

## ORIGINAL ARTICLE

# Kikuchi-Fujimoto disease and systemic lupus erythematosus – an enigmatic association for clinicians and pathologists: Case report and short literature review

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## ABSTRACT

Kikuchi-Fujimoto disease or histiocytic necrotizing lymphadenitis is a benign condition of the lymphatic tissue whose cause has not been fully elucidated. Although it has been thought that various viral infections are involved in the onset of the disease, its immunological characteristics expressed by the proliferation of cytotoxic CD8-positive T lymphocytes and histiocytic phagocytosis place it at the border of autoimmunity. Sharing immunological mechanisms, clinical manifestations, and epidemiological data (both are described in young women) with systemic lupus erythematosus (SLE), the association of the two pathologies represents a challenge for both clinicians and pathologists.

We present the case of a young woman with SLE with immunological, haematological and articular involvement, who associates a few months after diagnosis the significant swelling of the submandibular glands and latero-cervical lymphadenopathy. Histopathological and immunohistochemical examinations subsequently certify the diagnosis of histiocytic necrotizing lymphadenitis associated with the autoimmune disease.

**KEYWORDS:** Kikuchi-Fujimoto disease, systemic lupus erythematosus, submandibular glands enlargement, lymphadenitis.

## INTRODUCTION

Kikuchi-Fujimoto disease (KFD), also known as histiocytic necrotizing lymphadenitis, first described in 1972, represents a rare, benign and self-limiting disorder which affects predominantly young Asiatic women, but it can affect both genders and any race<sup>1</sup>. The etiology of the disease is not yet elucidated. There are two theories regarding the etiology of KFD, the first one involving microbial or viral infections that trigger a cytotoxic T cell-mediated immune response

and the second one assuming an autoimmune cause<sup>2</sup>. Although KFD can be associated with various autoimmune diseases, such as Sjogren’s syndrome, rheumatoid arthritis, Wegener’s granulomatosis, or Still’s disease, systemic lupus erythematosus (SLE) is the most common autoimmune condition associated with it<sup>3</sup>.

The most common clinical presentation of Kikuchi-Fujimoto disease is fever accompanied by unilateral or bilateral cervical lymphadenopathy. Generalized lymphadenopathy may be seen in 1-22% of cases<sup>2</sup>. Systemic manifestations rep-

resented by weight loss, nausea, vomiting, headache, weakness and arthralgia may occur<sup>4</sup>. In 40% of the cases, nonspecific skin and mucosal ulcerations may be present<sup>2</sup>. Hepatomegaly and splenomegaly can also be present in 5% of the cases<sup>4</sup>. Usually, the symptoms of KFD last one to four months and the recurrence rate is about 3-4%. Regarding laboratory findings, they most often indicate leukopenia. The diagnosis of KFD is a histopathological one, following the microscopic and immunohistochemical findings of the lymph nodes after the excisional biopsy<sup>3</sup>.

No specific treatment is available yet, but analgesics, antipyretics and corticosteroids represent the supportive treatment of the KFD. For non-responsive cases, treatment with immunoglobulins or with hydroxychloroquine can be considered<sup>5</sup>.

## CASE REPORT

We present the case of a 20-year-old female with systemic lupus erythematosus (SLE) under treatment with hydroxychloroquine and corticosteroids for immunological, haematological and articular involvement, who addressed the ENT Department for painful bilateral swelling of the submandibular glands, latero-cervical lymphadenopathy and xerostomia.

Two months before the presentation she was admitted in another medical unit for fever (40<sup>o</sup> C), headache, muscle pain and night sweats without any response to antibiotics and NSAIDs. At that time, blood tests revealed severe leukopenia (WBC-2300/mcL); normocytic, hyporegenerative anemia (Hb - 9.1 g/dl); high level of ferritin (1800 mcg/ml); high levels of alkaline phosphatase (ALP) and lactate dehydrogenase (LDH - 1600 U/L); hepatic cytolysis (elevated transaminases levels four times the normal value). The ionogram, the lipid panel and the folic acid, vitamin B12 and TSH levels were normal. Tests of renal function showed no modifications. In addition, multiple bacteriological and viral tests (Epstein-Barr virus (EBV), Cytomegalovirus (CMV), Rubella, HIV) were negative. Immunological assays were also performed, showing positive antinuclear antibodies and anti-double-stranded DNA (anti-dsDNA) antibody, positive antiphospholipid antibodies and lupus anticoagulant. Also, the Coombs test for Immunoglobulin G (IgG) and C3 was positive. The analysis of the smear revealed Howell-Jolly bodies. Hematologic tests (bone marrow aspiration smear, immunophenotyping of the bone marrow aspiration and bone marrow biopsy) did not show any evidence of hematologic malignancies.

Following the above-mentioned investigations, the diagnosis of SLE with immunological and haematological manifestations was established and the treatment with prednisone (60 mg/day) and hydroxychloroquine (400 mg/day) was initiated. Under this therapeutic regimen, her evolution was favourable and the blood count returned to normal.

