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Original articles

Soft tissue vascular malformations: differentiating flow types by MR imaging and comparison with histopathology

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ABSTRACT

Objective: To evaluate the MR imaging features of pathologically diagnosed high and low flow vascular malformations.

Materials and methods: The MR images and pathological diagnosis of soft tissue vascular malformations between January 2008 and July 2013 were retrospectively review. The radiologist recorded the MRI appearances, including the flow void artifact, hypersignal intensity on T1W GRE images, phlebolith, and arterial enhancement on contrast-enhanced MRA images that aided in classifying the flow types. The musculoskeletal pathologist re-evaluated the pathological specimens and classified the flow types according to the ISSVA classification. The MR imaging findings and the pathological diagnoses of the high and low flow vascular anomalies were then compared.

Results: A total of 27 patients were included in this study. Eleven patients had a final histopathologic diagnosis of low flow vascular malformations and 16 patients had a diagnosis of high flow lesions. The MRI features such as flow void artifact, phleboliths, hypersignal intensity on T1W GRE images, arterial enhancement on dynamic post-gadolinium MRA, showed no difference between these two groups. Nine of 11 (81.8%) low flow vascular anomalies and 7 of 16 (43.8%) high flow vascular malformations had concordant MR imaging diagnosis with pathological result. The characteristics of the patients, lesion size and presence or absence of specific pulse sequences were not different between the groups of concordant and discordant flow type classification.

Conclusion: We have documented the MR imaging features, which shared by low flow and high flow vascular malformations. The ability of MRI to distinguish low flow from high flow lesions based on pathologic diagnosis was limited in our study.

Keywords: MRI, AVM, venous malformation, vascular anomaly

Abbrevations: T1W GRE = T1-weighted gradient recalled echo, T1W FS = T1-weighted fat suppression, ISSVA = International Society for the Study of Vascular Anomalies, PPV = positive predictive value, NPV = negative predictive value

INTRODUCTION

Vascular anomalies comprise a broad spectrum of lesion that causes significant morbidity and mortality in children and adults. The biological classification of vascular anomalies proposed by Mulliken et al. [1, 2] is based on cellular turnover, histology, natural history, and physical findings. It clearly separates hemangiomas of infancy (tumors with an early proliferative and later involuting stage) from vascular malformations: capillary, lymphatic, venous, arterial, or combined (e.g. capillary venous, lymphaticovenous, arteriovenous malformation [AVM]). This classification has been useful clinically and accepted as official nomenclature by the International Workshop for the Study of Vascular Anomalies[2]. In such classification, hemangiomas are defined as benign proliferative tumors of the endothelial cells. All other congenital and developmental vascular lesions that lack of endothelial cellular proliferation are classified as vascular malformations[3].

Vascular malformations are categorized based on their flow dynamics into high flow and low flow lesions (Table 1)[4, 5]. The treatment of low flow vascular malformations is percutaneous sclerotherapy[6, 7]. However, percutaneous sclerotherapy alone is not effective for high flow lesions since the infused agents are rapidly washed away from the endothelial lining. The most effective treatment for high flow lesions is transarterial embolization[8, 9]. Occasionally, high and low flow vascular malformations are treated with surgical resection[10-16].

Table 1 Classification of vascular malformations adapted from the international society for the study of vascular anomalies

Types of vascular malformations	Diseases
Slow-flow	Capillary malformation
	Venous malformation
	Lymphatic malformation
Fast-flow	Arterial malformation
	Arteriovenous malformation
	Arteriovenous fistula
Combined vascular malformations	(Various combination of the above)

This table was adapted from table 1 of Lowe LH, Marchant TC, Rivard DC, Scherbel AJ. Vascular malformations: Classification and terminology the radiologist needs to know. Semin Roentgenol 2012; 47:106-117[5]

Magnetic resonance (MR) imaging is a non-invasive effective tool to characterize and classify vascular malformations based on the signal intensity, signal voids, contrast enhancement and hemodynamic flow characteristics. MR imaging also provides anatomic extent of the lesions, proximity to vital structures and involvement of multiple tissue planes[3].

We performed a retrospective study of soft tissue vascular malformations and aimed to determine the MR imaging characteristics that can help to distinguish slow flow and high flow vascular malformations based on histopathologic diagnosis. An awareness of the morphologic and dynamic MR pattern of soft-tissue vascular malformations will aid in recognition of these lesions and leads to proper planning of management.

MATERIALS AND METHODS

Patient population

The patients were retrieved by searching pathological report using the search terms of "arteriovenous malformation", "hemangioma", "venous malformation", and "lymphatic malformation" and searching radiology reports by the same search terms from radiology database of Ramathibodi Hospital between January 2008 and July 2013. The patients who had available both pre-operative MR images and tissue specimen were included in this study.

MR Imaging

All MR examinations were retrospective evaluation. They were performed on a 1.5-T MR system (Signa HDxt, GE Healthcare or Achieva, Philips) by using corresponding 8-channel torso, cardiac, extremity, knee or ankle array coils depending on locations of the lesions. The standard protocol of pulse sequence parameters are T1-weighted spin echo (SE), T2-weighted fast spine echo (FSE), and T2-weighted fat suppression (FS) or short tau inversion recovery (STIR). Twenty five of MR examinations had gadolinium-enhanced T1-weighted with fat suppression (FS) images, with contrast enhanced MR angiography (MRA) of 17 cases. Eight cases had T1-weighted gradient recalled echo (GRE) images.

