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CASE REPORT

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Kikuchi-Fujimoto disease: a case report

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Abstract Kikuchi-Fujimoto disease is a rare benign cervical lymphadenopathy, which often affects young adult women. Its etiology and pathogenesis are unknown. We present the case of Kikuchi-Fujimoto disease in the Polish population and analyse the difficulties in differentiating this disease from the systemic lupus erythematosus.

Keywords Kikuchi-Fujimoto disease · Systemic lupus erythematosus

Introduction

Kikuchi-Fujimoto disease is a benign self-limiting cervical lymphadenopathy of unknown etiology first described in Japan in 1972 [1–7]. It often affects young adult women [2–5, 7, 8] sometimes as a secondary effect of viral infection [Epstein-Barr virus (EBV)], human T cell lymphotropic virus, human cytomegalovirus (CMV), human herpes virus-6 and others] [1–3, 6].

Pathogenesis of this disease is still not fully understood. It is supposed that the primary event may be the activation of T lymphocytes and histiocytes. Proliferating T cells enter the cycle of apoptosis, which may form the areas of necrosis in lymph nodes and then the cellular debris is removed by histiocytes [2, 6, 8].

Clinically, an unilateral cervical lymphadenopathy in Kikuchi-Fujimoto disease is observed [1, 2, 6–8], but enlargement of lymph nodes in other regions may also be seen [5, 6, 8] sometimes in the form of generalized lymphadenopathy [1, 5, 9]. The affected lymph nodes vary in size from 0.5 to 7 cm of diameter with median size of 1.5 cm [5], and may be tender or painful [2, 5, 6, 8]. The other, most common clinical symptoms of this disease are low-grade fever [1, 2, 5–8], arthralgia and variety of skin rashes, which usually precede lymphadenopathy [1, 2]. However, non-specific symptoms, e.g. weakness, night sweats, weight loss, diarrhoea, anorexia, chills, nausea, vomiting, chest and abdominal pain have also been reported [1, 2, 6]. Sometimes splenomegaly and hepatomegaly are encountered [1, 2]. Laboratory findings are not specific including elevated ESR, leukopenia with mild lymphocytosis and atypical lymphocytes [1, 2, 5–8]. Moreover, in less than 5% of cases leukocytosis is found [5, 9]. The Kikuchi-Fujimoto disease tends to resolve spontaneously within 1 week to 3 years [6, 7] but it may also recur in about 3% of cases [2, 5, 9].

The aim of the present study is the presentation of Kikuchi-Fujimoto disease case that has occurred in the Polish population as well as the difficulties in differentiating this disease from the systemic lupus erythematosus (SLE). The existing probability, that the ancestors of the affected person were Tartars dwelling the Polish territory in the past ages let us understand better the fact of recognizing this disease in Poland.

Case report

A 50-year-old female with Raynaud phenomenon, xerostomia, symmetrical joint and muscle pain, mild dysphagia and fever of 6-month duration was admitted to the medical ward. She also occasionally suffered from severe headache. Clinical examination revealed skin rashes, and symmetrical arthritis affecting small joints and cervical lymphadenopathy localized in right posterior triangle (the lymph node diameter was about 3 cm). Other enlarged lymph nodes were also found and localized at the left mandibular and right axillary region. All of them were solid and painful.

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Laboratory examinations showed—HCT 35.4%; HB 11.2 g%; trombocyte count 420×10^9 cells/L; WBC 3.7×10^9 cells/L with 80% neutrophils, 15% lymphocytes, 4% monocytes, 1% eosinophils. The ESR was 52 mm after the first hour. Elevated levels of acute phase protein i.e. C-reactive protein, alpha-antitrypsin, ceruloplasmin, and fibrinogen were observed. The serum iron concentration was markedly decreased (16 μg/dL). Slightly elevated polyclonal IgG level (2294 mg/dL) and positive rheumatoid factor were noted. Antinuclear antibody test (ANA, HEp2 test) was positive. The remaining autoantibodies tested such as anti-DNA, AMA, APCA, ASMA, LKM, pANCA and cANCA were negative. Bacteriological analysis of blood, urea and stool did not reveal any pathogenic agents. The Mantoux test using ten units of PPD was negative. Serological examination showed positive CMV IgG antibody and Chlamydia IgG antibody, whereas CMV IgM antibody, Borelia IgG and EBV IgG tests were negative. Serum concentration of complement factor—C3 was 125 mg/dL (normal limit: 70–120 mg/dL)