The patient was subsequently admitted to the Rheumatology Department for further investigations, treatment review and disease monitoring. Blood tests (Table 1) and investigations supported the diagnosis of SLE with immunological (positive antinuclear antibodies - anti-Ro/SSA and anti-La/SSB antibodies, anti-dsDNA antibodies, and anti-Smith antibodies) and haematological (leukopenia) manifestations. Antiphospholipid syndrome (APS) was also observed, defined by the presence of antibeta-2 glycoprotein I antibodies, anticardiolipin antibodies and lupus anticoagulants (LA), but without the presence of any thrombotic event to date. It was decided to gradually reduce the dose of cortisone to the minimum required dose.

Physical exam performed on the first day of hospitalization in the ENT Department revealed painful symmetrical swelling of the submandibular glands (Figure 1), with firm strong consistency, mobile on the superficial planes; intact overlying skin tissue with no signs of inflammation and multiple bilateral, mobile and painless laterocervical lymph nodes. Respiratory, cardiovascular and abdominal examinations were within normal parameters. The patient admitted that she observed a progressive enlargement of the submandibular glands after the cortisone dose was reduced.

Laboratory tests results, summarized in Table 2 and Table 3, showed lymphocytopenia, neutrophilia and inflammation (high levels of C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR)). The urine sediment analysis was normal. Serological tests for CMV, EBV, Rubella, HIV, syphilis, toxoplasmosis and toxocarid were all negative. Also, the interferon-gamma release assay for tuberculosis screening was negative. Physical findings and laboratory findings did not suggest any infectious etiology.

Ultrasound of the submandibular glands (Figure 2) showed homogeneous, symmetrical enlargement of the submandibular glands with a disorganized architectural structure. No signs of abscesses or calcifications were visible on the ultrasonography at the moment of examination.

Initially, the presence of Sjogren's syndrome was suspected, but the Schirmer test and the specific antibodies (anti-Ro, anti-La) were all nega-

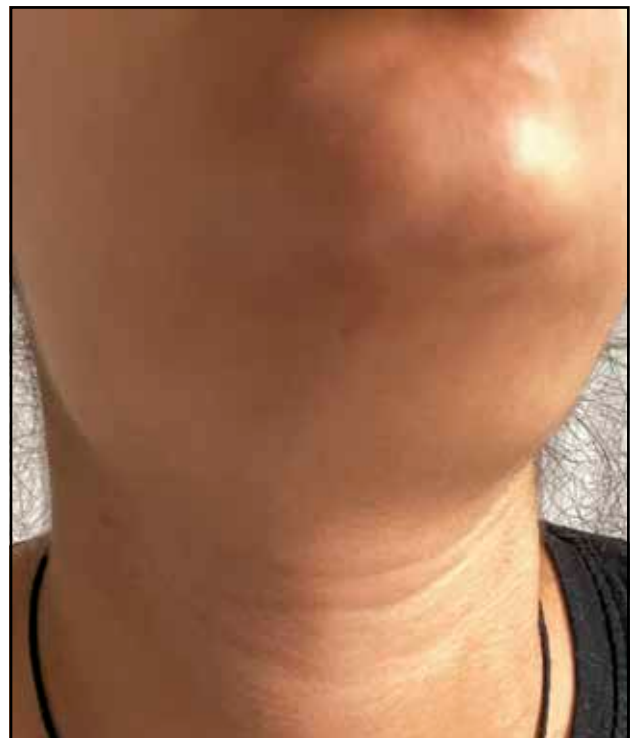
**Table 1. Immunologic tests results.**

	Value	Normal value (reference range)	Unit of measurement
Anti-double-stranded DNA antibody (anti-dsDNA antibody)	<25	<25	U/ml
Antibeta-2 glycoprotein I antibodies - IgG	64.8	negative < 5	U/ml
Antibeta-2 glycoprotein I antibodies - IgM	8.4	negative < 5	U/ml
Anticardiolipin antibody IgG	51.2	normal < 10	GPL-U/ml
Anticardiolipin antibody IgM	7.5	normal < 7	MPL-U/ml
Anti-Nuclear antibody (ANA)	4.3	negative < 1.0	Index
Anti-Smith antibody (anti-Sm antibody)	20.9	normal <15	U/ml
Anti-Ro/SSA antibody	3.5	normal <15	U/ml
Anti-La/SSB antibody	<0.1	normal <15	U/ml
Lupus anticoagulants (LA)			
- LA1/LA2	1.6	1.01 – 1.41	
- LA1	45.6	30.40 – 45.30	s
- LA2	28.40	27.70 – 33.50	s

tive. Moreover, the histopathological result of the biopsy performed on the minor salivary glands was “uncertain for a salivary component of Sjogren’s syndrome.”

The head and neck CT scan with contrast described an enlargement of the submandibular glands and multiple homogenous laterocervical lymphadenopathies (of maximum 12/17 mm) (Figure 3). In addition, the thoracic-abdominal-pelvic contrast-enhanced CT scan pointed out: homogenous hepatomegaly, non-homogenous splenomegaly and the presence of multiple splenic nodules less than 1 cm in diameter. Also, a small hilar hepatic lymphadenopathy and a thin blade of pelvic ascitic fluid were visible.