On the SE pre-saturation sequences, the protons flowing rapidly into the imaging volume were pre-saturated and therefore appeared as flow voids relative to the unaffected slow-flow blood or stationary tissue that were in the volume. On GRE sequences with gradient-moment nulling, the rapidly flowing protons are re-phased and appear as a very intense signal. Lesions demonstrating vascular flow voids on SE images or vascular high-intensity flow enhancement on GRE images with gradient-moment nulling or enhancement in arterial phase of contrast-enhanced MRA were designated high flow anomalies[17].

Image review

Each MRI study was evaluated collectively by a musculoskeletal radiologist (WV) and a third year radiology resident (SW) with consensus. The reviewers understood that patients had vascular anomalies, but were blinded to the pathological diagnosis. The reviewers evaluated each MRI study two times in 2-month interval and were asked to record the presence or absence of the following imaging features of the lesions: (a) flow void artifact, (b) hypersignal intensity on T1-weighted GRE images, (c) arterial enhancement on dynamic post-gadolinium-chelate enhanced MR angiography (MRA) images, and (d) phlebolith. The presence of the first three imaging features were used to classify high flow vascular malformations (Figure 1). The cases without high flow MR features were classified

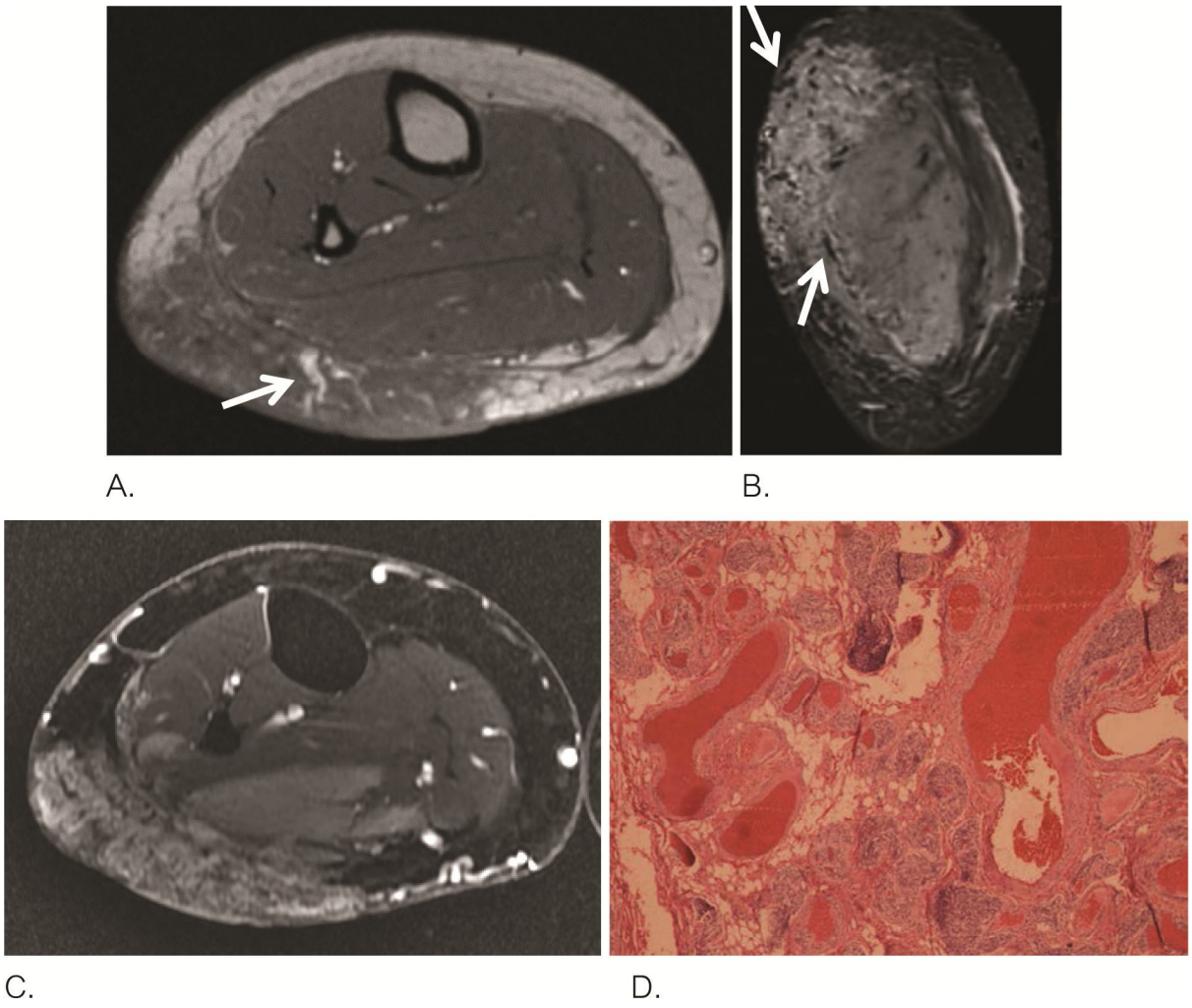


Figure 1 Typical MR characteristics of AVM in right calf of 17-year old woman.
A.) Axial T1-weighted GRE image shows tubular-shaped hypersignal intensity (arrow) representing high flow.
B.) Flow void artifacts (arrows) are seen on coronal short tau inversion recovery (STIR) image.
C.) Axial first phase of dynamic post-contrast image shows arterial enhancement of the lesion.
D.) The pathological diagnosis is AVM.

as low flow vascular malformations. In addition, the presence of phlebolith helped to suggest the diagnosis of low flow vascular malformations (Figure 2). Additional MRI findings such as the affecting organ/location, size, and involvement of skin, subcutaneous tissue, muscles or osseous structures were also recorded for each patient.

