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Kikuchi - Fujimoto Disease Presenting with Abnormal Liver Function Test Results: Case Report

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Authors' contributions

This work was carried out in collaboration between all authors. Author YML wrote the draft of the manuscript. Authors YJC and YML managed the literature searches. Author AYK designed the figures, managed literature searches and contributed to the correction of the draft. Author SJJ provided the case, the figures and supervised the work. All authors read and approved the final manuscript.

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Case Study

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ABSTRACT

Kikuchi - Fujimoto disease (KFD) also called histiocytic necrotizing lymphadenitis, characterized by lymphadenopathy (0.5-4 cm) and pain for 1-3 weeks. It mainly occurs in the posterior cervical triangle of the neck. The cause of KFD is unknown. Although viral or autoimmune causes have been suggested, none have been confirmed. Accurate differential diagnosis to rule out other conditions such Kawasaki disease, tuberculosis, lymphoma or infectious mononucleosis must be performed. Thus, histological analysis is essential to accurately diagnose KFD. Although an increase in liver enzyme levels is rarely associated with KFD, it has been associated with systemic lupus erythematosus, which in turn is typically associated with abnormal liver function test results. Here, we report a case of KFD with elevated liver enzyme levels, and positive antinuclear antibody results in an 11-year-old girl with a 1-month history of a palpable lump on the left side of the neck.

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Keywords: Histiocytic necrotizing lymphadenitis; lupus erythematosus, systemic, abnormal liver function tests.

1. INTRODUCTION

Kikuchi - Fujimoto disease (KFD), also called histiocytic necrotizing lymphadenitis, was first described by Kikuchi and Fujimoto et al. in 1972. Since then, many cases have been reported worldwide, especially from Asian countries such as Japan, Korea, and Taiwan. Reportedly, KFD predominantly occurs in women younger than 30 years old (3-4:1), and is seldom reported to occur in children. The condition is a benign and self-limiting disease, of unknown etiology [1]. Several reports have suggested a possible association with viruses, although no study has definitively identified the causative agent. Some authors have suggested an autoimmune pathogenesis for KFD, as it is often associated with autoimmune hepatitis (AIH), Kawasaki disease, and systemic lupus erythematosus (SLE) [2]. Here, we report an 11-year-old girl who presented with elevated liver enzyme levels and positive antinuclear antibody (ANA) results and was diagnosed with KFD based on histological analysis of the needle biopsy on left neck lymph nodes. We also provide a brief literature review.

2. CASE REPORT

An 11-year-old girl was referred to the Pediatric Infectious Disease division of the Cha Bundang Medical Center with a 1-month history of a palpable lump on the left side of her neck. There was no specific medical or family history. The lump was slightly tender on palpation, but the patient exhibited no other symptoms. The patient was referred to the pediatric gastroenterology division because of her high aspartate aminotransferase (AST) and alanine aminotransferase (ALT) levels. When the external neck was examined, a lump approximately 3 cm x 3 cm x 3 cm was palpable, hard, fixed, and slightly bigger than that at the previous visit. Upon application of hard pressure, pain was observed but no sense of heat. Several larger lymph nodes around the lump were also noted. Around the tonsil, injection was shown, but overall no exudates, skin rash, nor periorbital edema were observed. No disease-specific findings were obtained from abdominal examinations, such as hepatomegaly, splenomegaly, and ascites. The day prior to her second visit to the hospital, she had a fever with a body axillary temperature of 38℃, abdominal pain with nausea, and a mild sore throat. The patient did not appear distressed but complained of mild fatigue. Body temperature did not decrease despite antipyretic use.

Biochemical tests showed increased aspartate aminotransferase (AST) and alanine aminotransferase (ALT) levels at 75 IU/L and 106 IU/L, respectively. Complete blood count (CBC) showed white blood cell (WBC) count at 4.12 x 10^3/UL with 36.0% segmented neutrophils, 55% lymphocytes, and 9% monocytes. Antistreptolysin O titer was positive, and mycoplasma pneumonia IgM was negative. C-reactive protein level was 0.18 mg/dL, but was within normal range. Erythrocyte sedimentation rate was slightly above normal level at 46 mm/h. Considering the possibility of infectious mononucleosis with viral or bacterial infection, additional tests were performed, including Epstein-Barr virus (EBV) polymerase chain reaction (PCR), cytomegalo virus (CMV) PCR, lactate dehydrogenase (LDH), abdomen ultrasonography, and r-glutamyl transpeptidase (r-GTP) and direct bilirubin level tests. The CBC, taken 3 days after admission, due to persistent fever with a body temperature >38℃ showed a WBC count of 3.96 x 10^3/UL 70.0% with segmented neutrophils, 24% lymphocyte, and 6% monocytes. Levels of AST, ALT, and LDH had increased further to 69 IU/L, 70 IU/L, and 1176 IU/L, respectively; Other liver function test results, including total bilirubin, direct bilirubin and r-GTP levels were within normal ranges. The results of the EBV PCR and CMV PCR, performed under suspicion of infectious mononucleosis, were negative. In addition, ANA testing showed weakly positive results, whereas anti-dsDNA, anti-neutrophil cytoplasmic antibody and anti-Sm tests gave negative results. Results of C3, C4, and rheumatoid factor (RF) test were all within normal range, at 113.00 mg/dL, at 23.40 mg/dL, and 17.31 IU/L, respectively.

