OLGU SUNUMU CASE REPORT

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Kikuchi-Fujimoto Disease: A Report of Four Cases and Review of Relevant Literature

Kikuchi-Fujimoto Hastalığı: Dört Olgu Raporu ve Literatüre Genel Bakış

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ABSTRACT Kikuchi-Fujimoto Disease (KFD) is a rare, benign disease of unknown etiology characterized by cervical lymphadenopathy and fever. We herein report 4 cases, 3 women and a man, aged 25-45 years. The clinical and laboratory findings of the cases indicated autoimmune diseases and hematological malignancies. The histopathological examination clarified the diagnosis, despite the nonspecific character of the clinical presentation. Otolaryngologists should be familiar with this rare disease and consider the disease in differential diagnosis in order to provide full recovery and avoid further examinations and unnecessary interventions.

Keywords: Histiocytic necrotizing lymphadenitis; lymphatic diseases; Kikuchi-Fujimoto disease; cervical lymphadenopathy

ÖZET Kikuchi-Fujimoto hastalığı (KFH) etiyolojisi bilinmeyen, nadir görülen ve servikal lenfadenopati ve ateş ile seyreden benign bir hastalıktır. Biz bu makalede yaşları 25-45 arasında olan 3 kadın ve 1 erkek, 4 olguyu inceledik. Olguların klinik ve laboratuar bulguları otoimmun hastalıkları ve hematolojik maligniteleri işaret etmekteydi. Nonspesifik klinik prezentasyona rağmen, tüm olgularda tanı patolojik inceleme ile netleştirildi. Uygun tedavi yaklaşımı ile tam kür sağlamak, gereksiz ileri inceleme ve tedavi yaklaşımlarından hastayı korumak amacı ile otolaringologlar bu nadir hastalığa aşina olmalı ve ayırıcı tanıda akılda tutmalıdır.

Anahtar Kelimeler: Histiositik nekrotizan lenfadenit; lenfatik hastalıklar; Kikuchi-Fujimoto hastalığı; servikal lenfadenopati

Kikuchi-Fujimoto Disease (KFD) is a benign form of necrotizing histiocytic lymphadenitis with unknown etiology. Kikuchi-Fujimoto Disease usually presents with fever and cervical lymphadenopathy (LAP).[1] Disease can be associated with other systemic manifestations such as arthralgia, fatigue, weight loss, hepatosplenomegaly and heterogeneous skin rash.[2] Considering KFD in the differential diagnosis prevents the patients from aggressive treatment hence the symptomatology is similar with malign and autoimmune diseases. There is no specific laboratory test for the disease, however an increase in erythrocyte sedimentation rate and lactate dehydrogenase levels, leukopenia, atypical lymphocytosis have been observed in most cases.[3] With these findings, KFD often confused with lymphoma thus histopathological examination is crucial in diagnosis.

In this article, we presented 4 cases with KFD, discussed differential diagnosis and treatment options of KFD.

CASE REPORTS

CASE 1

Twenty seven years old male patient admitted to our clinic complaining of night sweats, fever, weakness and swelling on the right sight of the neck for more than 1 month. The symptoms did not relieve after multiple courses of antibiotic treatment. There were multiple, fixed, palpable LAPs in the neck. Neck computed tomography (CT) showed multiple LAPs located bilaterally around the upper third of the internal jugular vein (Figure 1). Leukopenia (3.8/mm^3) and lymphocytosis (56%) were observed in the complete blood count. The patient was referred to the hematology department. Peripheral blood smear examination was normal. Bone marrow biopsy results were normocellular. Excisional biopsy was performed for diagnosis. Histopathologic findings were reported as histiocytic necrotizing lymphadenitis (Figure 2). The symptoms relieved after excision. Patient was asymptomatic during the year following excision.

CASE 2

Forty five year old female patient admitted to our clinic complaining of fatigue and neck mass, present for more than 2 weeks. Despite antibiotic therapy neck mass was persistent. Fixed and painful LAP, which was approximately at the diameter of 3 cm, detected in the physical examination of the neck. Ultrasonographic (USG) examination revealed conglomerated lymphs nodes which had a 34×26 mm diameter in its largest size in bilateral upper jugular chain. Fine-needle aspiration biopsy (FNA) results showed atypical lymphocytes for which excisional biopsy was required. Pathological examination was reported as histiocytic necrotizing lymphadenitis. After excision, the symptoms of the patient relieved but widespread artralgia and myalgia persisted. The patient was consulted to rheumatology department. Investigations did not reveal any evidence of additional pathology. Her complaints resolved completely after two months of non-steroidal anti-inflammatory drug (NSAID) administration.