Lymph node microscopic examination showed large zones of coagulative necrosis in paracortical areas with karyorrhexis of the necrotic cells (Fig. 1). Necrosis was present within blood vessel walls with mononuclear cell infiltrations and fibrin deposits in the lumen (Fig. 2). Inconspicuous germinal centres with activated lymphocytes, histiocytes and occasionally plasmocytoid monocytes were found close to the necrotic areas of lymph node. Single granulocytes were observed only within the lymph node capsule and perinodular tissues. A Kikuchi-Fujimoto necrotizing lymphadenitis was diagnosed.

The patient was treated with non-steroid anti-inflammatory drugs, co-trimoxazole (1.92 g/day p.o., as an average dosage accepted in Poland), and prednisolone (0.02 g/day p.o.) with improvement after 2 weeks. She had no fever, arthritis, skin rashes and enlarged lymph nodes subsided.

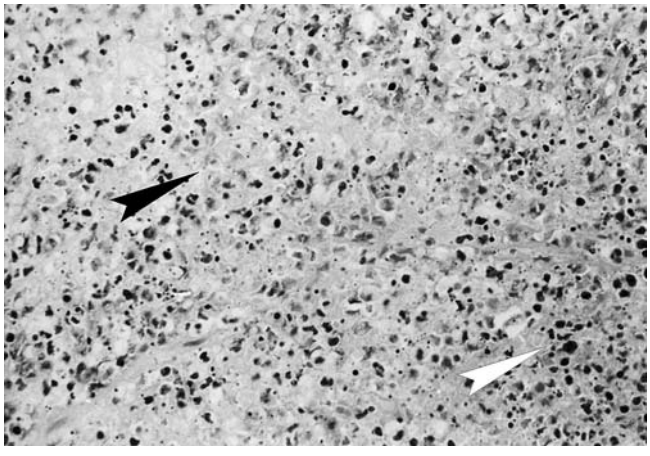

Fig. 1 Necrotic area without a polymorphonuclear leukocyte in the lymph node (➤). Karryorrhectic debris with histiocytes, monocytes and lymphoid cells (▷). H & E, 280 times

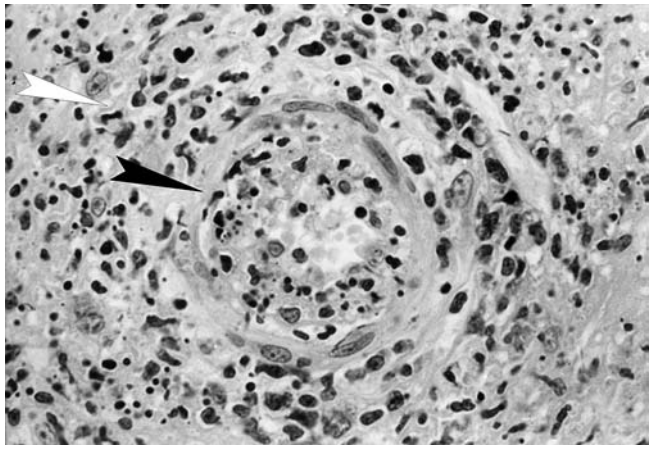

Fig. 2 Necrosis of the blood vessel walls with mononuclear infiltrations (➤). Histiocytes and plasmacytoid monocytes in the necrotic area around the blood vessel (▷). H & E, 330 times

Discussion

Kikuchi-Fujimoto disease was regarded to be very rare in non-Asian countries but it was reported in patients from Germany, Italy, Spain, Iran, the United States of America [2]. The patients of non Asian origin with Kikuchi-Fujimoto disease have recently been described in Greece, Portugal and Czech Republic [2, 10, 11] indicating a world wide geographical distribution of this disease.

