

## Kikuchi-Fujimoto's Disease and Tubulo-Interstitial Nephropathy: another form of systemic impairment

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### **Abstract:**

#### *Introduction:*

*Kikuchi-Fujimoto disease, or histiocytic necrotizing lymphadenitis, is a benign disease most commonly affecting adult females. It generally causing febrile cervical lymphadenopathy, the systemic forms associated with kidney injury is not common*

*This diagnosis must be considered in some African country where etiology of lymph node is dominated by a high prevalence of tuberculous lymphadenitis and haematological malignancies.*

*Case report: The authors report the case of a 35 year-old woman who presented with acute cervical lymphadenopathy associated with Gougerot Sjogren disease and kidney injury due to tubulo-interstitial nephropathy. Histopathological examination of a lymph node biopsy, concluded on a diagnosis of Kikuchi-Fujimoto disease*

*A favourable course was observed in response to corticosteroid therapy.*

*Conclusion: The association of cervical polyadenitis in its systemic form with Gougerot Sjogren disease causing kidney injury is rare. Lymph node, kidney and salivary gland biopsies have been installing the diagnosis after excluding tuberculosis and lymphomas, the prognostic could be spontaneously good but in our case a necessity of immunosuppressive therapy was indicated.*

**Keywords:** *Kikuchi-Fujimoto disease, histiocytic necrotizing lymphadenitis, cervical lymphadenopathy, tubulo-interstitial nephropathy*

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### **I. Introduction:**

Kikuchi-Fujimoto's disease or necrotizing histiocytic lymphadenitis is an anatomoclinical entity of unknown etiology [1]. It is a rare and benign cause of cervical lymphadenopathy usually in young people. It occurs during various autoimmune diseases such as lupus disease or Sjogren's disease or various infectious diseases. We report a case of Kikuchi-Fujimoto disease secondary to Sjogren's syndrome with multi-visceral injury. Physicians need to be aware of this rare disease often neglected as a diagnosis of fever and cervical lymph node in our context of endemic country of tuberculosis with the possibility of several injury including renal damage. The authors report a case of Kikuchi-Fujimoto disease with renal injury

### **II. Observation:**

A young female patient aged 35 years old was followed for asthma during 6 years, she has been suffering for several months from asthenia with cutaneous xerosis, oral, vaginal and ocular dryness and a red eye due to a superficial keratitis, with periodic fever without loss of weight. Clinical examination revealed multiple firm, regular, non-inflammatory, 1cm diameter cervical lymphadenopathies measured in the spinal, carotid-jugular and right axillary ganglionic chain,

The biologic abnormalities have been showed: accelerated VS with normal CRP, normochromic normocytic anemia at 10.5 g / dl without neutropenia or lymphopenia. Alanine aminotransferase concentration 170 IU/L, lactate dehydrogenase 745 IU/L, Moderate renal insufficiency: creatinine was 140µmol/l

corresponding to 60 ml/min MDRD clearance. Tubular proteinuria with 1g/24hours made of  $\beta$ 2 microglobulin without hematuria or leucocyturia

The cyto-bacteriological study of urine: was sterile. Serologies: of toxoplasmosis, EBV, HSV, Wright, Vidal and Felix, hepatitis B, C, CMV and HIV were negative. The search for *Bacillus koch* in sputum and tuberculin IDR were negative too.

The antibody anti-native DNA, anti-Sm, anti-SSA and anti-SSB were positive. Rheumatoid factor, cryoglobulinemia, search for circulating immune complexes, and direct Coombs were negative. Serum complement fractions (C3 and C4) were low

Chest X-ray, echocardiography, and abdominal ultrasound didn't show any abnormalities or presence of lymphadenopathies.

During admission she received multiple regimens of broad-spectrum antibiotics with persistence of cervical lymphadenopathies and renal insufficiency. Histopathology of kidney biopsy revealed a chronic tubulo-interstitial nephropathy with microscopic showing foci of tubular atrophy and necrosis of epithelial cells, with interstitial edema and fibrosis (figure 1)

While lymph node biopsy showed: a few necrotic, histiocytic lymphadenitis predominantly T cells expressing CD3 and histiocytic cells with CD68-positive to immunohistochemistry.

The salivary glands revealed sialadenitis stage 3 of Chisholm and Masson.

At the end of this data, the diagnosis of Gougerot disease or dry syndrome associated with Kikuchi Fujimoto's disease was made. The patient is treated with prednisone 1 mg / kg / day for 1 month and then degressing gradually during 3 months up to the dose of 5 mg/day before finally stopping; leading to the disappearance of lymphadenopathy, improvement of dry syndrome, with resolution of symptoms and degression of antinuclear antibody, antiSm, antiSSa and antiSSb antibody titre; and stabilisation of the renal function.

She had not developed features of connective tissue disease, but remains at risk of doing so. We have a current decline of 18 months

### **III. Discussion:**

Kikuchi-Fujimoto's disease or necrotizing histiocytic lymphadenitis is a rare and benign condition, described for the first time in 1972 in Japan simultaneously by two pathologists Kikuchi and Fujimoto. The neck is the site of predilection of Kikuchi-Fujimoto disease [1,2].

