Ultrasound Characteristics of Kimura Disease: Retrospective Analysis of 30 cases

Bingyan Liu, MD*, Shaoqing Fu, MD, Dongni Luo, MD, Shengxin Fu, MD, Donglin Wang, MD, Wei Liao, MD

Department of ultrasonography, Hainan General Hospital, Haikou, Hainan, China.
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Objective: To demonstrate the characteristics of the lesion in Kimura disease on ultrasound imaging and compare with clinical features in patients with pathologically-approved Kimura disease.

Methods: A total of 30 patients (29 men and 1 woman; a mean age of 35.4 years) with Kimura disease confirmed by surgery and pathology were enrolled in the study. Ultrasonographic findings were analyzed retrospectively and compared with clinical features and laboratory examinations to better understand the relationship among them.

Results: All patients presented with painless, progressively enlarged soft tissue masses in head and neck, axillary, inguinal regions or limb extremities. Laboratory results showed elevation of eosinophils in both peripheral blood and serum IgE in 12 of 30 cases. Ultrasound findings of the lesions in Kimura disease were divided into three types: Type I: characterized by simple lymph node enlargement; Type II: characterized by flake-like thickening of the lesion without mass effect, and enlargement of nearby lymph nodes; Type III: a tumor-like lesion associate with enlargement of nearby lymph nodes.

Conclusion: The Kimura disease has specific ultrasonographic characteristics of lymph node and adjacent structures. When combined with patient’s clinical information and laboratory tests, ultrasound examination can provide useful information for making clinical diagnosis and management.

Key words: Kimura disease; eosinophilic lymphogranuloma; ultrasound

Kimura disease was first reported in 1937 by Chinese Korean ethnic scholars Kimm and Szeto [1], which was originally known as eosinophilic hyperplastic lymphogranuloma. In 1948, Kimura et al [2] reported this disease as an unusual granulation combined with hyperplastic changes of lymphatic tissue; and provided a systematic description. Naturally, the disease was penned after his name for bringing academic awareness to the condition [3]. Kimura disease is also known as eosinophilic lymphogranuloma, a chronic inflammatory disease characterized by damage to lymph nodes, soft tissue, and salivary glands. It often presents as a painless subcutaneous mass, mostly located in the head and neck, and can involve the respiratory and urinary systems. It is easy to misdiagnose because of the slow progression and unapparent early symptoms [4].

The treatment of Kimura disease includes hormonal therapy, cyclophosphamide, surgery, and radiation therapy. Kimura disease may remit spontaneously but can recur at a rate as high as 17% [5]. The aim of this study was to demonstrate the characteristics of Kimura disease on ultrasound imaging and compare with the clinical features in 30 patients with pathologically-approved Kimura disease.

Patients and methods

Patients

The study was approved by our hospital ethical review board with exception of the consent from patients. This retrospective study included 30 patients (29 men
and 1 woman; with age from 4 to 58 years, a mean age of 35.4±14.3 years) with Kimura disease diagnosed by surgery and pathology in our hospital between January 2013 and June 2018. Clinical information of all patients including medical history, laboratory tests were obtained from medical records. All patients had ultrasound examination for superficial masses before the surgery and biopsy.

**Ultrasound evaluation**

Gray-scale and color Doppler ultrasound was used to image the superficial masses located at head and neck, axillary areas, inguinal regions or limb extremities. High resolution ultrasound systems including Aixplorer (Supersonic Imaging, France) and Logic 9 (General Electric, USA) machines with transducer frequency of 4–15 MHz were utilized in this study. The ultrasound systems were optimized in term of adequate settings of frequency, gain, depth and dynamic range as well as flow mapping parameters. The targeted areas and lesions were scanned in transverse, sagittal and oblique sections by experienced ultrasound doctors. Ultrasound characteristics of the lesions including size, shape, blood supply, and involvement of surrounding tissues were observed and documented for analysis.

**Results**

Of 30 cases, the lesions were involved at single location in 28 patients and two locations in 2 cases. There were 20 cases which the lesions were involved in the head and neck, two in the armpit, three in the groin, two in the upper limbs, two in the lower limbs, and one in male external genitalia. Ultrasound findings of Kimura disease included lymph nodes and extranodal lesions, which were classified into three types: Type I: characterized by simple lymph node enlargement; Type II: flake-like thickening of the lesion without mass effect, and enlargement of nearby lymph nodes; Type III: a tumor-like lesion associate with enlargement of nearby lymph nodes.