During hospitalization, the patient received hydrocortisone hemisuccinate (200 mg/day) and continued taking hydroxychloroquine (400 mg/day) along with symptomatic treatment. Despite this treatment, the patient’s general condition did not improve after 5 days of hospitalization. Moreover, she started accusing headache, arthralgia and myalgia of the lower limbs. In this case, it was decided to replace the hydrocortisone hemisuccinate with methylprednisolone

**Figure 1.** Bilateral swelling of the submandibular glands.

pulse therapy (250 mg/day), under which the evolution of the patient was favourable.

For a precise diagnosis, an excisional biopsy of two laterocervical lymph nodes was made (Figure 4).

Histological findings indicated extensive areas of necrosis surrounded by histiocytes, fibrinous exudate without neutrophils, karyorrhexis, reactive follicular hyperplasia and the presence of tingling bodies (Figure 5).

Immunohistochemical assays showed: CD3 evi-

dencing multiple T-cells, predominantly CD8+, but also CD4+, CD68 co-expressing myeloperoxidase (MPO) positive histiocytes, CD123 highlighting numerous plasmacytoid dendritic cells and CD20 indicating the presence of B lymphoid follicles (Figure 6).

The pathologist's report stated that these findings (histological and immunohistochemical) in association with SLE confirmed the diagnosis of KFD, and that the salivary gland involvement was

**Table 2. Usual laboratory tests.**

	Value	Normal value (reference range)	Unit of measurement
Hemoglobin	12.1	11.6 - 15.5	g/dL
Hematocrit	37.9	33.5 - 46	%
Leukocytes	3.94*10 <sup>3</sup>	3.5 - 10*10 <sup>3</sup>	μL
Lymphocytes	0.43*10 <sup>3</sup>	1 - 4.8*10 <sup>3</sup>	μL
Lymphocytes %	10.9 %	17 - 49	%
Neutrophils	7.83*10 <sup>3</sup>	1.7 - 7.7*10 <sup>3</sup>	μL
Neutrophils %	85.8%	35 - 75	%
Erythrocyte Sedimentation Rate (ESR)	52	2 - 20	mm/h
C-reactive protein (CRP)	5.50	0 - 5	mg/L
Lactate dehydrogenases (LDH)	447.00	105 - 247	U/L
D-dimer	1544	<0.55	mg/L
Ferritin	422.4	13 - 232	ng/mL
Procalcitonin (PCT)	<0.5	<0.5	ng/mL
Glutamate oxaloacetate transaminase (GOT)	24	0 - 35	U/L
Glutamate pyruvate transaminase (GPT)	52	0 - 34	U/L
Chloride	104	99.0 - 109.0	mmol/L
Serum creatinine	0.77	0.6 - 1.2	mg/dL
Glycaemia	82.04	70 - 115	mg/dL
C3	113.37	90 - 180	mg/dL
C4	22.919	10 - 40	mg/dL

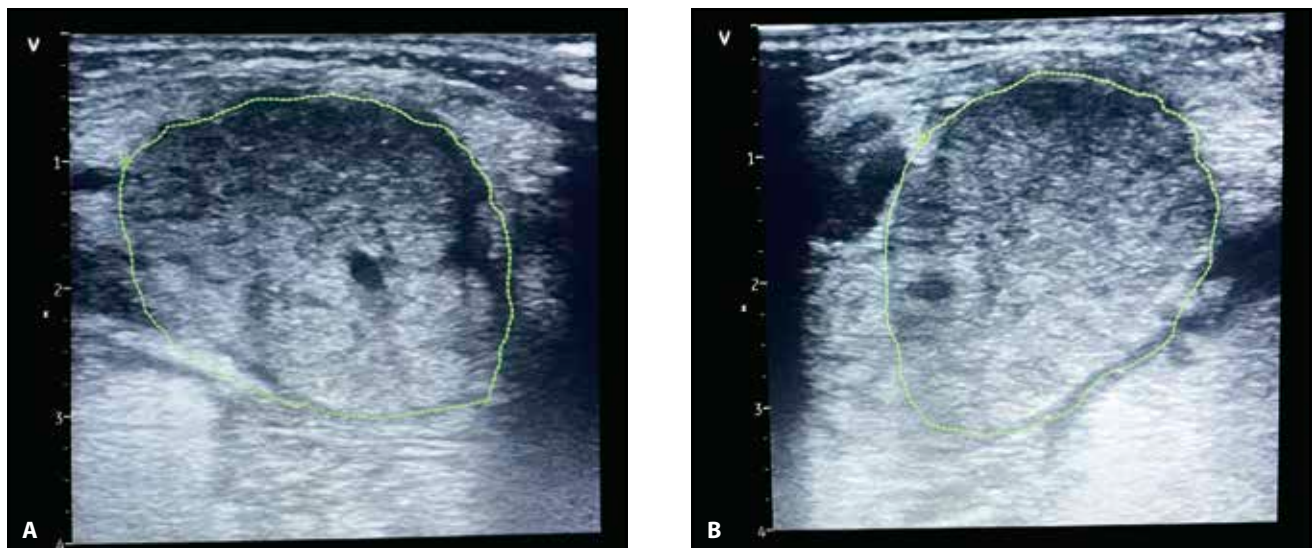
**Table 3. Serological tests for infectious diseases.**

