

# Kimura's Disease in Unusual Anatomical Locations: Clinical and Radiological Characteristics

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**Purpose:** To explore the clinical and imaging features of rare site Kimura's disease (KD).

**Methods:** Retrospective analysis was conducted on the clinical manifestations, laboratory examinations, and imaging features of five patients with rare site KD. All imaging data, including the location, quantity, size, uniformity, boundary, and enhanced appearance of the lesion were evaluated by two independent radiologists.

**Results:** Of the five patients, four were asymptomatic, and one experienced localized skin itching. Four cases involved subcutaneous nodules in the upper arm, while one was in the inguinal region. The main manifestations were single (three cases) or multiple (two cases) subcutaneous nodules/masses, with three patients accompanied by local lymph node enlargement. Four patients exhibited elevated eosinophil counts in their peripheral blood. Four patients had lesions with vascular flow voids; in three of these, the lesions also showed prominent enhancement. Notably, the lesion in a 5-year-old did not show vascular flow voids but displayed significant enhancement. Additionally, two patients showed edema around the lesions.

**Conclusion:** The presence of solitary or multiple subcutaneous nodules/masses in the upper arm or inguinal area, accompanied by lymph node enlargement, elevated eosinophils in the peripheral blood, and the observation of internal vascular within the lesion, can aid in the diagnosis of KD occurring in uncommon anatomical locations.

**Keywords:** Kimura disease, increased eosinophils, image, uncommon anatomical locations

## Introduction

Kimura's disease (KD) is a rare idiopathic chronic lymphoproliferative disease of unknown etiology.<sup>1</sup> It mainly occurs in young men in Asia, affecting areas such as the salivary glands, and oral and cervical lymph node chains. Other rare areas include the armpit, groin, trunk, abdomen, and subcutaneous areas of the limbs.<sup>2-6</sup> The main clinical features include painless subcutaneous soft tissue masses, local lymph node enlargement, increased peripheral blood immunoglobulin E, and eosinophilia.<sup>4,7</sup>

Given that KD is clinically similar to tumors,<sup>8</sup> especially in rare areas, differential diagnosis can be challenging. This study collected clinical data and imaging examination information of five rare sites KD patients admitted and confirmed in our hospital from 2015 to 2023, aiming to summarize the clinical and imaging features of rare site KD and achieve early and accurate diagnosis.

## Materials and Methods

### General Information

Five KD patients with lesions occurring in rare areas (outside the head and neck) between 2015 and 2023 were included, and all lesions were confirmed by pathology after puncture biopsy or surgical resection. All five patients were male, aged 5–48 years, with a median age of 34. The duration of their disease course varied from 0.5 to 240 months.

### Research Method

Retrospective analysis of clinical manifestations, laboratory examinations, pathological and imaging characteristics, and comprehensive evaluation were conducted for the included patients. The Sun Yat-sen University's Fifth Affiliated Hospital Medical Ethics Committee approved the study. Being retrospective, the study involved no alterations to treatment protocols and maintained patient confidentiality by anonymizing information during clinical and imaging analyses. The Ethics Committee exempted the need for informed consent forms to be signed. All imaging data were evaluated by two radiologists, with 15 and 6 years of imaging diagnosis experience, respectively. The evaluation included the location, number (single and multiple), size (maximum diameter or sum of maximum diameters) of the lesion, density/ intensity (compared to skeletal muscle density/intensity), uniformity, degree of enhancement (compared to skeletal muscle), margin (clear or unclear), peripheral edema, and whether lymph node enlargement was present. If there is a disagreement between the two physicians, it can be resolved through negotiation.

