Kimura Disease Simulating Hodgkin's Lymphoma on ^{18}F FDG PET-CT: Report of a Case

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Abstract We report the case of a 16-year-old male patient presenting with several mass lesions on the left side of his neck that had been there for weeks. Whole-body ^{18}F -fluorodeoxyglucose positron emission tomography and computed tomography (^{18}F FDG PET-CT) revealed multiple focal areas of increased uptake of fluorodeoxyglucose (FDG) on the left side of the neck, left supraclavicular fossa, left axilla, and mediastinum, simulating the imaging findings of Hodgkin's lymphoma. Subsequent incisional biopsy of lymph nodes in the left supraclavicular fossa with histologic examination confirmed the diagnosis of Kimura disease. The differential diagnoses should include Kimura disease when evaluating regional or generalized lymphadenopathy seen on ^{18}F FDG PET-CT because it also may show prominent uptake of FDG.

Keywords Kimura disease · Lymphadenopathy · Hodgkin's lymphoma · ^{18}F FDG PET-CT

Introduction

Kimura disease, a rare, benign, chronic inflammatory disorder of the soft tissue, was first described in China in 1937 and then more widely recognized after Kimura's description in the

Japanese literature in 1948 [1, 2]. A subcutaneous mass in the head and neck with regional lymphadenopathy and salivary gland involvement is the most common clinical finding. The manifestation of the disease, however, varies and may resemble lymphadenopathy of many different etiologies including lymphoma. ^{18}F FDG PET-CT is a useful technique and currently has been recommended for the clinical workup in selected patients with Hodgkin's and non-Hodgkin's lymphoma [3, 4]. However, it may sometimes be difficult for ^{18}F FDG PET-CT scans to differentiate benign conditions from lymphoma. We present the case of a young Asian boy with Kimura disease, whose clinical condition and imaging findings on ^{18}F FDG PET-CT mimicked Hodgkin's lymphoma.

Case Report

A 16-year-old male patient was admitted to our hospital with the complaint of a mass on the left side of his neck, which had been noted for 3 weeks and turned painful 1 week ago. Physical examination revealed an 8 cm×8 cm, fixed, confluent, and tender mass lying over level IV and level V of the left side of the neck. Nasal endoscopy and laryngoscopy performed to discover any possible primary malignancy showed only smooth mucosa. Laboratory data disclosed leukocytosis (12,670 cells/ μl) with segmented neutrophil predominance (80.0 %), an elevated serum level of C-reactive protein (4.67 mg/dl), and a normal serum level of lactic dehydrogenase (162 IU/l). Computed tomography (CT) of the head and neck revealed multiple enlarged, necrotic, and confluent lymph nodes on the left side of the posterior lower neck, left supraclavicular fossa, and left axilla, and an extensive soft tissue mass with central necrotic change involving the retrosternal and mediastinal regions (Fig. 1). On ^{18}F FDG PET-CT, multiple focal areas of increased FDG uptake were demonstrated involving the left side of the posterior lower

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Fig. 1 Post-contrast CT of the head and neck in (a, b) axial and (c) coronal views showed multiple enlarged, necrotic, and confluent lymph nodes with variable enhancement on the left side of the posterior lower neck and supraclavicular fossa. **d** A large extensive mass with necrotic change in the retrosternal and mediastinal regions was also visualized

neck and left supraclavicular fossa (SUVmax: 11.09), mediastinum (SUVmax: 11.84), and left axillary region (SUVmax: 9.72) (Fig. 2), suggesting Hodgkin's lymphoma. Incisional biopsy of lymph nodes in the left supraclavicular fossa and histological examination revealed soft tissue with fibrosis, histiocytic eosinophilic infiltration, and microabscess, compatible with the findings of Kimura disease (Fig. 3); immunohistochemical stain of CD30 showed no Reed-Sternberg cells

or variant forms, not supporting the differential diagnosis of Hodgkin's lymphoma. This patient, therefore, received intravenous steroid therapy followed by immunomodulating treatment with hydroxychloroquine and cyclosporin. The size of the mass on the left side of lower neck and left supraclavicular fossa gradually decreased, and the tenderness also subsided. His condition remained stable in follow-up for more than 1 year.

Fig. 2 Maximum intensity projection (MIP) image of whole-body ^{18}F FDG PET revealed multiple focal areas of increased FDG uptake in the left side of the posterior lower neck, left supraclavicular fossa, mediastinum, and left axilla. Transverse sections through the lower neck and upper chest areas demonstrated hypermetabolic uptake on fused PET/CT and PET images in the (a) left side of the posterior lower neck and supraclavicular fossa (SUVmax: 11.09), (b) mediastinum (SUVmax: 11.84, arrow), and left axillary region (SUVmax: 9.72, arrowhead)

Fig. 3 Photomicrograph of a lymph node in the left supraclavicular fossa showed (a) hyperplasia of the germinal center with histiocytic and eosinophilic infiltration; (b) fibrosis and proliferating endothelial cells were also seen. These features are compatible with Kimura disease

Discussion

We report the case of a teenage boy, who had a prominent mediastinal mass and lymphadenopathy on the left side of the neck, left supraclavicular fossa, and left axillary region. Combining head and neck CT and whole-body ^{18}F FDG PET-CT, the clinical picture initially resembled Hodgkin's lymphoma. Biopsy and histological examination, however, finally identified Kimura disease.