	Value	Normal value (reference range)	Unit of measurement
Rubella IgM	0.39	negative <1.2	index
Rubella IgG	228.5	negative < 4.9	IU/ml
CMV IgM	0.32	negative < 0.85	index
CMV IgG	245.1	negative <6.0	AU/ml
EBV anti-VCA IgM	0.48	negative < 0.5	S/CO
HIV 1+2	negative		
Toxoplasmosis IgG	negative	negative <5.0	IU/ml
Toxoplasmosis IgM	0.071	negative <0.9	S/CO
Toxocarid IgG	0.22	negative < 0.9	S/CO
Toxocarid IgM	negative		
Syphilis - VDRL	<1/2	negative <1/2	
Ig G4	12.6	5.2 – 125	mg/dl

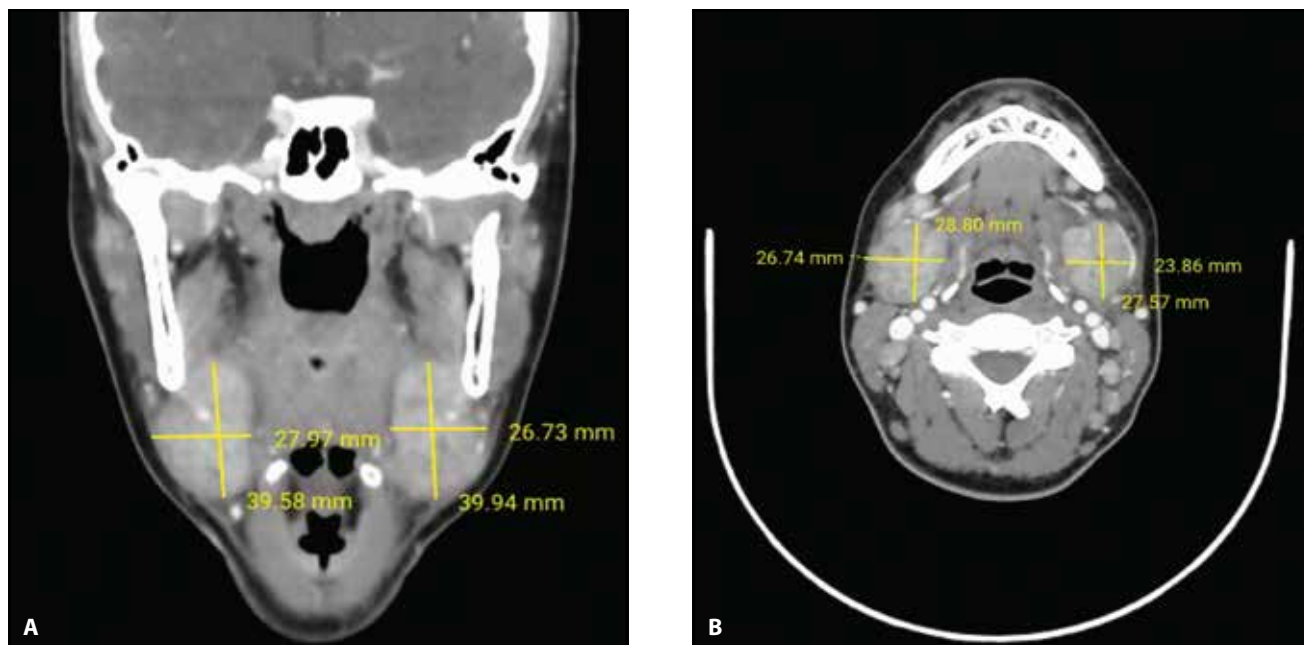
potentially related to KFD.

Under methylprednisolone pulse therapy (250 mg/day) for 5 days, the patient's progress was favourable and she was discharged from the hos-

pital. Furthermore, treatment with methylprednisolone (40 mg/day), hydroxychloroquine (400 mg/day), acetylsalicylic acid (75 mg/day) and symptomatic treatment were recommended. For



**Figure 2.** Ultrasonography aspect of the enlargement of the submandibular glands: A. right submandibular gland (diameter - 9.71 cm); B. left submandibular gland (diameter - 9.26 cm).



**Figure 3.** Cranio-facial CT scan, coronal view (A) and axial view (B), showing the enlargement of the submandibular glands and the multiple latero-cervical lymphadenopathies.

follow-up, the patient remained in the evidence of the Rheumatology Department.

## DISCUSSIONS

Kikuchi-Fujimoto disease, also known as histiocytic necrotizing lymphadenitis, was first described in Japan by the pathologists Y. Fujimoto and M. Kikuchi et al. in 1972<sup>6</sup>. KFD is a benign, self-limiting lymphadenopathy that usually af-