Abdomen ultrasonography was performed to test for hepatitis, which revealed normal findings. Computed tomography (CT) of the neck revealed an oval-shaped, well-defined lump approximately 2.1 X 1.5 X 2.5 cm in size, no necrosis, and an enlarged lymph node in the left cervical chain. The results of neck ultrasonography (Fig. 1) performed on the day of admission revealed an increased number of lymph nodes. The lump had also increased by approximately 3.8 cm.

Finally, to test for definite diagnosis, we decided to perform a needle aspiration biopsy. We used an 18 G gun to obtain four biopsy samples from the most prominent visible lump, composed of many united left neck lymph nodes. Histological analysis of the biopsy specimen confirmed a diagnosis of KFD (Fig. 2). PCR performed for *Mycobacterium tuberculosis* in the same samples showed negative results.

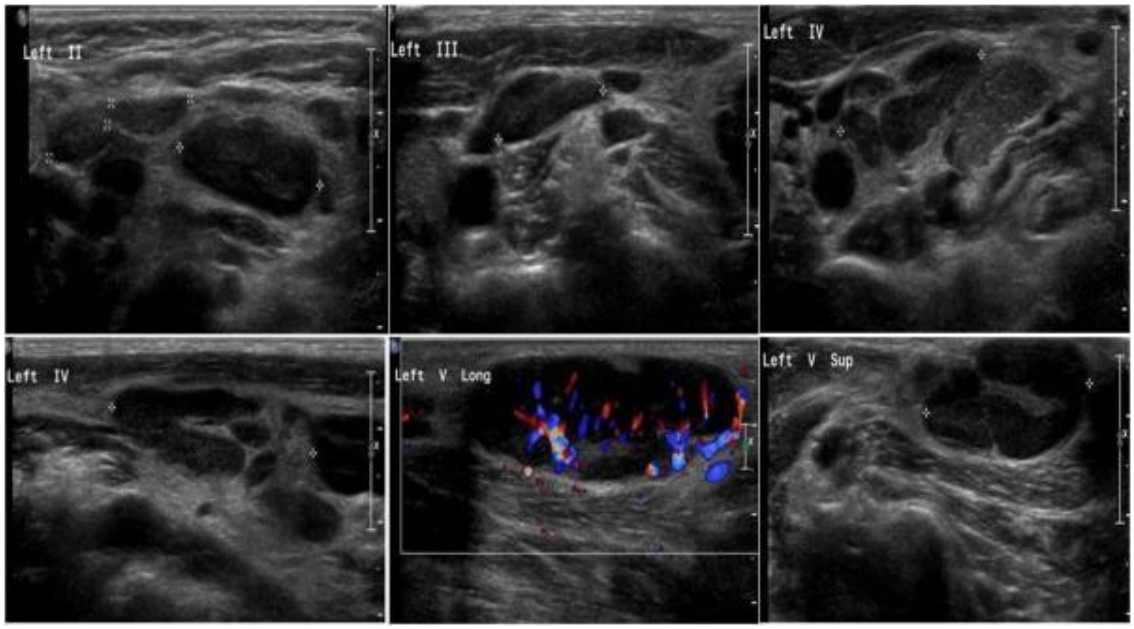

Fig. 1. Routine neck ultrasonography shows multiple enlarged lymph nodes along the left internal jugular chain (level II–V). The largest node at level V measures 3.8 cm and shows perinodal infiltration and increased vascularity. Well-preserved fatty hilum of multiple enlarged nodes is seen. Several small (less than 1 cm diameter) nodes are seen in the right internal jugular chain (level II–V). No perinodal infiltrations, intranodal necrosis, or abscesses are seen

