Kikuchi Disease Manifesting as Multifocal Lymphadenopathy and Splenomegaly: Ultrasonography, CT, and 18F-FDG PET/CT Findings Mimicking Lymphoma

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Kikuchi disease is a type of benign, self-limiting necrotizing lymphadenitis that occurs most commonly in young women and usually manifests as palpable cervical lymph nodes and fever. Patients with an unusual location of lymph node involvement can be misdiagnosed with malignant disease. Here, we report a case of Kikuchi disease in a 15-year-old girl presenting with persistent fever for 2 weeks. Imaging studies, including ultrasonography, CT, and 18F-fluorodeoxyglucose PET/CT, revealed splenomegaly and enlarged lymph nodes in the neck, axilla, abdomen, retroperitoneum, and inguinal region. Laparoscopic excision of the celiac lymph nodes confirmed histiocytic necrotizing lymphadenitis, also known as Kikuchi disease. Conservative treatment with corticosteroids improved the patient’s condition.

Index terms Kikuchi Disease; Histiocytic Necrotizing Lymphadenitis; Ultrasonography; Tomography, X-Ray Computed; Positron Emission Tomography Computed Tomography

INTRODUCTION

Kikuchi-Fujimoto disease (KFD), also known as necrotizing histiocytic lymphadenitis, is a rare self-limiting disease that was first described by Kikuchi (1) and Fujimoto et al.
Imaging Features of Kikuchi Disease Mimicking Lymphoma

(2). It usually occurs in Asian young women’s cervical lymph nodes accompanied by prolonged fever and uncommonly is found in the axillary or abdominal lymph nodes (3). Since KFD shows hypermetabolic features on ¹⁸F-fluorodeoxyglucose (FDG) PET/CT, particularly when presented as generalized lymphadenopathy, it can be confused with an infection or primary malignancy, such as lymphoma or metastatic lymphadenopathy (4). Herein, we report on a 15-year-old girl diagnosed with KFD presenting with prolonged fever, splenomegaly, and generalized lymph node enlargement that show bright uptake on ¹⁸F-FDG PET/CT, mimicking lymphoma.

CASE REPORT

Our Institutional Review Board approved this case report, and informed consent was waived because of the retrospective nature of this report. A 15-year-old girl presented with a 2-week history of fever, chills, and sweating. There was no headache, cough, abdominal pain, dysuria, vomiting, loose stools or weight loss and no previous history of similar complaints. Physical examination revealed no palpable mass in neck and no abnormalities in other parts of the body. The patient had a fever (38.7℃), but her other vital signs were within the normal range (pulse rate 90 beats/min, blood pressure 130/80 mm Hg, and respiratory rate 18 breaths/min). The patient’s hemoglobin count was 9.5 g/dL, which is lower than normal range, but leukocyte and platelet counts were within normal range (leukocyte count 4.43 × 10³/µL with distribution of lymphocyte 36.8%, monocyte 4.1%, and eosinophil 0.7% and platelet count 203 × 10³/µL). The patient’s serum electrolytes, liver function test, and routine urinalysis were also within normal limits. Lactate dehydrogenase, C-reactive protein, and erythrocyte sedimentation rate were elevated (413 IU/L, 0.890 mg/dL, and 76 mm/h, respectively). Serologic and microbiologic tests for tuberculosis, systemic lupus erythematosus, and infectious mononucleosis were all negative. Chest and abdominal plain radiographs were unremarkable. The abdominal ultrasonography (US) revealed mild splenomegaly, measuring 12 cm on the long axis and multiple enlarged homogeneously hypoechoic lymph nodes near the celiac axis and para-aortic space, measuring up to 1.3 cm on the short axis (Fig. 1A, B). The abdominal CT scan showed similar findings with US that the enlarged lymph nodes showed homogeneous density without internal necrotic foci, but with only mild perinodal infiltration. With the suspicion of lymphoma, the patient underwent ¹⁸F-FDG PET/CT that demonstrated an increased FDG uptake on the enlarged lymph nodes in both neck, both supravclavicular, both axillary, retro-pancreatic, mesenteric, left para-aortic, aortocaval, both iliac, and both inguinal areas, with a maximum standardized uptake value (SUVmax) of 10 (Fig. 1C). Although the lymph nodes in both neck also showed FDG uptake, those were not significantly large in size. Therefore, for accurate diagnosis, laparoscopic excision of the celiac lymph nodes and bone marrow biopsy were performed to exclude malignancy. Histopathologic evaluation of the resected lymph node revealed extensive necrosis, especially in the paracortical areas. There were collections of transformed lymphocytes, histiocytes, and plasmacytoid monocytes in the cortical areas around the germinal centers (Fig. 1D). In addition, immunohistochemical staining of the paraffin blocks revealed strong positivity for CD3 (Fig. 1E) and CD68, indicating a predominance of T lymphoid cells and histiocytes, and negative
results for CD20, CD79a, CD5, cyclin D1, BCL2, BCL6, CD10, C138, MUM-1, CD30, ALK, MPO, Ki-67, EBER, and AFB, consistent with histiocytic necrotizing lymphadenitis, also known as KFD (Fig. 1E). The bone marrow biopsy showed a normal complement of precursor cells with normal cellularity. After the administration of a low dose corticosteroid, the patient became afebrile and was discharged without any complications.