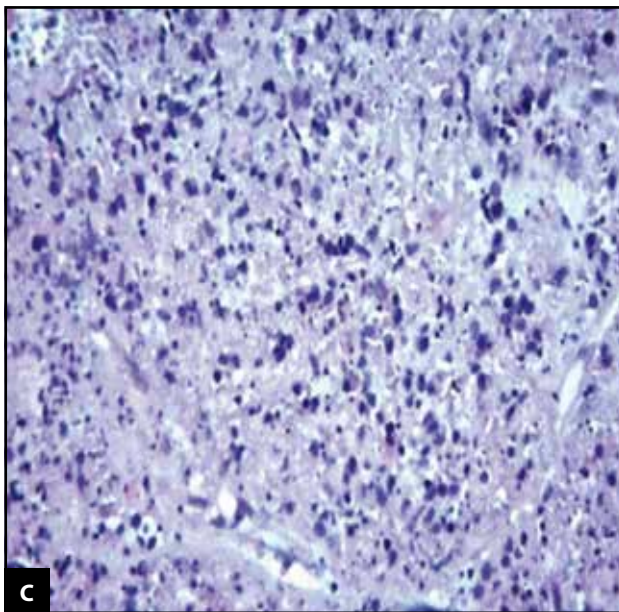
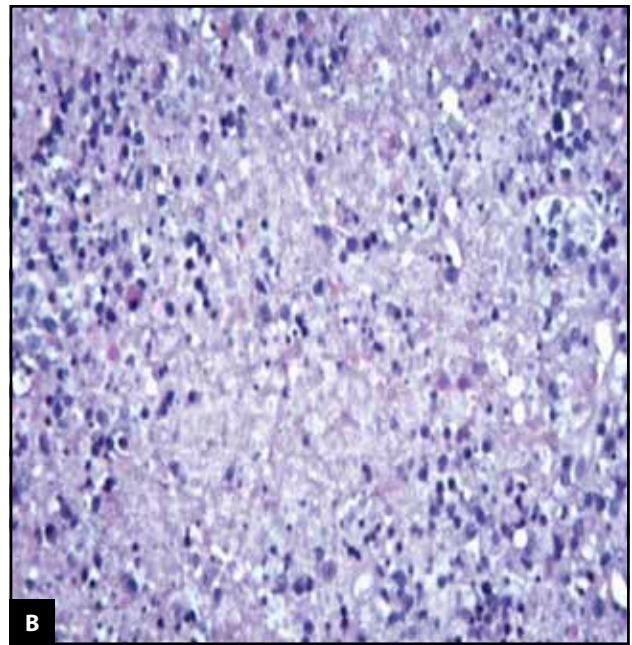
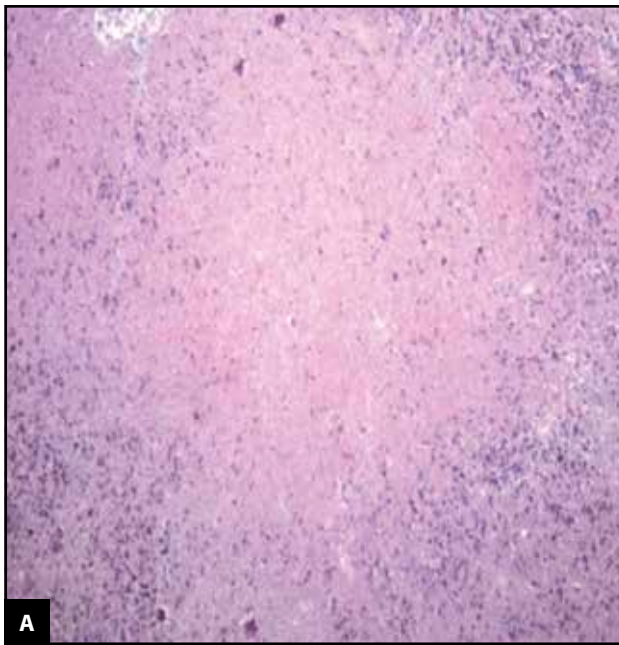
fects young adults and it seems to have a higher prevalence in females (female:male ratio of 2:1)<sup>7</sup>. Kikuchi disease is reported to affect people all around the world, with a higher prevalence in Asians<sup>8</sup>. Among the Caucasian population, the disease is very rarely reported in the literature and its true incidence is still unknown<sup>9</sup>.

The cause and the pathogenesis of Kikuchi-Fujimoto disease is still unclear. At this moment, there are speculated infectious and autoimmune causes<sup>10</sup>. Regarding the infectious theory, various causative agents, such as human herpes virus, Epstein-Barr virus, hepatitis B, simplex virus, human T-lymphotropic virus 1, toxoplasma and *Yersinia enterocolitica* are frequently involved, but the findings are ambiguous and, for the moment, there are not enough data to state with certainty that infections are responsible for the pathogenesis of the disease<sup>11</sup>. The autoimmune theory is based on the fact that there are several cases of KFD that occur simultaneously or follow SLE, but also other autoimmune diseases like Sjogren's syndrome, rheumatoid arthritis, Wegener's granulomatosis and Still's disease<sup>12</sup>.