### Imaging Examination

Two cases underwent CT examination, four cases underwent MR examination, and one case underwent both CT and MR examinations. The CT examination was performed using a German Siemens Somatom Definition Flash 256-row spiral CT machine, with scanning conditions of 120 kV, 210 mAs, and matrix  $512 \times 512$ , pitch 1.0, layer thickness 2mm. The contrast agent for enhanced scanning is iodohexanol (containing 300 mg/mL of iodine), approximately 90.0 mL, with an injection flow rate of 2.5mL/s. The MRI adopts the Siemens Vero 3.0 T MR scanner, and the scanning sequence includes T1-weighted Imaging (T1WI) in-phase, out-phase, and fat suppression sequences, T2-weighted Imaging (T2WI) and T2WI-fat suppression sequences, Proton Density-weighted imaging (PDWI), Diffusion-weighted imaging (DWI), and T1WI enhanced sequence. Scanning parameters: layer thickness 4 mm, layer spacing 1 mm, matrix  $256 \times 256$ ; T1WI, Repetition Time (TR) 500 ms, Echo Time (TE) 12 ms; T2WI, TR 3000 ms, TE 58 ms; PDWI, TR2800 ms, TE 28ms; DWI, TR 3700 ms, TE 74 ms; enhanced scanning contrast agent Gd - DTPA, dose 0.1 mmol/kg, flow rate 1.0–2.0 mL/s.

## Results

### Clinical Manifestation

Among the five patients, four cases had no symptoms, one case had local skin itching, and all five patients had no history of keeping pets such as cats or dogs. The lesion occurred subcutaneously in the upper arm (four cases) and inguinal area (one case), presenting as single (three cases) or multiple (two cases) subcutaneous nodules/masses. During palpation, the lesion was tough, with moderate activity and no tenderness, and three patients were accompanied by lymph node enlargement. The clinical data of five patients at admission are shown in [Table 1](#).

### Laboratory Examination

Among the five patients, four had increased eosinophils in peripheral blood, with an absolute count of  $(0.35\text{--}3.97) \times 10^9/\text{L}$  (normal reference value range  $(0.02\text{--}0.52) \times 10^9/\text{L}$ ), with a percentage of 6.1% to 42.3% (normal reference value range of 0.4% to 8%). The white blood cell count of all five patients was normal. The specific laboratory inspection results are shown in [Table 1](#). None of the five patients underwent peripheral blood IgE testing.

### Imaging Features

KD patients exhibit single or multiple iso-dense nodules or masses on CT ([Figure 1](#)), with mild enhancement on contrast-enhanced scans. MR imaging ([Figure 2](#)) showed lobulated nodules/masses, with lesions showing iso-intense on T1WI,