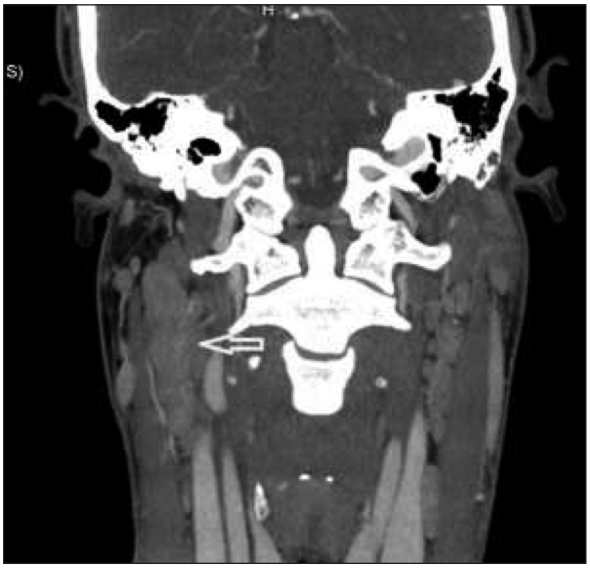

FIGURE 1: The right jugular chain lymph nodes of neck in coronal CT sections arrow (Case-1).

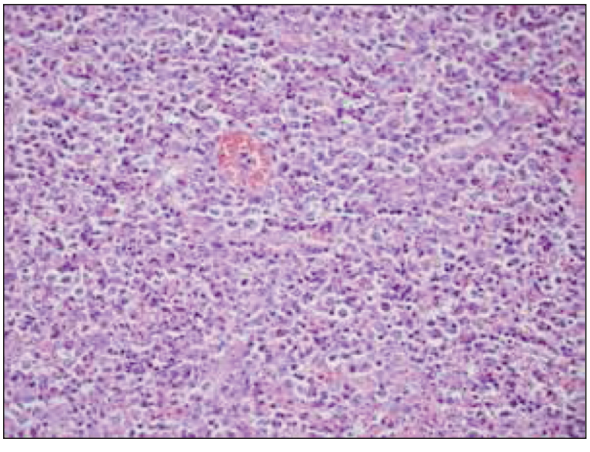

FIGURE 2: Large amount of apoptotic bodies, necrotic areas and some phagocytic histiocytes with characteristic crescentic nucleus (HE×20) (Case-1).

CASE 3

Twenty-five-year-old female patient presented with swelling on the left side of the neck. Physical examination revealed a hard, painful, LAP which was approximately 2 cm in diameter in left upper jugular chain. Tru-cut biopsy was performed in another medical center and was reported as Kikuchi lymphadenitis. We had reexamined the specimen histopathologically; T lymphocytes, histiocytes, as well as areas with plasma cell necrosis were observed

and diagnosis of Kikuchi lymphadenitis was confirmed. Patient did not accept the excision. She was symptom free after 3 month NSAID medication. After one-year follow up patient is asymptomatic.

CASE 4

Thirty-three-year-old female patient presented with swelling on the neck for more than 2 months. In the physical examination painful LAP was detected in both right and left anterior jugular chain. The lymphadenopathy was measured as 21×7 mm in it its largest diameter at the USG. Excisional biopsy was performed to obtain certain diagnosis. Pathological examination was reported as histiocytic necrotizing lymphadenitis (Figure 3). The patient had no systemic symptoms nevertheless she was given NSAID treatment to control possible multiple foci in the neck. Patient was symptom free after 6 months.

Informed consents have been obtained from the patients for the use of their data for scientific purposes.

DISCUSSION

Two pathologists named Kikuchi and Fujimoto first described this disease in 1972.[1] Young Asian women aged around 30 are mostly affected from KFD.[1,2] We reported 3 women and 1 man, aged 25-45 years. The age and sex distrubition of this patient series is similar with literature.[2]

Kikuchi-Fujimoto Disease presents itself with fever and painful cervical LAP in its initial stage. Küçükardalı et al. published a series of 244 cases. They observed LAP in cervical region as the most common symptom in 100% of 244 patients.[1] The most common systemic symptom is fever, which is observed in 35% of cases. In our 4 cases, 1 patient (25%) had fever and night sweats. Hepatosplenomegaly is observed in 10% of cases and erythematous rash described in 3% of cases.[1] Cheng et al published a KFD series with 195 patients, in 183 (94%) of whom the disease resolved spontaneously while recurrence occurred in 14 cases (15%) during 6 months following diagnosis.[3] We did not observe any recurrence during our control period which was at least 6 months.