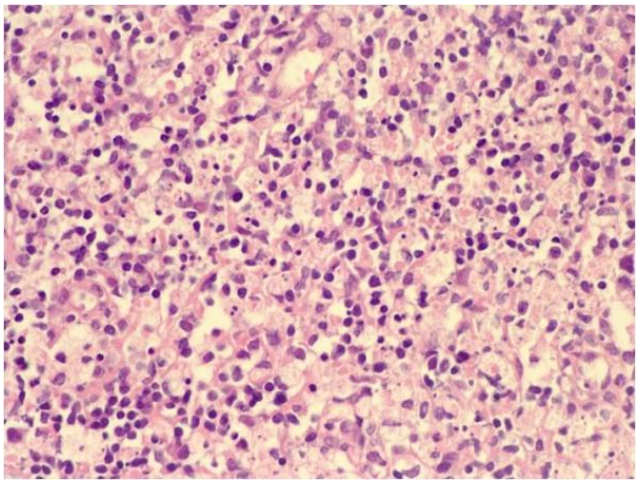

Fig. 2. The microphotograph shows mixed lymphoplasma cells and large number of pale-staining histiocytes among cellular debris and nuclear dust (Hematoxylin and eosin ×400). On histological findings, there were patchy areas of necrosis. The necrotic areas were composed of lymphoid cells in varying stage of maturation and sheets of proliferating histiocytes among karryorrhectic debris

During testing, the patient was allowed to take ibuprofen due to intermittent fever and H-2 receptor and dopamine antagonists for symptomatic treatment of intermittent abdominal pain. In the 2 days prior to discharge, she took 500 mg/day of combined non steroidal anti-inflammatory drug (naproxen) and esomeprazole and her symptoms improved. After confirming pathology results, the patient was discharged 6 days after admission. The patient continued to visit the Cha Bundang Medical Center as an outpatient for follow-up and medication maintenance. The lump size reduced, and the fever resolved.

3. DISCUSSION

Patients with KFD typically present with cervical lymphadenopathy, often accompanied by fever, sore throat, weight loss, chills, myalgias, arthralgias, splenomegaly, and skin rashes [3-6]. Although KFD was first described in Japanese patients, and a large number of cases have been described in Asian countries, few cases have been reported in Korean pediatric patients [1]. A 2007 review showed that females were affected twice as often as males; however, Korean pediatric data, show an equal distribution. Previous reports have suggested that the mean age of pediatric patients is 10±3.4 years, similar to our patient's age (11 years old). The cause of KFD is unknown and, although viral or autoimmune causes have been suggested, none have been confirmed [7]. We could not immediately rule out possibility of infectious mononucleosis in our case due to clinical features consistent with the condition, such as sore throat, abdominal pain, increased monocytes in CBC, and increased AST and ALT levels, but EBV serology/PCR and cytomegalovirus PCR results were negative. A meta-analysis revealed that the most suspected pathogen, EBV, was not any more likely to be associated with KFD than with normal controls, whereas Human herpes virus 8 positivity was more likely associated with KFD than with normal controls; however, further verification is necessary [8]. In patients with painful lymphadenopathy with or without fever, clinicians can exclude other diagnoses such as Kawasaki disease, tuberculosis, or lymphoma based on the node location, fever duration, laboratory studies, and patient age [3,6,9]. Unilateral cervical lymphadenopathy with a 2-3 cm diameter is typically seen in patients with KFD. Cervical involvement is the most common location, although, other lymph nodes, such as the axillary and abdominal nodes may be involved. Leukopenia, neutropenia, and lymphocytosis have been frequently reported in patients with KFD. Leukocytosis rarely occurs, and is seen in approximately 2-5% of cases. Our patient also showed leukopenia (WBC count: 36.0% segmented neutrophils, 55% lymphocytes, and 9% monocytes). Increases in liver enzyme levels are rarely seen in KFD patients [1,10]. Some cases if KFD with autoimmune hepatitis (AIH) have been reported. In such cases KFD was associated with SLE, which in turn can be associated with abnormal liver function test results. Thus, some authors have suggested that KFD may develop due to autoimmune dysfunction, since it is often associated with AIH, and SLE. Clear histologic differentiation between SLE and KFD is difficult, as classic findings are not always present, and pathologic results can be similar. In fact, a small percentage of pediatric KFD patients later develop SLE [2,7]. Our patient had a positive ANA test result. So it is clearly necessary for patients to be aware of the potential long term development of SLE. Histological analysis is essential to accurately diagnose KFD [9,11,12]. Early excisional biopsy or ultrasonography-guided needle biopsy can help minimize additional work-ups or unnecessary treatment [1,3,6,10]. Generally, KFD is self-limiting, resolves over 1-4 months, and has a recurrence rate around 3-4%. As a result, symptomatic and supportive treatments are typically adequate. Our patient fits this profile, completely recovering 3 months after presentation without medication except supportive treatment.

4. CONCLUSION

We report a case of KFD in a 11 years-old girl with abnormal liver function test results and positive ANA test results. Except for abnormal liver enzyme levels, the course of KFD was normal. However, it might progress to SLE, so long-term follow-up in our patient, and other similar cases, is recommended.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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