**Table 1** Clinical Data and Imaging Manifestations of Five KD Patients

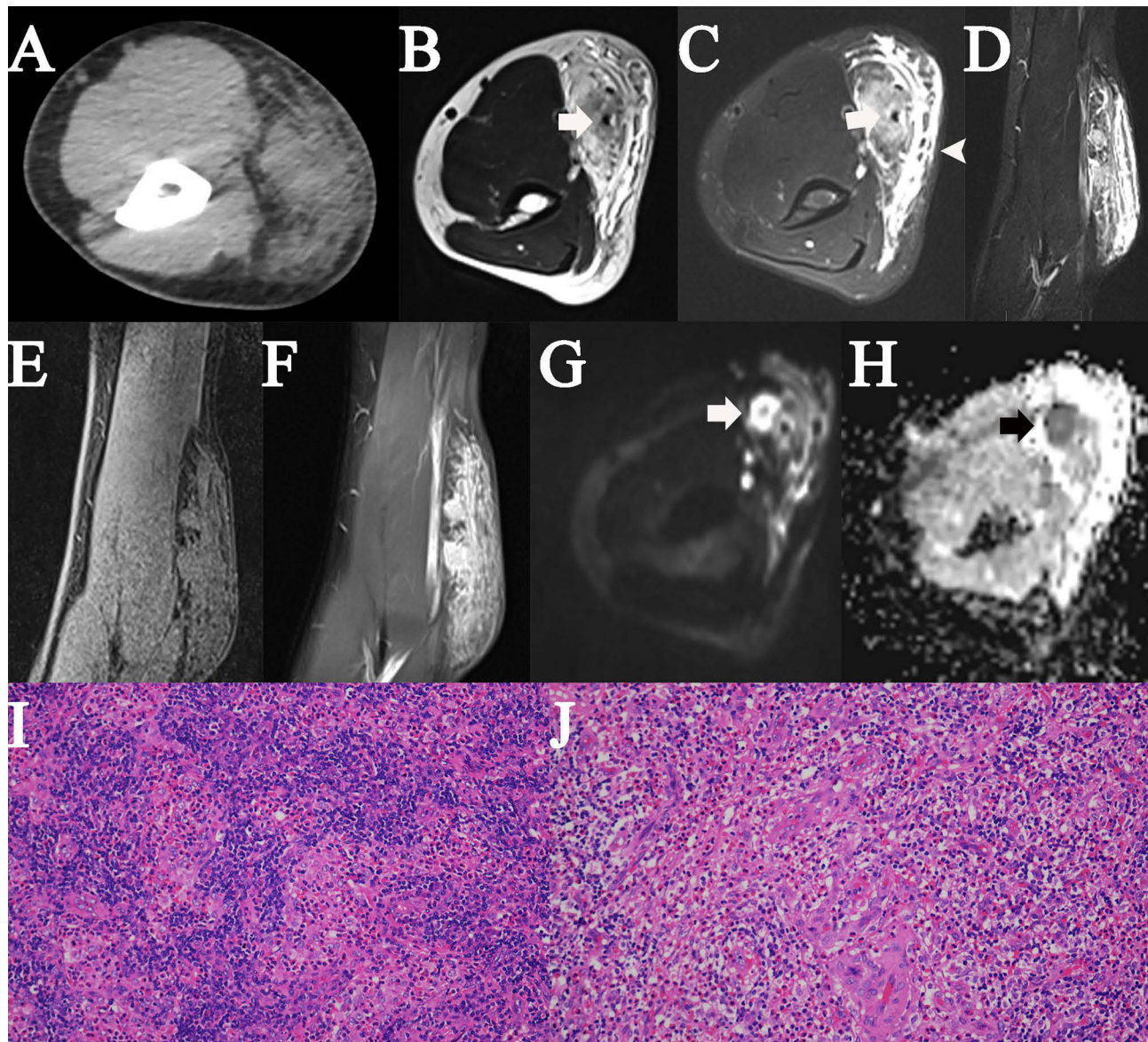
No.	1	2	3	4	5
Gender	Male	Male	Male	Male	Male
Age (year)	34	37	48	16	5
Interval between onset and examination (months)	240	48	0.5	24	0.5
Location and clinical manifestations	Subcutaneous mass on the inner side of the right upper arm	Progressive enlargement mass of the medial of the right upper arm	Subcutaneous mass in the right inguinal region with lymph node enlargement	Subcutaneous mass on the inner side of the left upper arm	Subcutaneous mass on the outer side of the right upper arm, accompanied by itching and axillary lymph node enlargement
Leukocyte count ( $\times 10^9/L$ )	5.77	9.39	6.74	8.48	7.77
Eosinophil count ( $\times 10^9/L$ ) and percentage	0.35 (6.1%)	3.97 (42.3%)	1.36 (20.2%)	1.88 (22.2%)	0.99 (12.7%)
Lymphadenopathy	None	Right iliac artery and inguinal area	Right inguinal region	None	Right armpit
Therapeutic method	Resection	Resection	Resection	Resection	Resection
Recurrence	None	None	None	None	None
Image findings					
CT plain scan findings	N	Iso-density	Iso-density	N	N
MR plain scan findings	TIWI iso, T2WI slightly hyper	TIWI iso, T2WI slightly hyper, DWI hyper, ADC slightly hypo	N	TIWI iso, T2WI slightly hyper, DWI hyper, ADC slightly hypo	TIWI iso, T2WI hyper, DWI hyper, ADC hyper
CT/MR enhance performance	Significant enhancement	Significant enhancement	Mild enhancement	Significant enhancement	Significant enhancement