There is no specific laboratory test for the disease but leukopenia, atypical lymphocytosis, increase in the sedimentation rate and LDH levels are the most common laboratory findings.[3] We observed leukopenia and lymphocytosis in one of 4 cases. In this particular case, the atypical laboratory and clinical findings directed us to perform a redundant bone marrow biopsy. We did not perform any further examination for the following cases considering KFD in the differential diagnosis. Majority of literature reports enounce that KFD can be confused with hematologic malignancies, infectious diseases and some autoimmune diseases because of the similar clinical manifestation Particularly non-Hodgkin's lymphomas, tuberculosis, toxoplasmosis, yersinia, cat-scratch disease, herpes, CMV and HIV virus infections are the other diseases to be considered in differential diagnosis.[1,2] Etiology of KFD is unknown; autoimmune causes have been discussed in the literature but none of them is clearly identified.[4] Another causative mechanism might be excessive response of T cells and histiocytes to some infectious agents such as *Toxoplasma gondii*, EBV, human herpes virus, parvovirus 6-7.[4]

KFD may be associated with certain autoimmune diseases, most commonly with systemic lupus erythematosus. Paradela et al observed 27 patients of KFD, 9 of whom were diagnosed as systemic lupus erythematosus (SLE).[5] They suggested

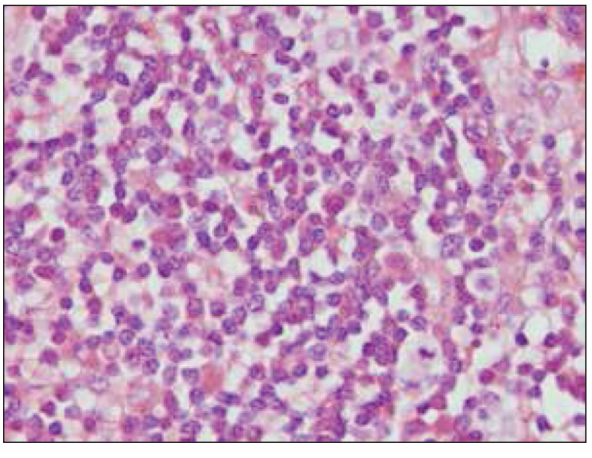

FIGURE 3: Lymphocytes, histiocytes as well as blast and plasmacytoid monocytes are seen, necrosis and apoptosis is not clear; typical for KFD's initial phase (HE× 40) (Case-4).

the investigation of SLE is essential especially in cases with skin rashes.[5] One of our patients suffered from muscle and joint pain after treatment. There was not any associated autoimmune disease and the symptoms relieved after 2 months of NSAID treatment. Patients with KFD who have recurrences or atypical symptoms should be followed closely due to their increased risk of SLE.[5]

In a study of 44 patients, Tong and colleagues detected a 56% of false positive and 37.5% of false negative diagnostic value of fine needle aspiration biopsy (FNAB).[6] Definitive diagnosis should be based on excisional biopsy and histopathological examination.

Since it is a self-limiting benign disease, observation of patient is considered to be the best option. Majority of patients present with spontaneous resolution over an average of 3 months (1-24 months).[1] NSAID drugs are first-line treatment option for symptomatic patients. Steroid treatment (0,025 to 1 mg/kg/day, methylprednisolone) might be an option for patients with systemic diseases or for the ones unresponsive to with NSAIDs.[7] Further treatment options are higher dose steroids or intravenous immunoglobulin (IVIG) which is necessary in extremely rare occasions.[8] Another treatment option is chloroquine treatment suggested by Rezai and colleagues. They reported a recurrence rate which is approximately 4% with chloroquine treatment.[9] In a 800 cases review published by Bogusz and Bhargava, recurrence was detected in 65 patients which is approximately 8%.[10] In our series, 3 patient treated by surgical excision and 1 patient treated with NSAID. All of our patients have been in remission for at least 6 months.

KFD is a self-limited benign disease. It should be kept in mind in differential diagnosis of malignancies, infectious or autoimmune diseases in order to avoid further unnecessary examinations and aggressive treatments.

Source of Finance

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Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: *Elif Dağlı, Kadriye Şerife Uğur;* ***Design:*** *Elif Dağlı, Kadriye Şerife Uğur, Hayriye Ergin Akkoz;* ***Control/Supervision:*** *Elif Dağlı, Kadriye Şerife Uğur;* ***Data Collection and/or Processing:*** *Elif Dağlı, Hayriye Ergin Akkoz;* ***Analysis and/or Interpretation:*** *Elif Dağlı, Kadriye Şerife Uğur, Hayriye Ergin Akkoz;* ***Literature Review:*** *Elif Dağlı;* ***Writing the Article:*** *Elif Dağlı, Kadriye Şerife Uğur, Hayriye Ergin Akkoz;* ***Critical Review:*** *Kadriye Şerife Uğur;* ***References and Fundings:*** *Kadriye Şerife Uğur, Hayriye Ergin Akkoz;* ***Materials:*** *Elif Dağlı, Kadriye Şerife Uğur.*

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