The onset of Kikuchi-Fujimoto disease is acute or subacute, typically evolves for 1-3 weeks, and the resolution is spontaneous after 1-4 months. The most common clinical presentation of KFD is unilateral or bilateral cervical lymphadenopathy (98% of cases) associated with fever (50% of the cases) and flulike prodrome. The posterior cervical lymph nodes are involved in about 65-



**Figure 4.** Macroscopic aspect of cervical lymph node post excisional biopsy.



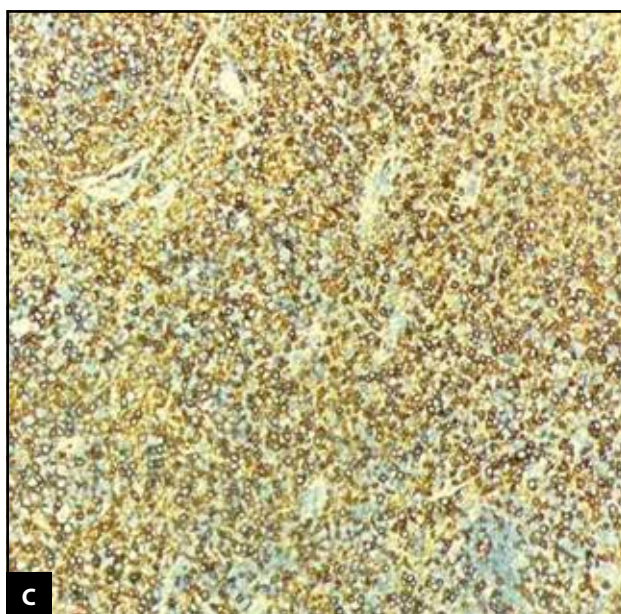
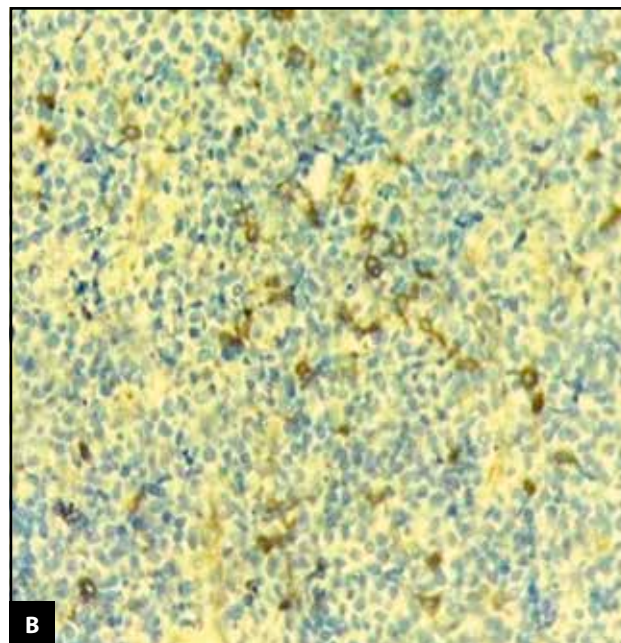
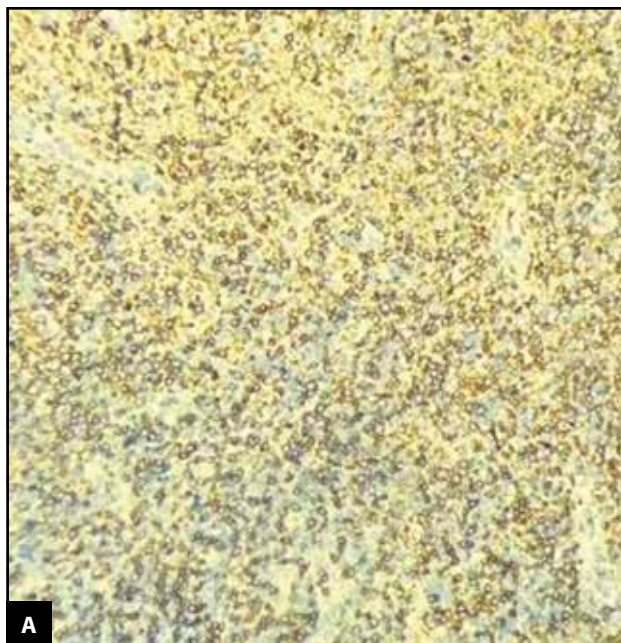
**Figure 5.** Microscopic aspects of the excisional cervical lymph node: A. necrosis (in the center) surrounded by histiocytes; nuclear debris (HE stain, x 10 magnification); B. plasmacytoid lymphocytes surrounding necrosis; nuclear detritus (HE stain, x 20 magnification); C. karyorrhectic debris and plasmacytoid lymphocytes (HE stain, x 40 magnification).

70% of the cases<sup>13</sup>. Usually, the size of the lymph nodes is about 0.5 - 4 cm in 93.4% of the cases, but occasionally they may reach 6 cm. Very often, the patients present painless or middle tender cervical adenopathy and the affected lymph nodes are usually firm, mobile and nonsuppurative. Generalized lymphadenopathy (mediastinal, axillar, peritoneal, retroperitoneal, splenic, inguinal) is quite uncommon and can be found in 1-22% of the patients<sup>14</sup>. Other less common signs and symptoms that can be associated with KFD are: nausea, vomiting, headache, wight loss, fatigue, night sweets, rush, arthralgias and myalgias<sup>15</sup>. Nonspecific cutaneous manifestation,

such as malar rash, maculopapular lesions, mucosal ulcerations, nodules, morbilliform rash and others lupus-like skin findings may be seen in 5-30% of the cases<sup>16</sup>. Hepatomegaly and splenomegaly can occur in 5% of the patients<sup>10</sup>. Very rarely, extranodal sites that include the myocardium, bone marrow, major salivary glands (parotid glands and submandibular glands), uvea and thyroid may be found. It is important to note that when extranodal involvement is present, systemic symptoms are more frequent<sup>17</sup>. In the presented case, extranodal damage was manifested by damage to the submandibular glands, with systemic symptoms (fatigue, headache, nausea, weight loss, arthralgia).