Kimura disease is a rare idiopathic chronic lymphoproliferative disorder of unknown etiology, mainly affecting young Asian men in the 3rd decade of life, with a male-to-female ratio of up to 3.5–6.0:1 [5, 6]. Clinically, non-tender subcutaneous masses involving the periauricular region, neck, salivary glands, epicranium, orbit, and eyelid are commonly observed. Masses in the tongue, earlobe, lacrimal gland, oral cavity, nasal sinuses, axilla, groin, extremities, long bones, and even abdomen have also been reported, often accompanied by regional lymphadenopathy [7, 8]. In laboratory studies, an increased number of eosinophils and mast cells may be seen in the peripheral blood, and the proportion of eosinophils may go up to 10–20 % [9]. Twelve to 16 percent of patients have nephrotic syndrome. Severe renal dysfunction has been found in rare cases [9]. Diagnosis is usually made by biopsy

and histological examination. Histopathologically, it is characterized by an abnormal proliferation of lymphoid follicles and vascular endothelium with eosinophilic infiltration in the mass and surrounding tissue, and the features of Asian and non-Asian cases are identical [6]. The pathophysiology of the disease remains uncertain. Production of IgE and cytokines such as TNF- α , IL-4, IL-5, and IL-13 is increased in the lesion tissue. This cytokine imbalance may be due to the predominance of Th2 and Tc1 cells. No specific culprit antigen, however, has yet been identified. Researchers now consider that Kimura disease is related to an unusual autoimmune response or immune response against parasitic infestation [10–12].

Some characteristic image findings of Kimura disease have been described. Without contrast, Kimura disease appears as ill-defined subcutaneous masses that are homogeneously isodense to slightly hypodense without necrosis, calcification, or cystic degeneration on CT. On magnetic resonance imaging (MRI), T1-weighted images show isointensity or slight hyperintensity and T2-weighted images reveal hyperintensity [13, 14]. With contrast, variable forms and degrees of enhancement may be seen on both CT and MRI images due to different degrees of fibrosis and vascular proliferation. In general, enhancement on MRI may be of greater degree than on CT because of the more delayed imaging protocol [14]. On ^{18}F FDG PET, Kimura disease shows remarkable uptake in the involved lymph node regions and resembles the picture seen in other inflammatory or neoplastic disorders, such as tuberculosis, lymphoma, or metastatic lymphadenopathy [15]. Patients with Kimura disease demonstrating unusual manifestations such as generalized lymphadenopathy or a pulmonary hilar tumor on ^{18}F FDG PET have also been reported [15, 16], highlighting the fact that Kimura disease should be considered as an alternative diagnosis in either regional or generalized lymphadenopathy.

In our patient, the age was relatively young, more approximating the first peak of the bimodal age distribution of Hodgkin's lymphoma rather than the usual age of onset between 20 to 40 years old for Kimura disease. There was no typical eosinophilia, elevated IgE level, or impaired renal function detected by laboratory tests. CT revealed a prominent soft tissue mass in the mediastinum with necrotic change instead of the more commonly reported subcutaneous mass in the parotid gland or other sites in the head and neck. ^{18}F FDG PET-CT demonstrated multiple focal areas of greatly increased FDG uptake involving lymph nodes. This information seemed to favor the diagnosis of Hodgkin's lymphoma until the histological examination was performed, which showed a negative immunohistochemical staining of Reed-Sternberg cells and provided the correct answer. In the literature, a case of Kimura disease initially diagnosed with Hodgkin's lymphoma by fine-needle aspiration cytology but later proven otherwise by excisional biopsy has also been

reported [17], underscoring the cautiousness required in the diagnosis of lymphadenopathy.

Conclusion

Kimura disease may demonstrate various manifestations in both the clinical setting and imaging findings. Therefore, it should be taken into consideration whenever evaluating regional or generalized lymphadenopathy demonstrated as intense FDG uptake on ^{18}F FDG PET-CT before it is proven related to malignancy or other etiologies, even at sites where Kimura disease does not typically occur. Biopsy with histological examination of the lesions should always be carried out to acquire the final diagnosis.

Ethical Standards

All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008 (5). Informed consent was obtained from all patients for inclusion in the study.

Conflict of Interest Tsung-Han Yang, Yu-Hsiang Chou, Woei-Yau Kao, and Shiou-Chi Cherng declare that they have no conflict of interest.

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