It typically affects people of Asian descent, and women are four-times more likely to be affected than are men although the geographical and ethnic correlation has not been clearly explained. Some authors have reported that HLA class II alleles (DPA101 and DPB102), which are more frequent in Asian populations, are associated with Kikuchi-Fujimoto disease [1-3].

The disease is more frequent in young people and is suspected to be caused by a virus, but no specific agents have been identified. [3]

The disease is characterised by a unilateral posterior cervical lymphadenopathy. In more than 80% of the cases most often the trapezial and jugulocarotidian chain, frequently associated with a procession of systemic manifestations.

Cervical lymph nodes do not present any specific features on imaging. Ultrasound and computed tomography reveal non-necrotic oval-shaped lymph nodes, generally measuring between 1 and 3 cm. [4]

Laboratory abnormalities associated with Kikuchi-Fujimoto disease consist of an inflammatory syndrome with Lactate dehydrogenase and alanine aminotransferase concentrations can be raised; neutropenia and lymphopenia are common.

Histologically, the dermatological manifestations of Kikuchi-Fujimoto disease have features in common with systemic lupus erythematosus. Rarer manifestations include serositis, aseptic meningitis, myocarditis, pneumonitis, hepatitis, and acute kidney injury. [5]

Various diagnosis have been difficult to eliminate before the association of adenopathies and fever including:

\* Hodgkin lymphoma or not Hodgkin lymphoma

\* Some infectious pathologies: • Tuberculosis, • cat scratch disease, • Infectious mononucleosis, • Toxoplasmosis, • Yersiniosis • Infection with herpes virus, cytomegalovirus or human immunodeficiency virus

\* Autoimmune disorders such as LES [6-7].

The diagnosis in our patient of the diseases of Kikuchi-Fujimoto and Gougerot Sjogren were concomitant with tubulo-interstitial renal injury. The indication for renal biopsy was made in the rarely reported case of renal failure [5]. Renal impairment in our patient did not show lupus nephropathy, lymphoma or other urinary tuberculosis disease. Our patient thus presents a renal insufficiency secondary to Sjogren's syndrome associated with the Kikuchi-Fujimoto disease whose diagnosis has been made by the immunohistochemical

lymph node examination showing a predominance of T cells expressing CD3 and positive histiocytes for the CD68

Treatment is supportive. Corticosteroids are considered if the clinical course is severe or persistent like in our case. Generally, the disease is self-limiting with recovery in weeks to months, but deaths have been observed in systemic forms of the disease [8-9]. Antibiotics have no impact on the course of the disease, as confirmed in our patient. Patients are at increased risk of developing autoimmune diseases; by 53% according to the results of one study [10] with an average of 10 years of follow-up.

Many treatments have been proposed, like biopsy-resection. Lymph node resection may accelerate cure by eliminating the stimulus responsible for the immunological reaction [1,4]. However, in systemic forms of the disease, a short course of corticosteroid therapy is recommended at a dosage 20 mg/day to 1 mg/kg/day; the duration of treatment could not be specified. Treatment with intravenous immunoglobulins has been proposed in severe forms resistant to high-dose corticosteroids (three bolus injections of 1 g of methylprednisolone) associated with thalidomide 200 mg/day.[4]

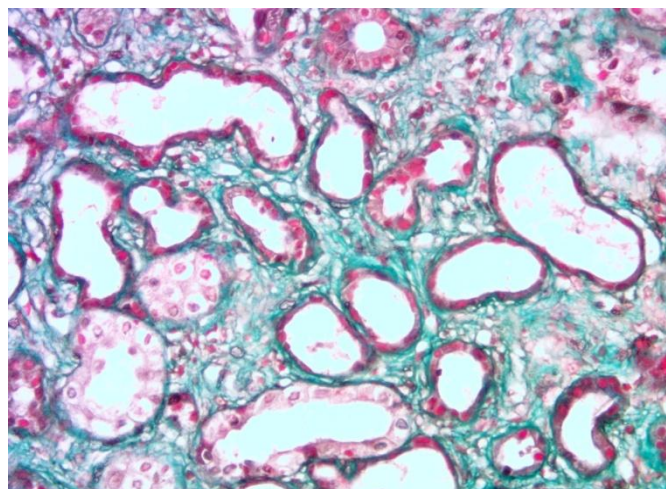
#### IV. Conclusion:

Kikuchi-fujimoto's disease is a rare, benign disease that is often poorly or undiagnosed, it could be isolated or accompanied to infectious or an autoimmune disease like in our case, and which causes clinical, biological and immunological disturbances that reestablish these lymphadenopathies and immunohistochemistry that demonstrates lymphocyte proliferation expressing CD3 and histiocyte for CD68 in our case the attack was secondary to Sjogren's Sjogroup disease responsible for tubulo-interstitial nephropathy.

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No conflicts of interest



**Figure I: showing foci of tubular atrophy and necrosis of epithelial cells, with interstitial edema and fibrosis (trichromatic colorings high magnification \* 40)**