Head and neck MRI of Kimura disease

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Objectives: The purpose of our study was to describe the MR appearance of Kimura disease and to interpret the differences in appearance from malignant parotid gland tumours.

Methods: MR studies of seven patients with Kimura disease were reviewed. The MR studies included T_1 weighted, T_2 weighted, short tau inversion-recovery, diffusion-weighted (DW) and dynamic contrast-enhanced imaging.

Results: Typical Kimura disease featured subcutaneous lesions, continuously infiltrated parotid lesions from the subcutaneous lesions with or without intraparotid lymphadenopathies, and reactive cervical lymphadenopathies. The subcutaneous lesions showed gradual upward enhancement on dynamic contrast-enhanced MR images.

Reactive lymph nodes showed early enhancement on contrast-enhanced MR images and marked high intensity and low apparent diffusion coefficient values on DW images.

Conclusion: An indication for making the diagnosis of Kimura disease should be the subcutaneous tissue of the head and neck showing gradual upward enhancement on dynamic contrast-enhanced MRI and a lack of high intensity on DW images, associated with reactive lymph nodes.

Received 26 September 2009
Revised 11 February 2010
Accepted 9 March 2010

DOI: 10.1259/bjr/42012793

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Kimura disease is an immune-mediated inflammatory disorder of unknown aetiology that predominantly occurs in Asian men in the second and third decades of life. Although it has been reported in Europe and America, the prevailing incidence is among Asians [1]. The head and neck region is typically involved, primarily affecting the salivary glands, adjacent subcutaneous tissues and regional lymph nodes. The commonly involved sites are the periauricular area, epicranium, orbit and eyelids. In non-Asian patients, the salivary glands are seldom affected, although the lachrymal glands are involved in some cases. The clinical course of Kimura disease is often progressive, and the main problem concerning treatment is disease recurrence [2]. The rarity of this disease makes a definitive treatment policy difficult to establish. This condition is benign and displays a predilection for young patients, therefore, use of irradiation is not common owing to concerns about secondary malignancy [3]. Surgical excision alone often results in relapse, so steroid therapy is usually employed; however, swelling tends to recur with the cessation of treatment [2]. Clinically, the lesion is often misdiagnosed as a salivary gland malignancy [4–6].

There are some reports on the radiological characteristics, including MR and CT, of Kimura disease [7–9]. Although the usefulness of dynamic contrast-enhanced MR and diffusion-weighted (DW) imaging in the characterisation of salivary gland tumours has been reported recently [10, 11], there are no reports of MR findings of Kimura disease, including in those studies.

Here, we describe MRI, including dynamic contrast-enhanced and DW imaging, of Kimura disease together with its pathological correlations.

Methods and materials

Between July 2003 and July 2008, we treated 7 patients with Kimura disease (6 males and 1 female; mean age 39 years; range 14–71 years), all of whom underwent MRI. Two patients underwent surgical excision (patients 2 and 5) and four underwent biopsy; pathological diagnosis of Kimura disease was made in six patients. The patient most recently diagnosed with Kimura disease (patient 7) has been followed-up clinically for 1 year.

All MR examinations were performed using a 1.5 T MR unit (GE Medical Systems, Milwaukee, WI) with a neurovascular array coil. T_1 weighted images, short tau inversion-recovery (STIR) images and DW images (spin-echo single-shot echoplanar sequence with b factors of 0 and 1000 s mm⁻²) of the same transverse plane were obtained. T_2 weighted images of the coronal plane were also obtained (Figure 1). Dynamic contrast-enhanced (dynamic) MRIs were obtained using three-dimensional fat suppression T_1 weighted multiphase spoiled gradient-recalled echo (SPGR) for 4 min, with each phase lasting 27 s followed by a 3 s interval. After the first set was obtained, contrast material injection was started immediately. A contrast agent (Omniscan; Daiichi Sankyo Co., Tokyo, Japan) was administered (0.2 ml kg⁻¹ body weight) at a rate of 2.0 ml s⁻¹ followed by a 20 ml saline flush into the antecubital vein. Seven sets of dynamic contrast-enhanced images were obtained serially. Soon after dynamic contrast-enhanced MRI, fat suppression T_2