Number of lesions	Single	Multiple	Single	Multiple	Single
Uniformity	Even	Even	Uneven	Even	Even
Long diameter (mm)	23	58	58	52	26
Internal vascular	Exist	Exist	Exist	Exist	Absent
Margin	Clear	Unclear	Unclear	Unclear	Unclear
Peripheral edema	Absent	Exist	Undetected	Exist	Absent
Subcutaneous fat reduction/thinning	Absent	Reduce	Absent	Absent	Thinning

**Abbreviations:** iso, iso-intensity; hyper, hyper-intensity; hypo, hypo-intensity; TIWI, T1 weighted imaging; T2WI, T2 weighted imaging; DWI, diffusion-weighted imaging; ADC, apparent diffusion coefficient.

slightly high or high intensity on T2WI, mild diffusion-limited or unrestricted on DWI, and significant enhancement on contrast-enhanced scans. Two cases (2/4) showed edema around the lesion, and two cases (2/4) had a subcutaneous fat reduction or thinning in the lesion area. The length/ total length of the lesion in five patients ranged from 23 mm to 58 mm, with abnormal blood vessels visible in the center of the lesion in four lesions. A 5-year-old child patient showed significant differences (Figure 3). First, the lesion was located subcutaneously on the lateral side of the upper arm, accompanied by clinical symptoms of itching. The remaining three cases of upper arm lesions were all located subcutaneously on the medial side, and there were no symptoms of local skin itching; Second, the T2WI signal of the lesion was higher; Third, there was no vascular flow void inside the lesion (Table 1).