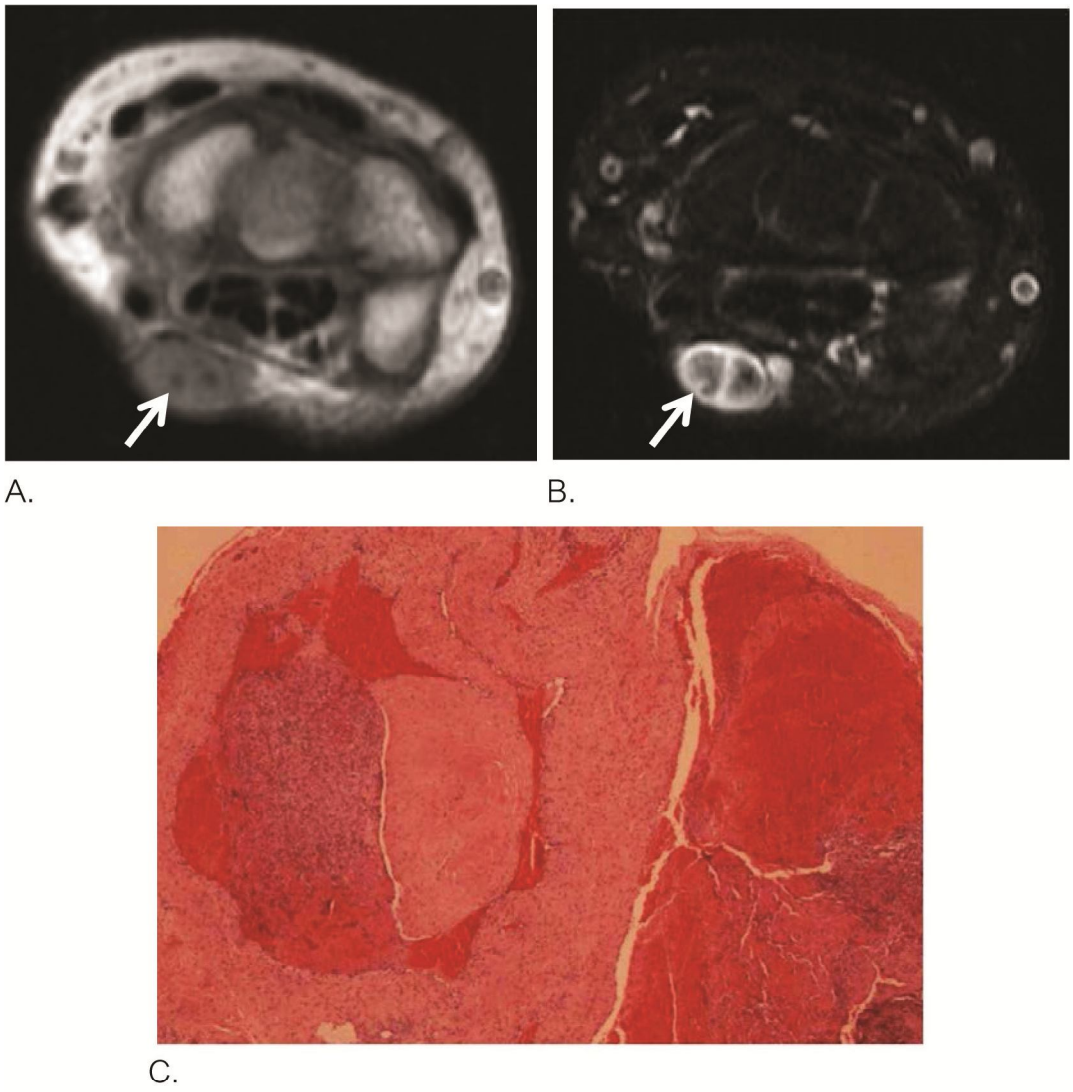


Figure 2 MR imaging of the left wrist of a 41-year old woman. Focal round hypointense areas on axial T1-weighted image A.) and axial STIR image B.) represent phleboliths (arrows). C.) The pathological diagnosis is venous malformation.

Pathological Analysis

Hematoxylin and eosin slides of all lesions were reviewed and re-diagnosed by a musculoskeletal pathologist who has an experience in this field more than 30 years. The lesions were defined in order to correlate with International Society for the Study of Vascular Anomalies Classification (ISSVA) as follows (Table 2): venous malformations, capillary malformation, and arteriovenous malformations (AVM)[18]. The criteria of diagnosis of each category were based on WHO classification of tumors, pathology and genetics of tumours of soft tissue and bone, 2002[19]. Venous and capillary malformations were regarded as low flow lesions whereas arteriovenous malformations as high flow lesions[5].