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Figure 1. Kimura disease of the right head and neck in a 14-year-old Japanese male (patient 2). (a) On axial T_1 weighted imaging, the periauricular subcutaneous lesion shows slightly high intensity for muscle (arrowheads). The subcutaneous lesion has invaded the posterior side of the right parotid gland. Intraparotid lymphadenopathy (arrow) shows low intensity for parenchyma of the right parotid gland. (b) On axial short tau inversion-recovery (STIR) imaging at the same level, the subcutaneous lesion (arrowheads) shows heterogeneous high intensities. Intraparotid and retropharyngeal lymphadenopathies also show marked high intensity (arrows). (c) On diffusion-weighted imaging, the intensities of the subcutaneous lesion (arrowheads) are lower than those of lymphadenopathies (arrows). (d) Fat suppression T_1 weighted imaging of the same axial plane as the pre-contrast enhanced T_1 weighted imaging shows a heterogeneously enhanced subcutaneous lesion (arrowheads) revealing gradual upward enhancement on dynamic contrast-enhanced MRI. The intraparotid lymph node (arrow) shows early enhancement with poor washout on dynamic MRI. (e) Axial STIR imaging of the caudal level shows ipsilateral cervical lymphadenopathies (arrows). Their minimum axial diameter is larger than 10 mm.

weighted images of the same transverse plane to pre-contrast enhanced T_1 weighted images were obtained. Apparent diffusion coefficient (ADC) maps were automatically constructed from DW images. Time-signal intensity curves (TICs) of the lesions on dynamic MRIs were plotted, and washout ratios were also calculated. TICs were divided into 4 types: Type A, curve peaks earlier than 120 s (<120 s) after administration of contrast material with a high washout ratio ($>30\%$); Type B, curve peaks earlier than 120 s (<120 s) with a low washout ratio ($<30\%$); Type C, curve peaks later than 120 s (>120 s); Type D, non-enhanced.

Results

The most common presenting complaint was a painless infiltrative mass in the subcutaneous tissue of the head and neck. None of the patients had facial nerve palsy.

We examined seven patients with Kimura disease arising in the head and neck region (Table 1). Six patients

had subcutaneous lesions: three lesions occurred in the right cheek (patients 1, 3, 4), one in the right auricular and occipital area (patient 2), one in the left submandibular area (patient 6) and one in the right temporal region (patient 7). Five of the patients with subcutaneous lesions in the cheek, auricular or temporal regions also had right parotid lesions. There were 3 patterns of parotid lesions: 1, infiltrative lesion from the subcutaneous lesion continuously; 2, enlargement of the intraparotid lymphadenopathies; and 3, a mixed pattern. Two patients had no salivary gland lesions (Table 2). All patients had ipsilateral cervical lymphadenopathies. All subcutaneous and parotid lesions showed heterogeneous high intensities on STIR and T_2 weighted images. Lymphadenopathies showed homogeneous high intensities on STIR and T_2 weighted images except in one patient (patient 5), who had lymphadenopathies only. The diameter of the largest was 42 mm, with heterogeneous high intensities (patient 5) on STIR and T_2 weighted images and with hypointense foci, suggesting that it was flow void. In the

Table 1. Clinical features of seven patients with Kimura disease

Patient	Age (years)	Gender	Site of lesions	Peripheral eosinophilia (%) ^a	Serum IgE levels (IU ml ⁻¹) ^b
1	32	M	R parotid, SC, R LNs	10.3	1100
2	14	M	R parotid, SC, R LNs	54	16 100
3	58	M	R parotid, SC, R LNs	36	15 100
4	36	M	R parotid, SC, R LNs	12	1190
5	37	F	R LNs	1.3	540
6	23	M	SC, L LNs	16.5	2901
7	71	M	R parotid, SC, R LNs	33	83 600

R, right; L, left; SC, subcutaneous; LNs, lymph nodes.

^aNormal range 1–5%.

^bNormal range ≤ 360 IU ml⁻¹.

other patients, the diameters of the lymphadenopathies were approximately 10 mm with homogeneous high intensities on STIR and T_2 weighted images. On T_1 weighted images, all lesions showed slightly high- or isointensity for muscle. On DW images, all subcutaneous and infiltrative parotid lesions showed moderately high intensities. On the other hand, intraparotid and cervical lymphadenopathies showed very high intensities on DW images. On dynamic MR images, all subcutaneous lesions had gradual upward enhancement (Type C, Table 2). One subcutaneous lesion (patient 6) also had another component that showed Type B perfusion on dynamic MRIs. Continuously infiltrated parotid lesions from subcutaneous lesions showed Type C perfusion on dynamic MR images, and enlarged intraparotid lymphadenopathies showed Type B perfusion. Cervical lymphadenopathies showed Type A or B perfusion on dynamic MR images except in one patient (patient 5), who had only lymphadenopathies, with the largest showing Type B and C perfusion. The component showing Type A and Type B perfusion on dynamic MRIs showed higher intensity and a lower ADC value on DW images than the component showing Type C perfusion. The mean values and standard deviation of the ADC values of the subcutaneous lesions and lymphadenopathies were as follows: subcutaneous lesions, $1.21 \pm 0.33 \times 10^{-3} \text{ mm}^2 \text{ s}^{-1}$; lymphadenopathies, $0.91 \pm 0.25 \times 10^{-3} \text{ mm}^2 \text{ s}^{-1}$.