Simple lymph node lesions accounted for 26.7% (8/30), including cervical nodes (n=3), axillary nodes (n=2), and inguinal nodes (n=3); while extranodal lesions accounted for 73.3% (22/30), including head and neck (n=17), upper limbs (n=2), lower limbs (n=2), and external genitalia (n=1). In two cases, lesions were distributed among two sites. In the first, one lesion was at the left posterior ear and the other was in the right axilla. In the second, one lesion was in the left spermatic cord and another was in the scrotum. The classification of types and location of Kimura disease is shown in Table 1.

All extranodal lesions had a common feature, i.e., they were accompanied by lymph node enlargement in nearby drainage area, accounting for 72.4% of 30 cases. Pathology confirmed that the lesion itself and lymph nodes in nearby drainage areas were all showed changes of Kimura disease. Table 1 shows that the 3 ultrasound types had unique characteristics (Fig 1-3): (1) Type I: hypoechoic lesions only occurred in the lymph nodes; which lesions were confined to the lymph nodes, and only a few broken through the lymph node capsule to invade surrounding adipose or muscle tissue (Fig 1). (2) Tape II: Flake-like thickening appearance (Fig.2): hypoechoic lesion was irregular in shape, and had no capsule or mass effect, and invaded into adjacent tissues. (3) Tape III: Tumor-like appearance (Fig.3): The shape of the lesion was mostly regular, i.e., circular, elliptic, or lobulated; the capsule can be intact or break through to invade surrounding tissues and form adhesion. Most of the above three types of Kimura disease lesions were abundant in tree branch-like blood flow, similar to acute lymphadenitis. No liquefaction or calcification occurred in any lesions of Kimura disease in this group. Simple lymph node lesions were mostly regular in shape, while extranodal lesions were mostly irregular (Table 2).

| Items                      | Ultrasound types (n) | Nearby node involvement (n) |
|---------------------------|----------------------|----------------------------|
|                           | Simple lymph node    | Flake-thickening type      | Tumor-like type |
| Lymph node lesions        | 8                    | 8                          | -              |
| Extranodal lesions        | 22                   | -                          | 16             | 6              | 22 |

**Discussion**

Kimura disease is also known as eosinophilic lymphogranuloma, and is a chronic inflammatory disease of unclear etiology with low incidence rate. Young and middle-aged males are at high-risk, especially Asians. There was only one female and the average age of all patients was 35.4±14.3 years in this study group, which consistent with literature reports [6]. Kimura disease starts slowly and persists for years to decades. It is easy to misdiagnose because obvious symptoms are lacking. In our study, only 12 patients completed laboratory examination at the beginning, of which five had received
By analyzing and summarizing data retrospectively, we found that there are certain rules to follow in the diagnosis of Kimura disease, especially with extranodal involvement. Regardless of flake-like thickening or tumor-like presentation, the combination of disease duration, benign course, chronic progression, young and middle-aged male, and lymph nodes enlargement in nearby drainage areas should be taken into account for consideration of Kimura disease. The diagnosis can be further supported by increased eosinophils in peripheral blood and elevated serum IgE levels. Ultrasound features from this study could be used to distinguish Kimura disease from inflammation, lymphoma, and metastatic cancer. The flake-like thickening of lesions (Type II) is easy to confuse with inflammation, but the patient has no inflammatory manifestations such as redness, swelling, hot, or pain. In the simple lymph node enlargement manifestation (Type I), the lymphoid medulla may thin or disappear completely, making it difficult to distinguish from lymphoma in terms of shape, echogenicity, or internal blood supply. Generally speaking, Kimura disease has no malignant tendency, but a report of the evolution of Kimura disease into non-Hodgkin’s lymphoma in one case should be noted [9]. The tumor-like subtype (Type III) of lesion in Kimura disease is easily misdiagnosed as cancer with lymph node metastasis due to enlargement of nearby lymph nodes. Knowledge of the duration and course of Kimura disease can help avoid omission. Core biopsy is optimal for making diagnosis of Kimura disease.

Additional laboratory examination after surgery. It can be seen that our knowledge of Kimura disease is far from enough and should be strengthened. Kimura disease mostly occurs in superficial tissues and organs [7], and is rare in internal organs [8]. No patients in our study had an evidence of internal organ involvement.