Table 2 ISSVA classification versus classical classification

ISSVA classification	Classical classification (including WHO classification)
Vascular malformations (High-flow)	
Arteriovenous malformation (AVM)	Arteriovenous hemangioma
Vascular malformations (Slow-flow)	
Venous malformation (VM)	Cavernous hemangioma
	Venous hemangioma
	Intramuscular hemangioma
Capillary malformation (CM)	Port-wine stain
	Hemangioma simplex
	Angiokeratoma
Lymphatic malformation (LM)	Lymphangioma
	Cystic hygroma
	Cavernous lymphangioma

This table was adapted from table 4 of Nozaki T, Matsusako M, Mimura H, Osuga K, Matsui M, Eto H, et. al. Imaging of vascular tumor with an emphasis on ISSVA classification. Jpn J Radiol 20138

Statistical analysis

Statistical software (STATA version 13) was used for all data analysis. A chi-square test or Fisher's exact test was used to compare the imaging findings between high and low flow vascular anomalies and Wilcoxon-rank sum test was used for comparing continuous variables. $P<0.05$ was considered statistically significant. The intraobserver reliability were calculated by using k coefficient, which defined k values for level of agreement as follows: 0.81–0.99, almost perfect agreement; 0.61–0.80, substantial agreement; 0.41–0.60, moderate agreement; 0.21–0.40, fair agreement; and 0.01–0.20, slight agreement[20].

RESULT

Between January 2008 and July 2013, 34 patients with vascular malformations were recruited, but there were 7 patients with missing pathological specimens. Therefore, 27 patients (16 years of median age; age range, 1-63 years) who fulfilled study inclusion criteria, were included: 8 men (15 years of median age; age range, 1–41 years) and 19 women (17 years of median age; age range, 8-63 years). Of these patients, 11 had a final histopathologic diagnosis of low flow vascular malformations (2 men and 9 women; 33 years of median age; age range, 12–63 years), composed of 10 venous malformations and 11 capillary malformations. The locations of low flow lesions were upper extremities (n=3), lower extremities (n=7) and trunk (n=1). Sixteen patients had a final histopathologic diagnosis of AVMs or high flow lesions (6 men and 10 women; 14 years of median age; age range, 1-55 years). In high flow lesions, the locations distribute in upper extremities (n=5), lower extremities (n=6) and trunk (n=5).

The involvement in depth of the lesions, size, margins and MR imaging features are summarized in Table 3. There is no difference of the MRI features

Table 3 Summary of the MR imaging findings of vascular malformations

MR Features	High flow vascular malformations (n=16)	Low flow vascular malformations (n=11)	P value
Involvement in depth			
Superficial[a]	5 (31.25%)	4 (36.36%)	1.000
Deep[b]	8 (50%)	6 (54.55%)	
Both	3 (18.75%)	1 (9.09%)	
Size, median (range) cm	7.5 (2.2-20.5)	11.4 (1.6-50.4)	0.340
Margin			
Well-defined	5 (31.25%)	6 (54.55%)	0.264
Ill-defined/infiltrative	11 (68.75%)	5 (45.45%)	
Specific pulse sequences			
Hypersignal T1 GRE (n=8)[c]	3 of 7 (42.86%)	0 of 1 (0%)	1.000
Arterial enhancement (n=17)[d]	4 of 9 (44.44%)	2 of 8 (25%)	0.620
Flow void artifact	7 (43.75%)	2 (18.18%)	0.231
Phlebolith	3 (18.8%)	2 (18.2%)	1.000

Note: Involvement in depth; a =skin/subcutaneous involvement; b =intramuscular, intraarticular or intraosseous involvement.

including flow void artifact, phleboliths, hypersignal intensity on T1-weighted GRE images, arterial enhancement on dynamic postgadolinium-chelate enhanced T1-weighted fat suppression images between the groups with pathologically diagnosed high flow and low flow lesions.

Intraobserver agreement tested by the Cohen k showed substantial agreement for the presence of hypersignal in T1W GRE (k = 0.71), almost perfect agreement for the presence of arterial enhancement (k =0.88) and flow void artifact (k =0.91), almost perfect agreement for the presence of phlebolith (k =0.89), and almost perfect agreement for the diagnosis of high and low flow types (k =0.82).

On the basis of the MR imaging features, 9 of 11 (81.8%) cases of low flow vascular anomalies had concordant diagnosis with pathological result. Alternatively, 7 of 16 (43.8%) patients with high flow vascular malformations had concordant diagnosis. The characteristics of the patients, size of the lesions and presence or absence of specific pulse sequences between the groups of concordant and discordant classification of flow type with pathological diagnosis are summarized in the Table 4. There is no statistically significant difference in age, gender, size of the lesions, involvement in depth, having T1-weighted GRE sequence, and having dynamic post-contrast imaging between the patients with concordant and discordant categorization of the flow types.

Table 4 MR characteristics with the concordant and discordant diagnosis of vascular malformations classification of MRI correlated with pathological diagnosis

Characteristics	Concordant MRI classification (n=16)	Discordant MRI classification (n=11)	P value
Age, median (range) years	17(9-63)	15 (1-55)	0.080
Gender			
Male	4 (25%)	4 (36.36%)	0.675
Female	12 (75%)	7 (63.64%)	
Involvement in depth			
Superficial	5 (31.25%)	4 (36.36%)	1.000
Deep	8 (50%)	6 (54.55%)	
Mixed	3 (18.75%)	1 (9.09%)	
Size, median (range) cm			
Minimal diameter	1.8 (0.7-6.2)	2.6 (0.5-6.4)	0.387
Maximal diameter	7.95 (1.6-50.4)	7.9 (4-24.1)	0.554
Pulse sequence			
Dynamic postcontrast enhancement	9 (56.25%)	8 (72.73%)	0.448
T1W GRE	4 (25%)	4 (36.36%)	0.675

DISCUSSION

Vascular malformations are categorized based on their flow dynamics into high flow and low flow with a variety of treatments. To our knowledge, there are a few articles studied MR imaging features to distinguish between the low flow and high flow vascular anomalies with histopatohlogical correlation[21, 22].