Histologically, subcutaneous lesions are characterised by dense collagen fibrosis, capillary proliferation and chronic inflammation by infiltrating plasma cells, lymphocytes, reactive lymphoid follicles and eosinophils. The largest cervical lesion of patient 5 also showed dense fibrosis and hyalinisation, capillary proliferation, chronic inflammation by infiltrates of plasma cells and lymphocytes with germinal centre formation. The prominent

fibrotic component reduced the intensity on DW images and showed Type C perfusion on dynamic MRIs. Cervical lymph nodes revealed follicular lymphoid hyperplasia with mild eosinophilic infiltrates.

Discussion

Kimura disease is a rare chronic inflammatory disease of unknown cause [1]. This disease has male predominance and occurs mostly during the second and third decades of life, endemically in Asia, especially in Japan and China. Clinically, the lesion is often misdiagnosed as salivary gland malignancy because of the diffuse nature of the disease [4–6, 12].

MRI is an established and useful way of demonstrating the morphology and extent of head and neck lesions, as well as their relationship with adjacent structures. Regarding the characteristics of malignant salivary gland tumours, static MRI, T_1 weighted, T_2 weighted and gadolinium-enhanced MRIs reportedly show irregular tumour margin, tumour infiltration into surrounding tissue and low signal intensity on both T_1 and T_2 weighted MRIs [13]. On the other hand, Freling et al [14] reported that tumour margins, homogeneity, signal intensity and infiltration into subcutaneous fat were not discriminating factors to correctly predict benign or malignant disease. Recently, the usefulness of dynamic MRI and DW imaging in the characterisation of salivary gland tumours was reported [10, 11]. Here, we describe MRI, including dynamic contrast material-enhanced and DW imaging, of Kimura disease together with its pathological correlations.

The literature on radiological features of Kimura disease is limited owing to its rarity. The previously reported imaging findings of Kimura disease were

Table 2. Time–signal intensity curves of lesions on dynamic MRIs and apparent diffusion coefficient (ADC) values of cervical lymphadenopathy

Patient	Subcutaneous lesions ($\times 10^{-3} \text{ mm}^2 \text{ s}^{-1}$)	Parotid lesions	Cervical lymphadenopathies	ADC values ($\times 10^{-3} \text{ mm}^2 \text{ s}^{-1}$)
1	NE	B	A	0.94
2	C	B, C	A	0.86
3	C	C	B	0.75
4	C	B	A	0.81
5	No lesion	No lesion	¹ B, ² C	¹ 0.89, ² 1.56
6	B, C	No lesion	A	0.71
7	C	C	B	0.82

ADC, apparent diffusion coefficient; NE, not examined.

non-specific and variable. On CT scans, subcutaneous masses with lymphadenopathy were reported as the typical findings. Gopinathan and Tan [9] recently reported that the lesions of Kimura disease could be classified into two specific morphological subtypes: relatively well-defined nodular lesions (Type 1) and ill-defined plaque-like lesions (Type 2). On static MRI, including T_1 weighted, T_2 weighted and gadolinium-enhanced MR, intense contrast enhancement and flow voids in the mass have been classically described by Som and Biller [7]. However, poorly and moderately enhancing lesions are also frequently seen [8, 15].

The lesions of Kimura disease tend to be heterogeneous, hypointense, sometimes slightly hyperintense on T_1 and T_2 weighted imaging and show heterogeneous enhancement [16]. Takahashi et al [8] reported that prominent fibrotic tissue influenced the intensity on T_2 weighted images, showing less T_2 hyperintensity. They had attributed the variable contrast enhancement to differing degrees of fibrosis and vascular proliferation [8]. Histopathologically, soft-tissue mass and lymphadenopathy in the parotid gland revealed extensive infiltration by eosinophils and lymphocytes with germinal centre formation surrounded by thick fibrotic tissue [8]. There may be different patterns of signal intensity in the lesions of Kimura disease depending on the variability of fibrosis and vascularity [4, 8].

In our study, although all lesions of Kimura disease showed heterogeneous hyperintensities on STIR and T_2 weighted images, there were some different MR characteristics among the lesion sites on DW and dynamic MRIs. The subcutaneous lesions and the infiltrative parotid lesions continuing from them showed gradual upward enhancement on dynamic MRIs (Type C) and not so high intensity on DW images (mean of ADC values of subcutaneous lesions was $1.21 \pm 0.33 \times 10^{-3} \text{ mm}^2 \text{ s}^{-1}$). On the other hand, intraparotid and cervical lymphadenopathies showed early enhancement on dynamic MRIs and marked high intensity on DW images. Subcutaneous lesions contained more prominent fibrotic tissue than lymph node lesions, and this prominent fibrotic tissue resulted in their gradual upward enhancement on dynamic MRIs. Hypercellularity in lymph node lesions caused the marked high intensity on DW images.