The clinical presentation and the laboratory findings of the KFD generally mimic situations that necessitate lengthy and expensive diagnostic and therapeutic interventions.

Given the disease's rarity and its various manifestations, diagnostic criteria for KFD have not yet been established. Usually, infectious, autoimmune and malignant etiologies of the lymphadenopathy must be ruled out. The excisional biopsy of the lymphadenopathy must be performed for an accurate diagnosis. Also, the laboratory tests and the imaging investigations are nonspecific. Biological findings may reveal anemia, leukopenia (20-58% of the cases) usually



**Figure 6.** Immunohistochemical assays: A. CD3 shows that the lymphoid infiltrate consists mostly of T cells; B. CD123 shows the hyperplasia of the interferon producing plasmacytoid dendritic cells; C. CD8 shows that most of the T cells are of the cytotoxic subtype.

Staphylococcus aureus, Tuberculosis, Brucella, Yersinia enterocolitica and Bartonella henselae), viral tests (Cytomegalovirus, Epstein-Barr Virus, Herpes Simplex, Hepatitis B, parvovirus B19), and also parasitic assays (Entamoeba histolytica and Toxoplasma gondii)<sup>12,18,19</sup>.

It is important to be noted if the patient presents any personal or family history of autoimmune disorders and an autoimmune serological evaluation should be performed, especially the evaluation of the SLE antibodies panel. Antinuclear antibodies, anti-double-stranded DNA antibodies, anti-Ro antibodies, anti-La antibodies and anti-Smith antibody can help the clinician to differentiate KFD from SLE. If the patient presents positive serology for SLE, histopathological examination is necessary to distinguish KFD from lupus lymphadenitis<sup>4</sup>. The reports highlighted the association of Kikuchi-Fujimoto disease with other autoimmune diseases, the association with SLE being the most common one<sup>20</sup>.

It is notable that, in the presented case, the patient displayed on the usual laboratory tests lymphocytopenia, neutrophilia and inflammation (high levels of CRP and ESR); the serological tests for CMV, EBV, Rubella, HIV, syphilis, toxoplasmosis and toxocariasis were all negative, also the interferon-gamma release assay for tuberculosis screening was negative. Thus, the laboratory findings excluded any infectious etiology.

with neutropenia, leucocytosis (2-5% of the cases) or thrombocytopenia. Elevated inflammatory markers such as erythrocyte sedimentation rate, C-reactive protein and ferritin may also be found. Elevated liver transaminases (alanine transaminase (ALT) and aspartate transaminase (AST)), increased levels of serum lactated dehydrogenases (LDH) and reduced values of C3 can be also present, but these findings are neither specific nor pathognomonic.

As it was mentioned before, various serological tests are required to exclude infectious causes of the cervical lymphadenopathy. They must include bacterial tests (Streptococcus pyogenes,

Due to the fact that the patient was already diagnosed with lupus, and the presence of this condition was known, the immunologic tests results confirmed once again the pre-existing condition – SLE with immunologic, hematologic (leukopenia) and articular manifestations.

Regarding KFD, imagistic investigations such as ultrasonography, computer tomography (CT) and magnetic resonance imaging (MRI) confirm the presence of lymphadenopathy in the affected areas, but the findings are not specific and cannot confirm the diagnosis<sup>18</sup>.

Ultrasonography of the enlarged lymph nodes may reveal hypervascularity, no intranodal calcification and echogenic hilum. The CT scanning might show homogenous lymph node enlargement in 83% of the patients and perinodal inflammation in 81% of the cases<sup>21</sup>. In the case of cervical adenopathy, to establish the etiology, a chest X-ray is indicated to rule out signs of malignancy. In 1-22% of the cases, generalized lymphadenopathy may be found on the CT scan and 5% of the patients could present hepatosplenomegaly<sup>9</sup>.

In the presented case, the cervical-thoracic-abdominal-pelvic CT scan pointed out enlargement of the submandibular glands, showing the extranodal involvement accompanied by the presence of multiple homogenous laterocervical lymphadenopathies with a maximum diameter of 12/17 mm, generalized lymphadenopathy and hepatosplenomegaly.

As we mentioned before, there is no specific criteria nor test for the diagnosis of Kikuchi-Fujimoto disease. The histological findings of the enlarged lymph node after excisional biopsy represents the only diagnosis method.

The histological examination highlights paracortical extensive areas of coagulative necrosis containing abundant karyorrhectic foci (histiocytes, plasmacytoid monocytes, immunoblasts and lymphocytes) that usually destroy the normal architecture inside the lymph node. Also, numerous histiocytes surrounding the necrotic area, reactive follicular hyperplasia and the absence of the neutrophils can be observed. In 10% of the cases, a follicular hyperplasia is present and in 50-60% of the cases reactive lymphoid follicles may be seen<sup>11</sup>. Several types of histiocytes may be noticed, including crescentic histiocytes, nonphagocytic histiocytes, foamy histiocytes and tingible body macrophages. The presence of crescentic histiocytes and the paracortical foci of plasmacytoid monocytes with karyorrhexis represent the minimum necessary criteria to make the diagnosis of KFD<sup>22</sup>.