In the previous studies, there were imaging features on MR imaging that help to characterize high flow type of vascular anomalies. These features include (a) hypersignal intensity on T1-weighted GRE images; (b) arterial enhancement on dynamic postgadolinium-chelate enhanced T1-weighted fat suppression images, and (c) flow void artifact [3, 23-26].

Meyer et al. [17] described MRI findings in correlation with pathological diagnosis of 23 cases of vascular anomalies. All three AVMs showed flow voids on SE presaturation images and 2 of 3 (66.7%) AVMs had hyperintense on GRE images. Our study shows flow void artifact in 7 of 16 (43.8%) high flow lesions and hyperintense T1 GRE in 3 of 7 (42.9%) high flow lesions.

Rak et al.[24] performed retrospective study to distinguish slow flow venous malformation from high flow arteriovenous malformation using conventional MR imaging correlated with angiography. Nine of 11 (81.81%) high flow vascular malformations presented flow-related signal void on SE images. Four of the 16 (25%) venous malformations had

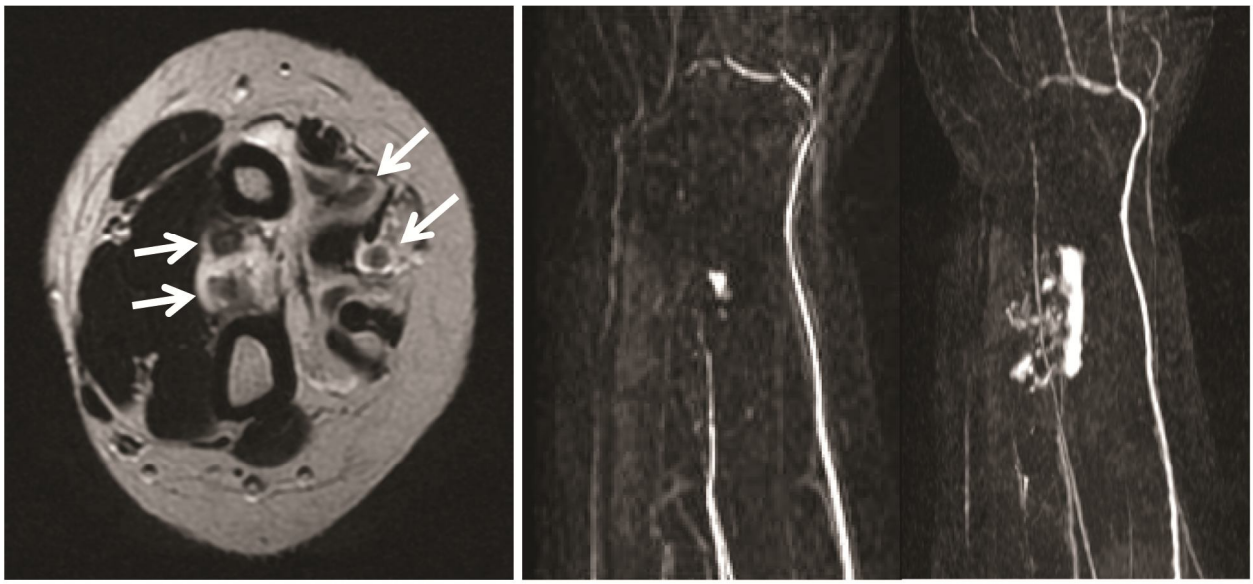
minor component of signal voids, whereas thrombosed vessels, phleboliths and linear, fibrous striations cut in cross section may mimic flow voids[14]. Two of 16 (12.5%) venous malformations found single AVFs on angiography, corresponding areas of higher signal intensity on GRE images. This might occasionally causes areas of signal void within venous malformations. Two of 16 (18.18%) of low flow vascular malformation in our study shows signal void.

Rijswijk et al.[25] performed prospective study to classify 27 cases of peripheral vascular malformations using dynamic contrast-enhanced MRI compared with angiography. The study showed that sensitivity of conventional MR imaging in differentiating venous and non-venous malformations was 100%, whereas specificity was 24–33%. Adding dynamic contrast-enhanced MR imaging increased specificity to 95%, but decreased sensitivity to 83%. All 8 cases of arterial malformations and arteriovenous malformation presented early enhancement (≤ 6 sec). Six of 8 cases have flow void artifacts. Ohgiya et al.[26] performed prospective study to distinguish low flow form high flow vascular malformations in 16 cases using dynamic contrast-enhanced MRI compared with angiography. The contrast rising time of high flow vascular malformation was shorter than in low flow vascular malformation.