Clinically, differential diagnoses include malignant salivary gland tumour with metastatic lymphadenopathies, lymphoma and angiolymphoid hyperplasia with eosinophilia (ALHE).

High-grade malignancy of salivary glands sometimes features soft-tissue invasion and metastatic lymphadenopathy [11]. Usually, cervical lymph nodes larger than 10 mm in minimal axial diameter are positive for

metastasis on static MRIs. Recently, the usefulness of dynamic MRI and DW imaging in the characterisation of cervical lymph nodes has been reported [11]. Reactive lymph nodes showed Type A TICs and metastatic lymph nodes showed Type B TICs on dynamic study, and the ADC value of metastatic lymph nodes ($1.23 \times 10^{-3} \text{ mm}^2 \text{ s}^{-1}$) was higher than that of reactive lymph nodes ($0.90 \times 10^{-3} \text{ mm}^2 \text{ s}^{-1}$) on DW images. Although reactive lymph nodes possess the whole normal lymph node structures except for size, metastatic lymph nodes are involved with malignant cells, and they also contain microscopic necrotic foci, haemorrhagic changes and reactive fibrosis. Lymph node lesions of Kimura disease had low ADC values, and were considered to be reactive lymphadenopathies. On dynamic MRIs, lymph node lesions showed Type A and Type B TICs. Although there were no biopsy specimens of any of the reactive lymphadenopathies except for the largest cervical lymphadenopathy in patient 5, one could surmise that some reactive lymph nodes of Kimura disease have fibrosis.

Malignant lymphoma, especially non-Hodgkin lymphoma, tends to be a homogeneous tumour that includes lymph nodes and soft-tissue lesions. King et al [17] observed that non-Hodgkin lymphoma showed intermediate signal intensity (similar to brain grey matter) on T_2 weighted images and intermediate signal intensity on T_1 weighted images, with mild or moderate enhancement following contrast medium administration. In our study, all subcutaneous and parotid lesions in patients with Kimura disease showed heterogeneous high intensities on STIR and T_2 weighted images. Lymphadenopathies showed homogeneous high intensities on STIR and T_2 weighted images except in one patient (patient 5). We speculated that the homogeneity of the intensity of Kimura disease on T_2 weighted and enhanced T_1 weighted images differed from that of malignant lymphoma (Table 3). Malignant lymphoma had marked high intensity on DW images [18, 19]. Wang et al [18] reported a very low mean ADC value in malignant lymphoma of 0.66 ± 0.17 (mean $\pm$ standard deviation), which is lower than the mean ADC values of Kimura disease in our study. In Kimura disease, the intensities of soft-tissue lesions on DW images appeared low compared with those of lymph node lesions around or in soft-tissue lesions (Table 3).

ALHE is considered to be a type of endothelial neoplasm related to inflammatory stimulation. It often affects middle-aged Western women, who present with a superficial, well-circumscribed mass without formation of lymphoid follicles and eosinophilic abscesses histologically. Patients with ALHE have normal immunoglobulin E (IgE) levels and no albuminuria [20–22].

Table 3. Differences between Kimura disease and malignant lymphoma by signal intensity

	SI on T_2 weighted image	SI of LNs on T_2 weighted image	SI on diffusion-weighted image	ADC values ($\times 10^{-3} \text{ mm}^2 \text{ s}^{-1}$)
Kimura disease	Heterogeneous intermediate	Homogeneous high	Heterogeneous intermediate high	SC, 1.21 ± 0.33 LNs, 0.91 ± 0.25
Malignant lymphoma	Homogeneous intermediate	Homogeneous intermediate	Homogeneous very high	0.66 ± 0.17

ADC, apparent diffusion coefficient; LN, lymphadenopathy; SC, subcutaneous lesions; SI, signal intensity.

The inflammatory masses in ALHE are mostly restricted to the dermis and have a tendency to bleed when irritated [9]. The diagnosis of Kimura disease should not be a problem when combined with the results of a pathological examination, together with markedly high levels of eosinophils in peripheral blood and serum IgE. Correlation with these clinicopathological findings is essential as differentiation on imaging alone may be difficult.

Conclusion

Subcutaneous tissue of the head and neck with gradual upward enhancement on dynamic MR and absence of high intensity on DW images, associated with reactive lymph nodes, was consistent with Kimura disease. Dynamic MRI and DW imaging can differentiate its precise nature from other soft-tissue tumours.

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