## Pathological Manifestations

All five patients underwent surgical resection. Macroscopic observation showed that the lesion was irregular in shape, without an obvious capsule. The cut surface is gray-white/gray-yellow. Under the microscope, it showed lymphoid tissue proliferation, and reactive lymphoid follicular hyperplasia, accompanied by high endothelial venule proliferation, eosinophil infiltration, and small focal necrosis. Immunohistochemical staining showed CD20 (+) and CD79a (+) in lymphoid follicles, BCL-6 (+) in lymphoid follicular germinal center, BCL-2 (+) in lymphoid follicular mantle and paracortical B cells, CD3 (+) and CD5 (+) in paracortical T cells, CD21 and CD23 showing FDC scaffold network (+), CD34 showing vascular endothelial cells (+), S-100 (-), CD1  $\alpha$  (-), Broad spectrum CK (-).

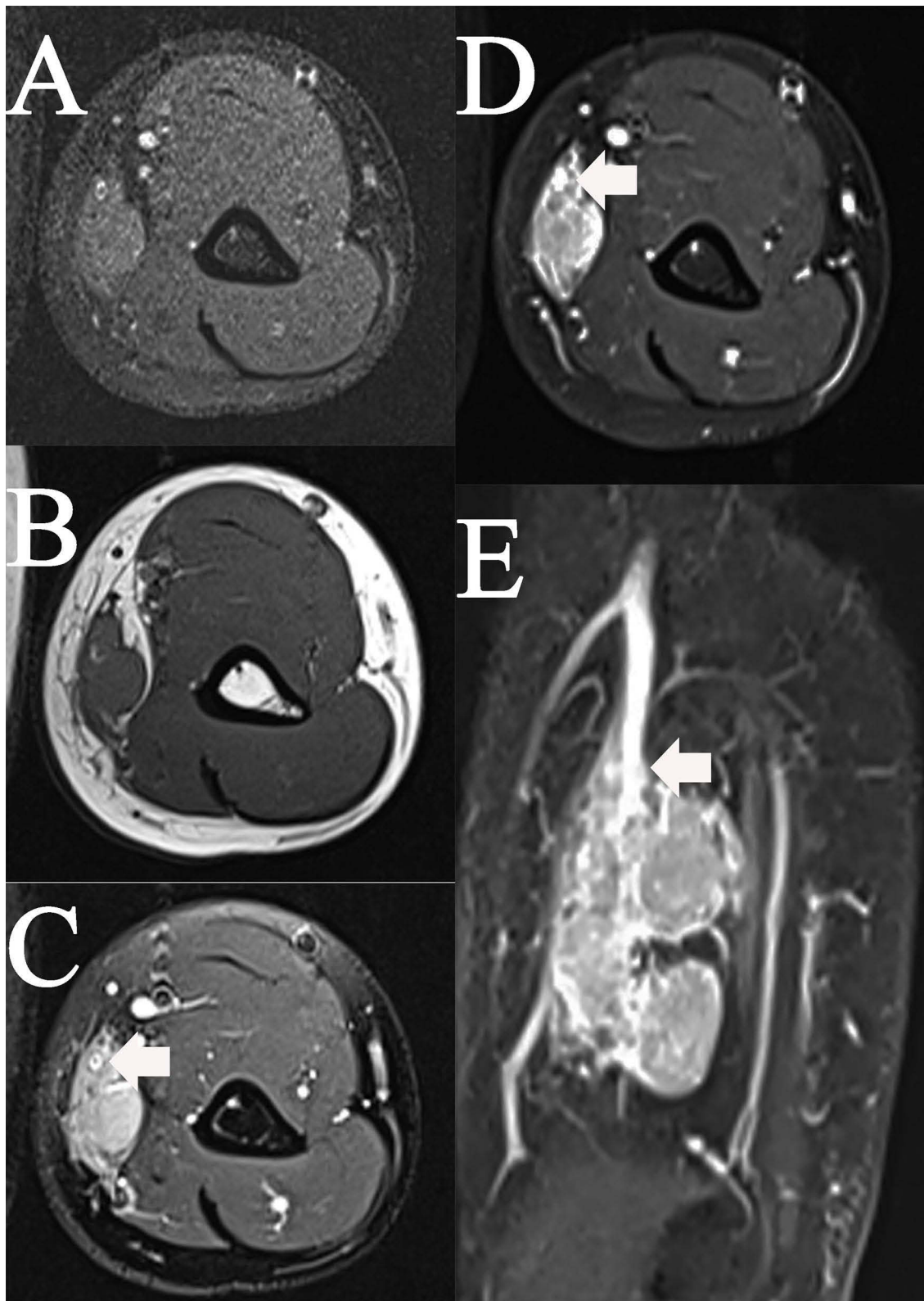


**Figure 1** A 37-year-old male. Non-contrast CT image (A) displays an iso-dense, irregular mass in the right upper arm's medial subcutaneous tissue, with indistinct surrounding fat planes. T2W (B) and fat-suppressed T2W images (C, axial; D, coronal) depict a slightly hyperintense mass with vascular flow voids (arrows) and peripheral subcutaneous edema (arrowhead). TIW fat-suppressed image (E) shows that the mass was isointense, and contrast-enhanced TIW imaging (F) revealed notable enhancement. On DWI (G), the mass exhibits hyperintensity, but on the ADC image (H), it shows localized hypo-intensity. Histopathology examinations (I and J) confirm lymphoid tissue proliferation, eosinophil infiltration, and high endothelial venule proliferation.