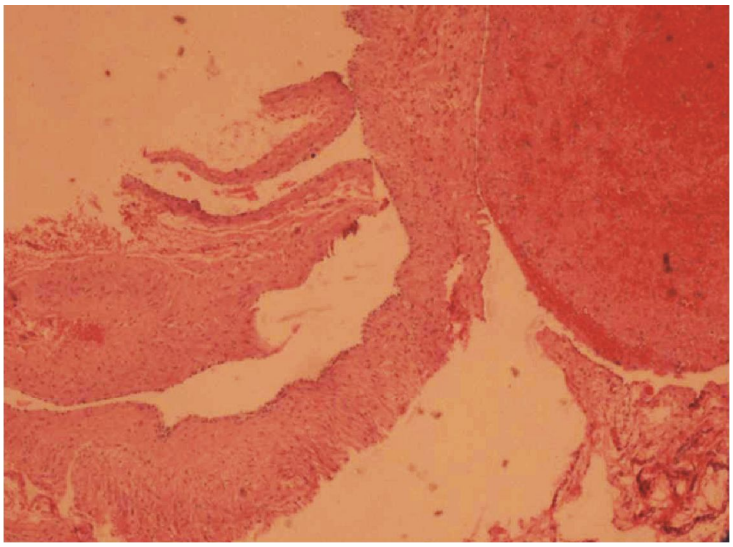
In our study, the MR imaging yielded the concordant diagnosis of flow types with pathological results in 16 of 27 cases (59.3%) and most of them (68.8%) were low flow vascular anomalies. Nine of 11 (81.8%) cases of low flow vascular anomalies had concordant diagnosis, whereas 7 of 16 (43.8%) cases with high flow vascular malformations had concordant diagnosis. Nine of 18 (50%) of patients with low flow MR imaging pattern were pathologically diagnosed as AVMs (Figure 3, 4, 5). Only 4 of 9 (44.44%) pathological diagnosed high flow vascular malformations showed early enhancement. Intraluminal thrombosis or hyalinization of the lesion may cause absence of flow void artifact, absence of hyperintensity in T1W GRE and absence of arterial enhancement. Two cases with high flow MRI pattern were diagnosed as venous malformations (Figure 6). The Table 3 shows no significant difference in any MR imaging features between pathological diagnoses of high and low flow vascular malformations. According to the prior cites, hemodynamic evaluation of vascular malformation by MRI may correlate better with angiography than the static pathological images and this may explain our unsatisfied results.

However, the MRI is valuable for differentiate vascular anomalies from soft tissue tumors[27] and defining the extent of the lesion, using STIR or contrast enhanced T1-weighted fat suppression[28]. These non-invasive techniques provide details of vascular anomalies for therapeutic planning. With incomplete resection, the residual lesion may become aggressive and symptomatic[6].

Our study has some limitations. First, this is retrospective study with difference in MR imaging protocol and pulse sequences, some study without contrast-enhanced MRA or T1-weighted GRE causing limitation to assessment the flow type. Second, there are small number of cases and only symptomatic cases who underwent surgery would have histological diagnosis. As such, asymptomatic vascular malformations might not undergo MR imaging and having different features.



A. B.



C.

Figure 3 MR imaging of the right forearm of a 15-year old woman. A.) Axial T2-weighted image shows serpiginous T2-hyperintense mass that infiltrates the muscles at dorsal aspect of the right forearm. Multiple round and oval T2 hypointense areas may also representing phleboliths or non-calcified thrombi (arrows). B.) Coronal subtraction maximum intensity projection (MIP) images from multi-phase magnetic resonance angiography (MRA) show delayed enhancement of the lesion, which suggested low flow type. C.) The pathological diagnosis is AVM.