In our case the diagnosis of Kikuchi-Fujimoto disease was based on histopathological examination of the lymph node (Figs. 1, 2). The microscopic picture was characterized by presence of coagulative necrosis with the proliferation of histiocytes without granulocytic infiltration. Such histological picture (Fig. 2) was typical enough to resign from carrying out any additional immunocytochemical tests. The presence of necrosis, karyorrhexis, and cellular debris (Fig. 1) enabled to recognize the necrotizing type of Kikuchi-Fujimoto disease [1, 2, 5, 7, 8]. The remaining histopathological types of the disease include: proliferative type with the presence of lymphocyte, immunoblasts and histiocytes infiltration with the coexisting lack of coagulative necrosis as well as the xanthomatous type characterized by the presence of foamy histiocytes [4, 5, 9]. Presumably they may form the following stages of the disease progression ranging from the proliferative type, through the necrotizing to the xanthomatous one [5, 9].

The lymph node evaluation let us exclude other diseases such as Kimura, Kawasaki or lymphatic system proliferating disorders as well as neoplastic metastases in this case [1, 2, 5, 8, 9]. Bacteriological analysis did not reveal any infective agents and Borelia IgG, CMV IgM, EBV IgG tests in serum were negative, whereas serological examination showed positive CMV IgG antibody and Chlamydia IgG antibody in the case under consideration. As CMV IgM and EBV IgG serological tests were negative, PCR analysis was not performed because

it is applied when false-positive results in serological tests are suspected [12].

A special attention should be paid to the differentiation between the Kikuchi-Fujimoto disease and lymphadenitis accompanying SLE [1–9]. The differentiating diagnosis of the Kikuchi-Fujimoto disease and SLE in this case has proved to be very difficult. It should be taken into account that the necrosis areas similar to those seen in the second type of Kikuchi-Fujimoto disease have been frequently found in the histopathological evaluation of SLE-related lymphadenopathy [3, 4, 7]. The diagnosis of SLE can be supported by the relatively great number of plasma cells, as well as hematoxyphilic bodies, DNA deposits in the vascular walls, neutrophilic infiltrations and the presence of diffuse a cellular coagulative necrosis [1, 3–5, 7]. It is worth noticing that the immunophenotype of the cells found in the SLE-related lymphadenopathy affected nodes can be similar to the one found in patients with the third histopathological type of Kikuchi-Fujimoto disease [5].

The existing similarities of the nodes histopathological picture regarding both described disorders may suggest the presence of pathogenetic analogies resulting from the immunological overreactivity against undetermined etiological factors [2, 7]. It should be noted that the cases of the Kikuchi-Fujimoto disease with the presence of ANA, anti-DNA and anti-U1-RNP antibodies were described [7]. In our case of Kikuchi-Fujimoto disease ANA antibodies were found.

Non specific clinical symptoms characteristic for both diseases such as mild fever, arthralgia, myalgia and skin rashes coexisting with lymphadenitis with the eventual existence of auto-antibodies cause that in many cases the diagnosis of SLE is made simultaneously or immediately after the recognition of the Kikuchi-Fujimoto disease [4, 5, 7]. On the other hand it is known that such association of phenomena occurs only in small percentage of cases of Kikuchi-Fujimoto disease [3].

It should be noticed that in the presented case the therapy resulted in evident subjective and objective improvement. The fever decrease, relief of the joint pains, skin changes disappearance and considerable diminishing of the lymph nodes sizes were observed.

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