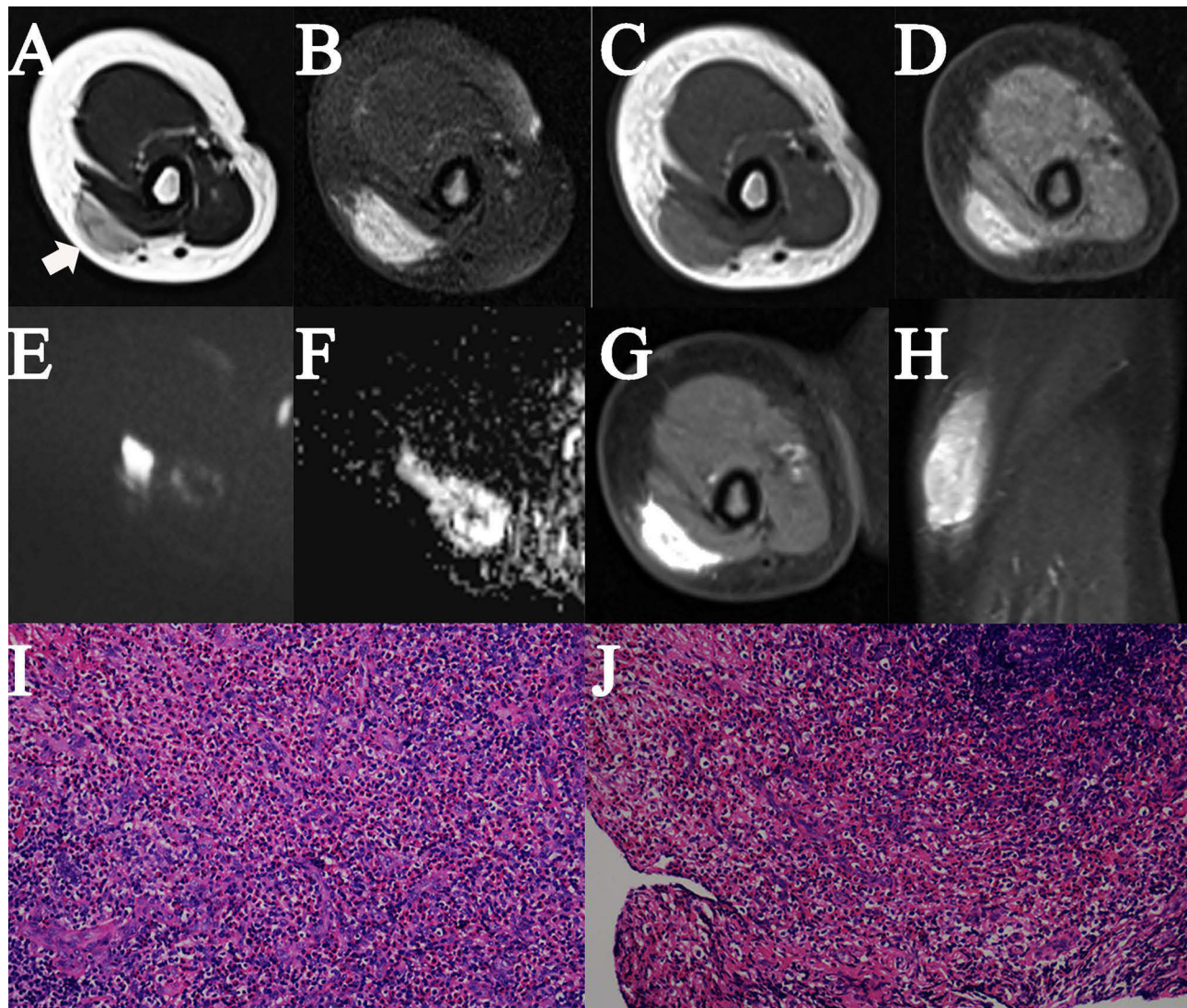
## Discussion

### Clinical Characteristics of KD

The incidence of KD in males is much higher than in females. KD presents as a long-term painless subcutaneous soft tissue mass in the head and neck in the clinical setting, often accompanied by involvement of salivary glands or regional lymph nodes, as well as isolated lymph node involvement. Inguinal areas and limbs are relatively rare. Some KD patients may also be accompanied by nephrotic syndrome, accompanied by eczema, Raynaud's phenomenon, mediastinal and hilar lymph node lesions, bronchial asthma, severe coronary artery spasm, thrombotic disease, ulcerative colitis, retinal and choroidal degeneration, temporal arteritis, main arteritis, and other manifestations, so some scholars believe that KD is a systemic disease.<sup>5,9-11</sup> KD has a long disease course and is prone to recurrence, characterized by an increase in peripheral blood eosinophils and elevated serum IgE.<sup>4,6,7,12</sup> Previous studies have shown that factors such as an increase

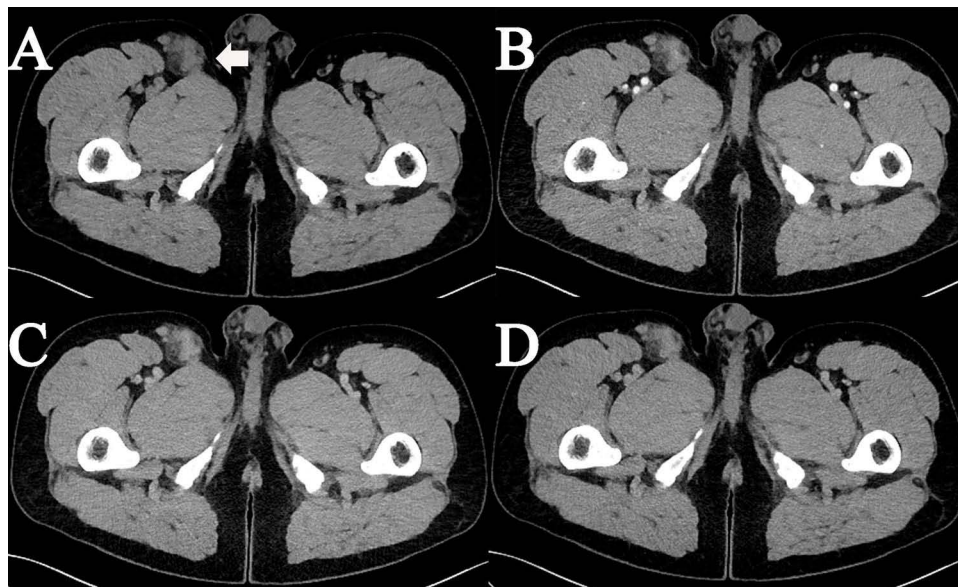


**Figure 2** A 16-year-old male. Fat-suppressed T1W (A) and T1W (B) images show a subcutaneous isointense mass on the inner side of the left upper arm, PDW (C) image shows the mass with vascular flow voids (arrows), contrast-enhanced T1W imaging (D and E) show significant enhancement, and a thick blood vessel passing through the lesion (arrows).



