทางชีวภาพดังกล่าวนี้มาจากวิธีอิมมูโนฮีสโตเคมี [Immunohistochemistry (IHC)] ซึ่งเป็นวิธีการทางเคมีด้านภูมิคุ้มกันวิทยาสำหรับตรวจสอบการแสดงออกของโปรตีนแต่ละชนิดที่ถูกสร้างมาจากยีนที่เกี่ยวข้องในเนื้อเยื่อ วิธีการนี้มีค่าใช้จ่ายที่ไม่แพง ขั้นตอนไม่ยุ่งยาก สามารถจำแนกแยกแยะและระบุชนิดของเซลล์ที่แสดงออกโปรตีนที่เป็นตัวบ่งชี้ทางชีวภาพ รวมถึงตำแหน่งในเซลล์ที่โปรตีนซึ่งเป็นตัวบ่งชี้ทางชีวภาพนั้นทำหน้าที่ด้วย[8] อย่างไรก็ตามมีปัจจัยหลายประการซึ่งมีอิทธิพลต่อความถูกต้อง (Accuracy) และความเที่ยงตรง (Reproducibility) ของผลลัพธ์ที่ได้จากวิธี IHC ได้แก่ การคงสภาพของเนื้อเยื่อ (Tissue fixation) ระยะเวลาและวิธีการสำหรับการคืนสภาพแอนติเจน (โปรตีนที่สนใจ) (Antigen retrieval) ความจำเพาะของแอนติบอดี้ (สารที่ใช้ตรวจโปรตีนที่สนใจ) (Antibody specificity) ความเจือจางของแอนติบอดี้ที่ใช้ (Antibody dilution) สารที่ใช้ตรวจสอบปฏิกิริยาทางอิมมูโนฮีสโตเคมีที่เกิดขึ้น (Detection systems) วิธีการให้คะแนนหรือร้อยละสำหรับผลลัพธ์ของปฏิกิริยาที่ปรากฏ (Scoring systems) และระดับของคะแนนหรือร้อยละซึ่งใช้เป็นเกณฑ์การวินิจฉัยว่าปฏิกิริยาที่เกิดขึ้นนั้นเป็น “ผลบวก”(Positive cut-off levels)[9]

ตัวบ่งชี้ทางชีวภาพจากการแสดงออกทางอิมมูโนฮีสโตเคมีของเซลล์มะเร็งเต้านมซึ่งใช้ในการทำนายผลการตอบสนองต่อการรักษามะเร็งเต้านมนั้น สามารถแบ่งออกได้เป็น 3 ประเภท[10] คือ

ประเภทที่ 1: ตัวบ่งชี้ทางชีวภาพซึ่งถูกยอมรับและใช้กันอย่างกว้างขวางในทางคลินิก ได้แก่

1.1. <u>โปรตีน Oestrogen receptor (ER)</u>

โปรตีน ER มีความสำคัญเป็นอย่างมาก เนื่องจากผู้ที่เป็นมะเร็งเต้านมที่มีการสังเคราะห์โปรตีน ER นั้น สามารถถูกกระตุ้นโดยฮอร์โมนเอสตราไดออล (Oestradiol) ได้ ปัจจุบันนี้ผู้ป่วยมะเร็งเต้านมที่พบการแสดงออกของโปรตีน ER บนเนื้อเยื่อมะเร็งจะได้รับการรักษาด้วยยาทาม็อคซิเฟน (Tamoxifen) ซึ่งเป็นยาที่ต่อต้านโปรตีน ER บนเซลล์มะเร็ง (Anti-oestrogen drugs) มีผลให้เกิดการระงับการเจริญเติบโตของเนื้อเยื่อมะเร็งได้[11]

1.2. <u>โปรตีน Progesterone receptor (PR)</u>

โดยทั่วไปการแสดงออกของโปรตีน PR จะแปรผันตามการแสดงออกของโปรตีน ER อย่างไรก็ตามในการตรวจทางอิมมูโนฮิสโตเคมีของเนื้อเยื่อมะเร็งเต้านมอาจพบว่าโปรตีน PR แสดงผลบวก แต่โปรตีน ER ยังคงแสดงผลลบเสมอแม้จะทำการตรวจยืนยันอีกครั้งแล้วก็ตาม ซึ่งการให้ยากลุ่มที่ต่อต้านโปรตีน ER บนเซลล์มะเร็งเช่น Tamoxifen ยังไม่เป็นที่แน่ชัดถึงประโยชน์ต่อการรักษาผู้ป่วยมะเร็งเต้านมกลุ่มนี้[12,13]