Immunohistochemistry in the case of KFD

shows the predominance of T lymphocytes (CD8+ are more common than CD4+), fewer B cells, histiocytes that co-express CD68+ and myeloperoxidase (MPO), but also CD123+ plasma dendritic cells. The certain diagnosis of KFD is an anatomopathological one, according to the microscopic and the immunohistochemical findings of the lymph node after excisional biopsy<sup>4</sup>. The histopathological and immunohistochemical results regarding the presented case, showed multiple characteristics for KFD.

Histopathological examination is very important also for the differential diagnosis. From this point of view, the differential diagnosis with lymphoma, especially with non-Hodgkin lymphoma (NHL) is crucial. KFD can be confused with a NHL because of the presence of T-cell immunoblasts and various atypical monocytes<sup>9</sup>. Few histopathological elements that argue for the diagnosis of KFD and not for a malignancy are represented by the absence of Reed-Sternberg cells, the presence of numerous histiocytes and the fact that the mitotic rates are relatively low<sup>17</sup>. Lupus lymphadenitis is also difficult to distinguish from KFD even from the histopathological point of view. The things that plead for the diagnosis of KFD and not for lupus lymphadenitis are the absence or the small rate of plasma cells, hematoxylin bodies and neutrophils. Additionally, to support the diagnosis, the absence of autoantibodies and anti-nuclear antibodies – ANA (antinuclear antibodies), anti-double-stranded DNA antibodies (anti-dsDNA), anti-Ro antibodies, anti-La antibodies and anti-Smith antibodies – is needed to rule out the possibility of an autoimmune disorder<sup>23</sup>. Due to the clinical and anatomopathological similarities between the two entities (SLE and KFD), the opinions regarding their association are divided, some authors claiming that Kikuchi-Fujimoto disease is in fact a characteristic or an incomplete phase of lupus lymphadenitis, while others consider that these diseases are two different entities which might coexist. For the moment, the real association between KFD and SLE continues to be a mystery<sup>20</sup>.

The differential diagnosis of Kikuchi-Fujimoto disease is extensive and includes a wide range of conditions that can cause cervical lymphadenopathy<sup>11,14</sup>. Regarding the differential diagnosis, in our patient, among the causes of cervical lymphadenopathies associated with the swelling of submandibular glands, we excluded the infectious causes – bacterial (*Streptococcus pyogenes* infection, *Staphylococcus aureus* infection, Tuberculosis), viral (Rubella, CMV infection, EBV infection, Herpes simplex infection, Hepatitis B

and C, HIV, Syphilis) and parasitic (Toxoplasmosis and Toxocariasis), as well as other autoimmune diseases that have a similar presentation to Kikuchi-Fujimoto disease, such as Sjogren's syndrome, IgG4-related disease and granulomatous causes such as sarcoidosis. Differential diagnosis with SLE was not necessary in our patient because this condition was already established in her case. To rule out the Sjogren's syndrome, various specific investigations were performed, such as Schirmer's test, serological tests for specific antibodies (anti-Ro, anti-La) and biopsy from the minor salivary glands, all of them being negative and demolished the hypothesis of the presence of the Sjogren's syndrome. The malignancy causes such as lymphoma – NHL and adenocarcinoma of submandibular glands, were excluded by the pathologist after the examination of the biopsied lymph nodes.

No specific treatment is available for patient with Kikuchi-Fujimoto disease due to the fact that the disease is self-limited. But supportive treatment is necessary. Analgesics, antipyretics, non-steroidal anti-inflammatory drugs (NAIDs) and corticosteroids are required to reduce the marked symptomatology<sup>24</sup>. The dose of corticosteroids depends on the severity of the symptoms and varies between 0.5mg and 1mg/kg of prednisone per day<sup>25</sup>. For the patients who have corticosteroid resistance and non-responsive cases, treatment with intravenous immunoglobulin and hydroxychloroquine must be taken into consideration<sup>17</sup>. In our case, considering that KFD disease is associated with SLE and the patient was already under chronic cortisone treatment, it was decided to increase the dose of cortisone (Medrol 40 mg/day) and to continue the therapy with Plaquenil (hydroxychloroquine) 400 mg/day.

## CONCLUSIONS

Kikuchi-Fujimoto disease or histiocytic necrotizing lymphadenitis is a benign and self-limiting disorder with unknown etiology, which can be associated with systemic lupus erythematosus, but the relationship between them is complex and is not yet elucidated.

The positive diagnosis of the disease is difficult, and it involves multiple etiologies (bacteriological, virological, parasitic, neoplastic, autoimmune) and multiple paraclinical tests are necessary in order to make the correct diagnosis.

Histological examination and immunochemistry of the biopsied lymph node are considered the gold standard methods for the diagnosis of the disease.

No specific treatment is available for this disease, but analgesics, antipyretics and corticosteroids represent the supportive treatment of the disease.

Our case highlights the significance of the interdisciplinary collaboration between specialties (otorhinolaryngology, rheumatology, haematology, radiology and anatomopathology) and this is very important in order to have a correct management of the patient.

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**Contribution of authors:** All authors have equally contributed to this work.

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