**DISCUSSION**

Typically, KFD is characterized by an acute or subacute febrile illness with regional lymphadenopathy. The most common site of lymphadenopathy is the neck, involving the posterior cervical triangle (99%), followed by the axilla (7%), inguinal region (6%), mesentery (2%), and retroperitoneal area (1%). Seventy-five percent of the patients with cervical lymphadenopathy show unilateral lymphadenopathy (5). The predominant symptom is fever (76%), the median duration of which is nine days. However, the clinical spectrum of KFD may vary and
thus, when the involved lymph nodes are located in unusual sites, diagnosis can be con-
founded and delayed. For example, the abdominal pain was the first symptom of KFD involv-
ing mesenteric lymph nodes, mimicking acute appendicitis or other causes of acute abdo-
men (6).

The common US findings of KFD are multiple conglomerated unilateral cervical lymph-
adenopathy showing perinodal fat swelling and even size distribution. Previous study sug-
gested lymph nodes in KFD have smaller size, less round, less heterogeneous echotexture,
more clustered feature and peripheral hyperechoic rim than those in lymphoma (7). In our 
case, the enlarged lymph nodes on abdominal US showed relatively round hypoechoic fea-
ture without definite evidence of hyperechoic rim and also were in unusual location for KFD.

The most common CT features of KFD are multiple, unilateral, homogeneous enlargement
of the cervical lymph nodes, frequently associated with perinodal infiltration (8). In addition,
the nodal necrosis appears as small eccentric foci with indistinct margins in the enlarged cer-
vical lymph nodes and shows a higher CT density than those seen in other diseases, such as tuberculous lymphadenitis, metastasis or lymphoma, which help in the differential diagnosis (9). The CT features of abdominal KFD were reported as the enlarged lymph nodes with marked perinodal infiltration with or without internal necrotic foci (6). However, sometimes, US and CT features of KFD are not characteristic, making a differential diagnosis challenging. Therefore, it was warned that nearly 30–40% of patients with KFD were initially misdiagnosed with malignant lymphoma and received unnecessary chemotherapy. In our case, lymphoma have been considered because the enlarged homogeneous lymph nodes with mild perinodal infiltration showed a bilateral and generalized distribution from the neck to the inguinal regions without nodal necrosis, accompanied by prolonged fever and mild splenomegaly.

18F-FDG PET/CT enables semi-quantitative analysis of lesions, usually by measuring the SUV and is known as an essential diagnostic and follow-up modality for malignant diseases (4). On the other hand, 18F-FDG uptake is nonspecific for some cancers because 18F-FDG avidity is due to increased glycolysis and glucose transporter activity. Thus, false-positive 18F-FDG uptakes have been reported even in benign lesions, including thyrotoxicosis, fat necrosis, tuberculosis, sarcoidosis, fungal infection, syphilis, infectious mononucleosis, and KFD (4). A recent study suggested that the SUVmax of lymph nodes was helpful for differentiating KFD from non-Hodgkin lymphoma (10); the highest SUVmax of KFD lymph nodes was significantly lower (8.4) than that of aggressive non-Hodgkin lymphoma (15.6). The SUVmax of our case was between the two values, making a differential diagnosis difficult.

For these reasons, the diagnosis of KFD is based on the histopathological evaluation of biopsied or excised lymph nodes. The characteristic histologic findings of KFD include patchy necrotizing features localized mainly in the paracortical areas of the involved lymph nodes (8). The necrotizing areas show abundant karyorrhectic debris and large numbers of different types of histiocytes at the margin. The immunophenotype of KFD typically consists of a predominance of T cells, among which CD8+ cells prevail over CD4+ cells (3, 8). The histopathological findings in our case were consistent with the characteristics of KFD and ruled out lymphoma. Once the diagnosis is confirmed histopathologically, conservative treatment with agents such as analgesics, antipyretics, and rest, usually improves the local or systemic symptoms. Occasionally, some patients require low dose steroid therapy (3).

In conclusion, KFD is a benign self-limiting disease with a good prognosis and thus, is possibly underdiagnosed. Rarely, it could mimic lymphoma when manifesting as the generalized involvement of lymphoid tissues. The pediatric radiologists should be aware of KFD when children and adolescents have persistent fever and lymphadenopathy, whether in the cervical or extra-cervical regions. Histopathologic diagnosis is often necessary when the differential diagnosis is not clear.

Author Contributions
Conceptualization, J.B.; investigation, H.M.; project administration, J.B.; supervision, J.B., L.S.W.; validation, L.E., L.S.W.; visualization, L.E.; writing—original draft, H.M.; and writing—review & editing, J.B., L.S.W.

Conflicts of Interest
The authors have no potential conflicts of interest to disclose.

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다발성 림프절염과 비장종대로 발현하여 림프종으로 오인된 기쿠치병의 초음파, CT, 18F-FDG PET/CT 소견

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기쿠치병은 주로 아시아에 거주하는 젊은 여성에서 경부 림프절 비대와 열을 주소로 나타나는 조직구 괴사성 림프절염이며 자연적으로 치유되는 양성질환이다. 기쿠치병이 전형적으로 발현하는 위치가 아닌 림프절에서 발생하면 진단이 어려워지고 악성 질환으로 오인되기도 한다. 저자들은 2주간 지속되는 발열을 주소로 내원하여 시행한 초음파와 CT, 18F-fluoro-deoxyglucose PET/CT에서 비장 종대와 경부, 엑라부, 복강, 후복강, 서해부 림프절 비대를 보여 림프종을 의심하였던 15세 여자 환아 증례를 보고한다. 복강 림프절 결제술로 기쿠치병을 진단하였다. 이후, 환자는 스테로이드로 보존적인 치료를 받고 발열 증상이 호전되어 퇴원하였다.

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