1.3. <u>โปรตีน Human epidermal growth factor receptor 2 (HER2)</u>

โดยปกติยีน *HER2* (*ERBB2*) จะอยู่บนคู่โครโมโซมคู่ที่ 17 ตรงตำแหน่งที่ 21.1 ของแขนยาว (q arm) (17q21.1) และเป็นยีนที่มีบทบาทสำคัญในควบคุมการเจริญเติบโตของเซลล์ (Cell growth) การเคลื่อนที่ของเซลล์ (Cell migration) และการเปลี่ยนแปลงของเซลล์เพื่อไปทำหน้าที่ต่างๆ (Cell differentiation) ซึ่งในเนื้อเยื่อมะเร็งเต้านมจะสามารถตรวจพบการแสดงออกที่มากเกิน (Over-expression) ของโปรตีน HER2 ที่ถูกสร้างจากยีนนี้ และ/หรือการเพิ่มจำนวนชุดของยีนนี้ (Amplification of gene copy number) ได้ประมาณร้อยละ 15 – 30 โดยปรากฏการณ์ดังกล่าวมีความเกี่ยวข้องกับการดำเนินโรคที่แย่ลง ในปัจจุบันนี้ผู้ป่วยมะเร็งเต้านมที่พบการแสดงออกของยีน *HER2* สามารถให้การรักษาด้วยยาทราสทูซูแม็บ (Trastuzumab) หรือชื่อในการค้าคือ เฮอร์เซ็พทิน (Herceptin®) ซึ่งเป็นยาที่มีความจำเพาะและต่อต้านโปรตีน HER2 บนเซลล์มะเร็งเต้านม (Humanised monoclonal antibody against HER2 protein)[14-16]

ประเภทที่ 2: ตัวบ่งชี้ทางชีวภาพซึ่งมีศักยภาพที่จะถูกนำไปใช้ในทางคลินิก แต่ยังมีความจำเป็นที่จะต้องทำการปรับปรุงความเข้มข้นของสารแอนติบอดี้ที่ใช้ตรวจวิเคราะห์และระบบการให้คะแนนสำหรับการวินิจฉัย ได้แก่

2.1. <u>โปรตีน Ki67</u>

โปรตีน Ki67 บ่งถึงสภาวะการแบ่งตัวเพิ่มจำนวนของเซลล์ (Cell proliferation) โดยจำนวนร้อยละของการแสดงออกของโปรตีนดังกล่าวบนเนื้อเยื่อมะเร็งเต้านม จะมีความสัมพันธ์กับระดับความแตกต่างทางจุลกายวิภาค[17] นอกจากนั้นแล้วจำนวนร้อยละดังกล่าว สามารถนำมาใช้ในการประเมินการแบ่งตัวเพิ่มจำนวนของเซลล์มะเร็งทั้งก่อนและหลังการรักษาด้วยยาทางต่อมไร้ท่อ (Endocrine therapy) รวมไปถึงการคาดคะเนการตอบสนองต่อการใช้ยาเคมีบำบัด[18-20]

2.2. <u>โปรตีน Epidermal growth factor receptor (EGFR)</u>

โปรตีน EGFR เป็นตัวรับที่สามารถพบการแสดงออกได้ในเนื้อเยื่อเต้านมปกติ[21] แต่การแสดงออกของตัวรับนี้ในมะเร็งเต้านมจะมีความสัมพันธ์กับการไม่ปรากฏการแสดงออกของโปรตีน ER และการดำเนินโรคที่แย่ลง[22,23]

2.3. <u>โปรตีน Topoisomerase II alpha (TOPO2A)</u>

ยาเคมีบำบัดกลุ่มแอนทราไซคลิน (Anthracycline chemotherapeutic drug) เป็นยาที่มีความจำเพาะต่อโปรตีน TOPO2A ดังนั้นในผู้ป่วยมะเร็งเต้านมที่ปรากฏการแสดงออกของโปรตีนชนิดนี้บนเซลล์มะเร็ง จะมีการตอบสนองต่อการรักษาด้วยยาเคมีบำบัดกลุ่ม anthracycline ได้ค่อนข้างดี[24]

ประเภทที่ 3: ตัวบ่งชี้ทางชีวภาพซึ่งยังอยู่ในระหว่างการวิจัยและถูกนำไปใช้ในทางคลินิกเป็นบางครั้ง[10] ได้แก่

3.1. <u>โปรตีน p53</u>

โปรตีน p53 ใช้สำหรับการวิเคราะห์การผ่าเหล่า (Mutation analysis) ของยีนทีพี 53 (*TP53* gene) ซึ่งปกติแล้วยีนนี้เป็นยีนที่ทำหน้าที่ยับยั้งการเติบโตของเนื้องอก (Tumour suppressor gene)

3.2. <u>โปรตีน Bcl-2 โปรตีน Bcl-x และโปรตีน Survivin</u>

โปรตีนเหล่านี้จะถูกนำมาใช้เป็นตัวบ่งชี้ (Marker) สำหรับการประเมินเซลล์มะเร็งที่ปรากฏกระบวนการตายเองของเซลล์ (Apoptosis) อันเป็นผลเนื่องมาจากการตอบสนองต่อการรักษาด้วยยาเคมีบำบัด

3.3. <u>โปรตีน Cyclin D1 โปรตีน Cyclin E โปรตีน p21 และโปรตีน p27</u>

โปรตีนเหล่านี้จะถูกใช้เป็นตัวบ่งชี้ต่อสภาวะการแบ่งตัวเพิ่มจำนวนของเซลล์มะเร็ง (Tumour cell proliferation)

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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 the members of the Editorial Board or the expert reviewers. 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. Conclusions

The Conclusions 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

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APPENDIX 3
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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.

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Thank you

Assistant Professor Dr Chetana Ruangpratheep
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Editor-in-Chief of Asian Archives of Pathology

ACADEMIC MEETINGS AND CONFERENCES

Announcements of academic meetings and conferences that are of interest to the readers of Asian Archives of Pathology (AAP) should be sent to the Editor-in-Chief at least 3 months before the first day of the month of issue. The contact information is shown below.

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