**Figure 3** A 5-year-old male. On the lateral side of the right upper arm, a subcutaneous mass shows hyperintensity on T2W (A) and fat-suppressed T2W (B) images, while it appears slightly hyperintense on both T1W (C) and fat-suppressed T1W (D) images. No prominent vascular flow void signals were observed within the mass, and no signs of edema were seen in the surrounding subcutaneous fat. Both DWI (E) and ADC (F) images show high intensity. Contrast-enhanced T1W (G, axial; H, coronal) image reveals marked enhancement of the mass. Histopathological examinations (I and J) revealed eosinophil infiltration and high endothelial venule proliferation.

in blood eosinophil count of  $> 20\%$ , a percentage of eosinophils of  $> 50\%$ , a blood IgE level of  $> 10,000$  IU/mL, multiple lesions outside the salivary gland, bilateral onset, lesion diameter greater than 3 cm, unclear lesion boundaries, and a disease course of more than five years are associated with disease recurrence. The size of the lesion is closely related to the peripheral blood eosinophil count, and the larger the lesion, the higher the eosinophil count.<sup>4</sup> In this study, all patients were male, with three cases occurring subcutaneously on the medial side of the upper arm, while only one case occurred subcutaneously on the lateral side of the upper arm. This is similar to the study by Park et al<sup>13</sup> and may be related to the large number of blood vessels located subcutaneously near the neurovascular bundle on the medial side of the upper arm.<sup>14,15</sup> KD patients tend bilateral occurrence, and it is necessary to evaluate whether there are signs of onset on the opposite side after finding of lesion on one side.<sup>7,13</sup> In this study, four cases were not evaluated on the opposite side due to limited examination sites and images, and one case underwent bilateral inguinal area scans, but no obvious lesions were found on the opposite side (Figure 4). In addition, all cases were not tested for serum IgE, indicating that clinical attention should be paid to the serological examination of relevant cases.



**Figure 4** A 48-year-old male. There is a subcutaneous mass in the right inguinal region. The non-contrast CT (A) shows a mass with uneven density and distinct boundaries. The mass demonstrates mild enhancement in the arterial (B), venous (C), and delayed phases (D).

**Abbreviations:** T1W, T1-weighted imaging; T2W, T2-weighted imaging; PDW, Proton Density-weighted; DWI, Diffusion-weighted imaging; ADC, Apparent diffusion coefficient.

## Imaging Features of KD

The imaging manifestations of KD in rare areas such as the upper arm and groin are roughly the same as those of common lesions. The lesion appears as a regular/irregular nodule or mass with uniform density or signal. MRI shows iso-intensity on T1WI and slightly high or high intensity on T2WI and PDWI. Some lesions on DWI show mild diffusion restriction and contrast-enhanced scans show mild or significant enhancement. The lesions that occur in the upper arm are mainly subcutaneous on the medial side, while the vascular bundles on the medial side of the upper arm are abundant. Due to different disease courses, the fiber composition and degree of vascular proliferation in the lesions may present different enhancement patterns.<sup>12,14</sup> In most lesions (4/5) in this study, blood vessels could be seen passing through the interior of the lesion, and there was no significant deviation in the course of blood vessels. There was no clear involvement or narrowing of the vascular lumen, which may be a characteristic imaging manifestation of KD.<sup>14,15</sup> In addition, the lesions were mostly lobulated, with varying degrees of edema visible around some lesions. Adjacent subcutaneous adipose tissue decreases or thins, while adjacent muscles, bones, and joints are not affected, which is consistent with findings from previous reports.<sup>2,4</sup>

KD rarely affects children, and such reports are rare.<sup>16</sup> In this study, there was a 5-year-old child with KD who had an atypical lesion located subcutaneously on the lateral side of the upper arm, accompanied by typical manifestations such as local skin itching, axillary lymph node enlargement, and increased eosinophils in peripheral blood. MR imaging showed iso-intensity on T1WI, hyperintensity on T2WI, and obvious enhancement on enhanced T1WI. There were no vascular flow voids in the center of the lesion. Compared to other cases, the T2WI intensity of this lesion is higher and the enhancement is more obvious, which may be related to the more vascular components of the lesion, which is consistent with other research reports. However, the lack of vascular flow voids within the central region of the lesion could potentially be attributed to factors such as the patient's age, timely identification, and the relatively diminutive volume of the lesion.