### Table 2  Ultrasound imaging features of Kimura disease

| Items                  | Simple lymph node | Extranodal lesion |
|------------------------|-------------------|-------------------|
| Total (n)              | 8                 | 22                |
| Shape (n)              |                   |                   |
| Regular                | 6                 | 4                 |
| Irregular              | 2                 | 18                |
| Capsule (n)            |                   |                   |
| Complete               | 5                 | 4                 |
| Incomplete             | 3                 | 18                |
| Internal echo (n)      |                   |                   |
| Hypoechoic             | 8                 | 22                |
| Calcification          | -                 | -                 |
| Liquefaction           | -                 | -                 |
| Blood supply (n)       |                   |                   |
| Plentiful              | 5                 | 22                |
| Not plentiful          | 3                 | -                 |

**Figure 1**  Type I lymph node of Kimura disease in right parotid gland.

**Figure 2**  Type II flake-like thickening of lesion of Kimura disease in right elbow (A), with troclear lymph node involvement (B).

**Figure 3**  Type III tumor-like of lesion in Kimura disease in left spermatic cord and scrotum (A), with abundant tree branch-like blood flow (B).
group had two concurrent lesions. In one case, the lesions were close to each other, but were separated in the other case, indicating that there is no consistent growth pattern in cases with multiple lesions.

Pathological diagnosis of Kimura disease with lymph node involvement is based on lymph node structure: (1) Lymphocyte follicles proliferate significantly, and a small number of follicles can undergo progressive transformation. Vascular hyperplasia and polynuclear giant cells are often found in the growth center with fibrosis and protein deposition are also observed. (2) The lymphoid follicular area is enlarged and the blood vessels show hyperplasia, accompanied by glass-like degeneration, infiltration of tissue cells, plasma cells and mast cells etc., and fibrosis can occur in the lymphoid sinus and follicular interstitium as the disease progresses. (3) The diagnosis focused on infiltration of a large number of mature eosinophils in the follicular interstitial area, the capsule, and even the adipose tissue outside the membrane. Most of these mature eosinophils formed eosinophilic abscesses. Although there is no lymph node structure in extranodal Kimura disease, lymphocyte follicular hyperplasia, enlargement of the growth center, infiltration by eosinophilic granulocytes, and the formation of eosinophilic abscesses and subsequent fibrosis all have the same characteristics. Hyperplasia of new blood vessels is the main reason for rich blood flow in lesions seen on ultrasound.

The histopathology of Kimura disease should be distinguished from angiolymphoid hyperplasia with eosinophilia (ALHE) [12], which is characterized by hyperplasia of vascular lymphoid tissue and increased eosinophils. These two diseases used to be considered the same, but now they are considered clinically and histologically separate diseases [13]. ALHE is also known as epithelioid hemangioendothelioma, which is mostly found in European and American, especially women; the onset peak is 20–40 years old, and the medical history is shorter, generally within a few months [14,15]. ALHE lesions often only invade the superficial skin, with a small lesion range, and do not invade lymph nodes or the parotid gland. ALHE is mainly characterized by vascular hyperplasia (new capillaries), accompanied by infiltration with lymphocytes and eosinophils, without glassy degeneration. In addition, there is no obvious tendency toward fibrosis in the pathology of ALHE. ALHE may represent an anatomical abnormality of a vascular secondary inflammation, while Kimura disease may represent a primary inflammatory process secondary to vascular hyperplasia. In recent years, there have been case reports of the co-existence of these two diseases [16]. Kimura disease is nominally similar to eosinophilic granuloma and needs to be identified. Eosinophilic granuloma mainly involves the skeleton and commonly occurs in children. Langerhans cells show patchy proliferation in the lesions, and the Langerhans cells are scattered among a large number of eosinophils, neutrophils, and lymphocytes. Occasionally polykaryotic cells are formed, and fibrotic hyperplasia is observed in advanced lesions. Although the names and microscopic pathologies of the diseases mentioned above are similar, familiarity with the common pathogenesis, age of onset, and other characteristics enables better differential diagnosis.

According to the literature, about 3% of patients with Kimura disease have kidney damage, mainly nephrotic syndrome [17]. However, none of the patients in this group had other systemic involvement.

**Conclusion**

Although the final diagnosis still requires pathological evidence [18], the Kimura disease has specific ultrasonographic characteristics of lymph node and adjacent structures. When combined with patient’s clinical information and laboratory tests, ultrasound examination can provide useful information for making clinical diagnosis and management.

**Conflict of Interest**

The authors have no conflict of interest to declare.

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