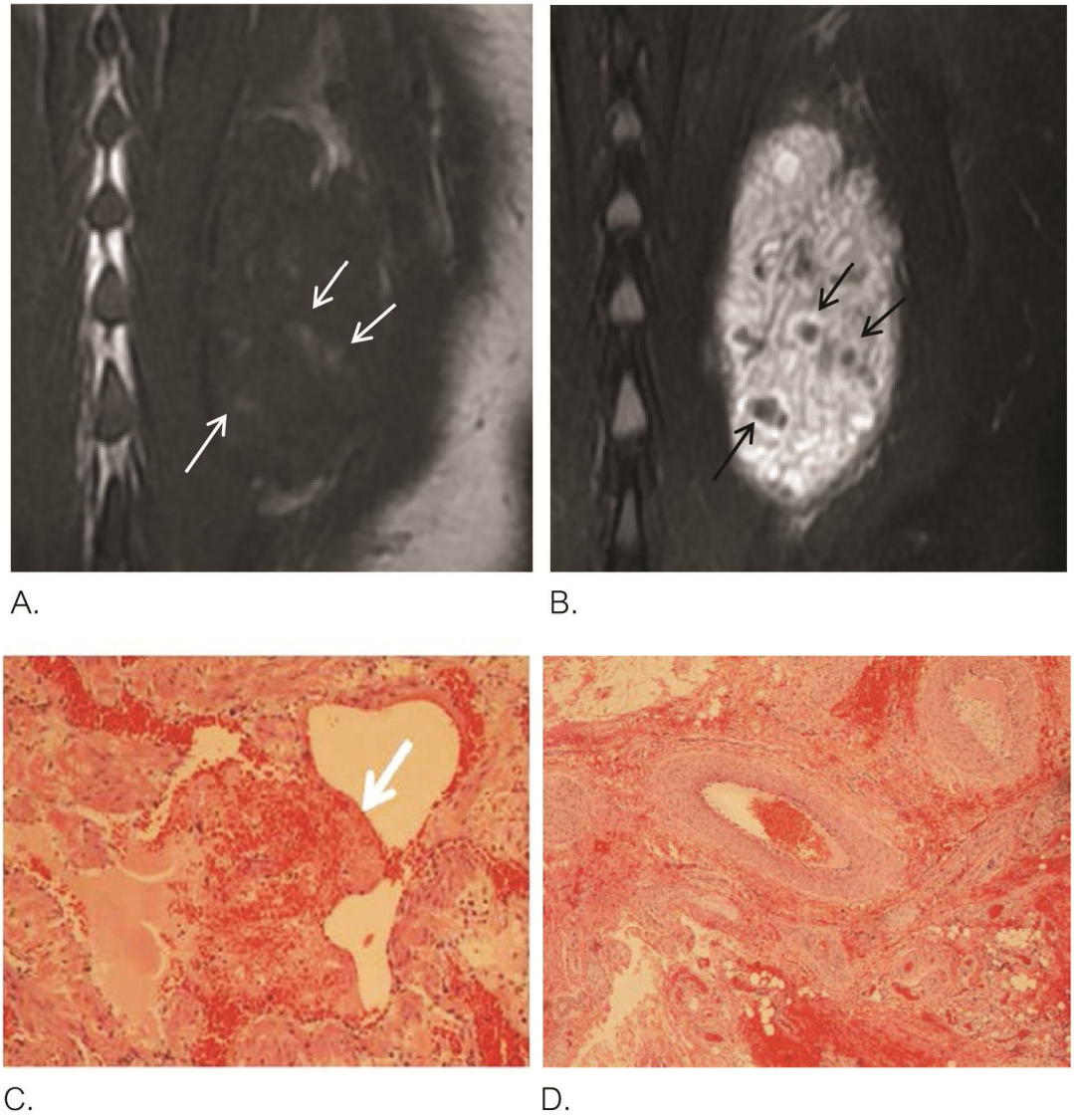


Figure 4 MR imaging of the back of a 1-year old boy. Multiple foci of hyperintense areas (white thin arrows) on coronal T1-weighted image A.) and hypointense areas (black thin arrows) on coronal T2-weighted image B.), which corresponded to intraluminal thrombi (arrow) on pathologic examination C.). D.) The pathological diagnosis is AVM.

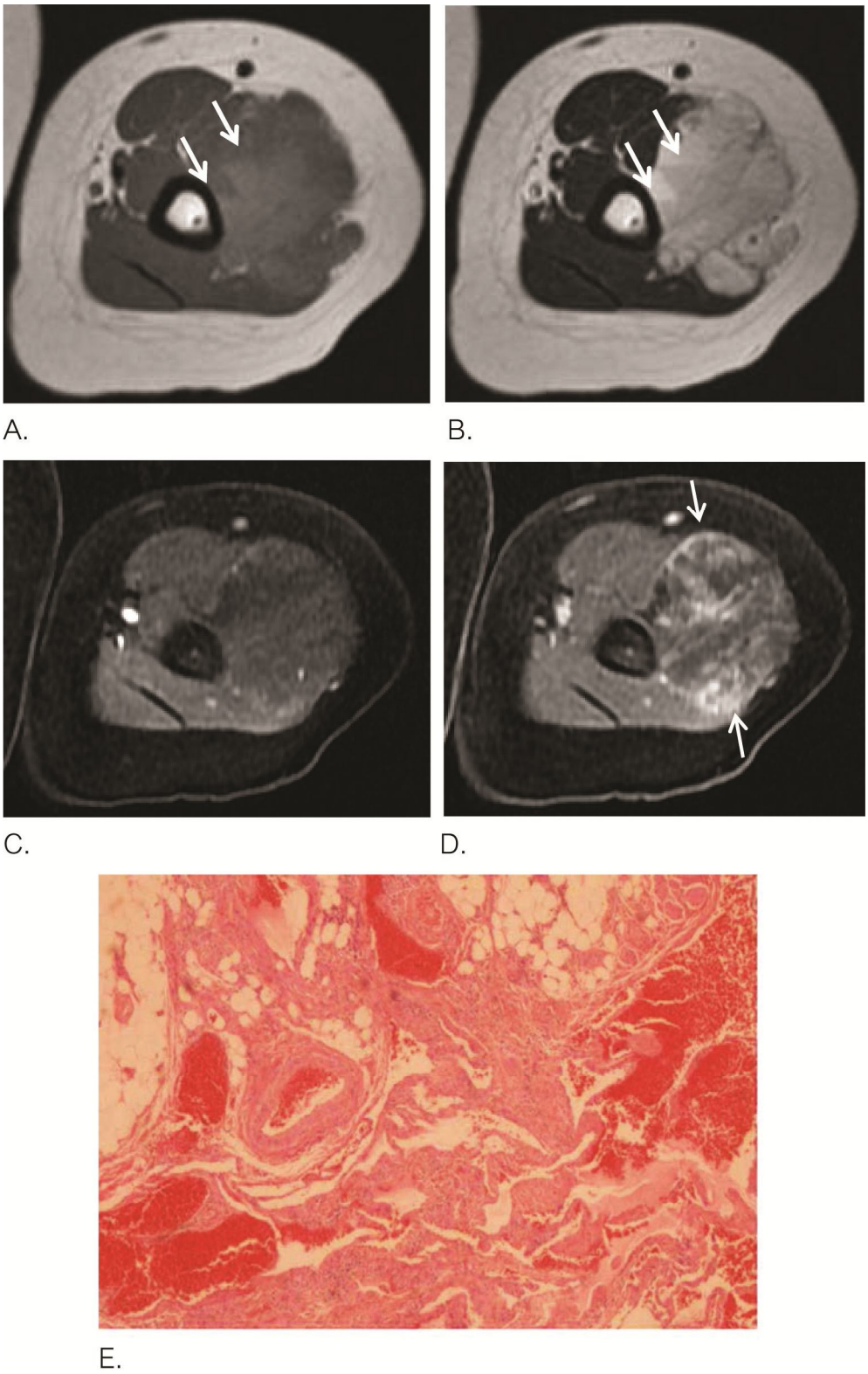
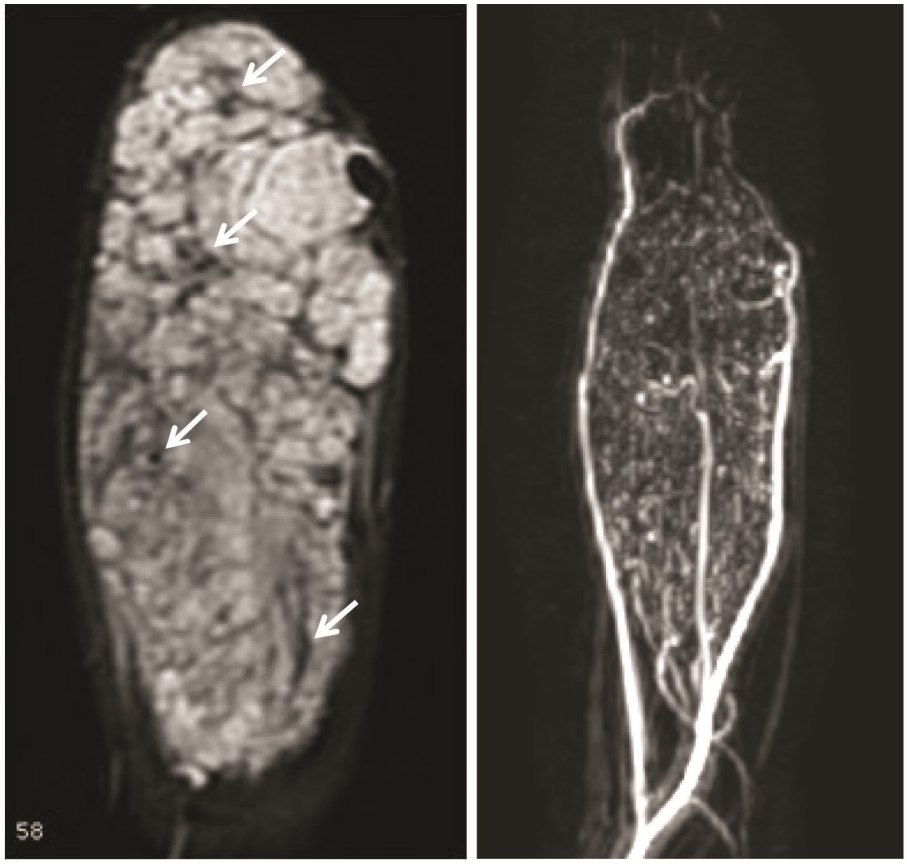