KD patients are usually accompanied by local lymph node involvement. In this study, the tumor on the inner side of the right upper arm in Patient 2 gradually increased, and there was no obvious enlargement of the lymph nodes in the right armpit. Instead, there was an enlargement of the lymph nodes adjacent to the right iliac artery and in the inguinal area, which is rarely reported.<sup>11,17</sup> This may be because KD is a systemic disease that can occur in various parts of the body, so there is a mismatch in spatial distribution.

## Differential Diagnosis of KD

KD should be differentiated from diseases such as lymphoma, cat scratch disease, lymph node tuberculosis, metastatic tumors, lymphadenitis, Castleman's disease, soft tissue sarcoma, etc.<sup>13,15,18</sup> Lymphoma usually presents as multiple nodules or masses with uniform density/intensity, clear boundaries, and uniform enhancement. Sometimes, lymphoma and KD have similar pathological manifestations and are difficult to distinguish; however, lymphoma is more common in middle-aged and elderly people, with areas rich in lymphoid tissue being more common. Multiple lymph nodes can significantly fuse, while rare sites such as KD are mostly located under the skin. In addition, eosinophilia and surrounding soft tissue changes can be used to differentiate from lymphoma.<sup>8,12,13,15,18</sup> Cat scratch disease is usually manifested as a mass in the soft tissue of the epicondylar humerus, often with subcutaneous edema, similar to KD. However, there is no history of contact with the cat, negative serological tests, and no necrosis in the center of the lymph nodes on the enhanced image, which can be used to rule out cat scratch disease.<sup>15</sup> In lymph node tuberculosis and metastatic tumors, swollen lymph nodes usually show central low-density necrosis and peripheral ring enhancement, and lymph node tuberculosis has a history of pulmonary tuberculosis, and metastatic tumors usually have a history of primary tumors.<sup>12,15</sup> Lymphadenitis has specific clinical manifestations of inflammation such as redness, swelling, heat, and pain, which helps clinical doctors differentiate it from KD. Castleman's disease can occur as single or multiple lesions in the neck, similar to KD. Still, the volume of Castleman's disease lesions is usually large, with single lesions being more common, and the degree of enhancement of the lesions on contrast-enhanced scans is significantly higher than that on KD.<sup>10</sup> A comprehensive evaluation of medical history, symptoms, laboratory tests, and radiologic features may aid in the diagnosis of KD; however, confirmation through pathological examination remains essential.

## Treatment for KD

Despite being considered a benign disease, KD exhibits a high rate of recurrence reported in up to 60% to 80%.<sup>19</sup> Surgical intervention has traditionally been the primary treatment modality. Patients with a maximal tumor diameter of  $\geq 3$  cm, disease duration of  $\geq 5$  years, peripheral eosinophil counts of  $\geq 20\%$ , or serum IgE levels of  $\geq 10,000$  IU/mL are at increased risk of relapse. In such cases, the consideration of adjuvant therapies, such as radiotherapy, systemic immunosuppressive medications, and targeted therapies, may be beneficial in improving the management of recurrence.<sup>1,20</sup>

## Conclusion

The imaging manifestations of KD in rare areas are non-specific. Suppose nodules/masses appear in rare areas such as the subcutaneous and inguinal areas on the inner side of the upper arm, with local skin itching or no symptoms. In that case, vascular flow voids can be seen inside the lesion, edema accompanied by local fat reduction, and peripheral blood eosinophilia, it is necessary to suspect the occurrence of KD highly and to perform relevant serological tests such as IgE. There are certain differences in imaging manifestations of KD between children and adults; therefore, further research is needed.

## Data Sharing Statement

The datasets used and analyzed during the current study are available from the corresponding author at an appropriate request.

## Ethics

Research conformed to the Declaration of Helsinki. Our local Institutional Review Board approved this study.

## Disclosure

The authors report no competing interests in this work.

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