Figure 5 MR imaging of the left arm of a 7-year-old boy. Axial T1-weighted A.) and axial T2-weighted images B.) reveal intramuscular multilobulated mass with internal fluid-fluid level (arrows). Axial images from multi-phase dynamic contrast-enhanced study show no enhancement of the lesion in arterial phase C.) and heterogeneous enhancement (thin arrows) on delayed phase D.). E.) The pathological diagnosis is AVM.



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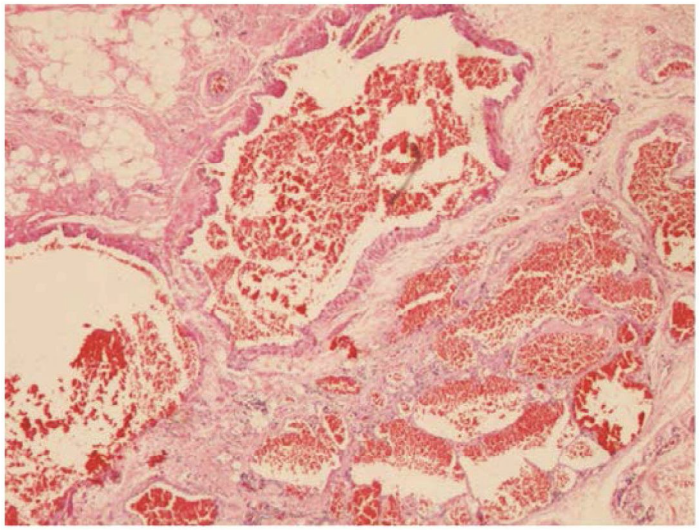

C.

Figure 6 MR imaging of the right forearm of a 22-year-old woman. A.) Coronal T2-weighted image with fat suppression shows the large mass with multiple flow void artifacts (arrows). B.) Coronal subtraction MIP image from multi-phase MRA shows enhancement of the mass in arterial phase. These findings suggest AVM. C.) The pathological diagnosis is venous malformation.

CONCLUSION

The MR imaging features showed no difference between pathologically diagnosed high and low flow vascular malformations. We have documented the MR imaging features which shared by the low flow and high flow vascular malformations including flow void artifact, hypersignal intensity on T1-weighted GRE images, early enhancement on dynamic postgadolinium images, and phlebolith. The ability of MR imaging to differentiate low flow from high flow lesions based on pathologic diagnosis was limited in our study.

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