Kikuchi-Fujimoto disease associated with type 1 Diabetes Mellitus: case report

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Abstract

Necrotizing lymphadenitis or Kikuchi-Fujimoto disease corresponds to the idiopathic and self-limited disorder, uncommon in clinical practice that affects elderly women of Asian ethnicity. It usually courses with painful cervical lymphadenopathy, persistent low fever, nocturnal sweating and leucopenia. It usually bears low risk of complications and recurrence, with spontaneous resolution in six months at most, with no need for interventions or specific treatment. The differential diagnosis, performed by histopathology exam of the affected lymph node, should be made with lymphoma and other infectious or autoimmune diseases that occur with cervical lymphadenopathy, in order to avoid iatrogenic outcomes caused by unnecessary interventions. This is the case of a 12 year-old otherwise healthy female, admitted to investigate a neck lymphadenopathy and weight loss, diagnosed with necrotizing lymphadenitis, and later progressed to Type 1 Diabetes Mellitus.

Keywords: Lymphadenitis, Histiocytic Necrotizing Lymphadenitis, Diabetes Mellitus, Type 1.
INTRODUCTION

Necrotizing lymphadenitis, also called Kikuchi-Fujimoto Disease (KFD), is an idiopathic and self-limited disorder; frequent in clinical practice. It is estimated that KFD corresponds to 0.5 to 5% of all histologically assessed lymphadenopathies. The most frequently found symptoms are: persistent low fever, lymphadenopathy, usually cervical, and leukopenia. Night sweats may also be present. It usually affects young patients and prognosis is commonly favorable, with low risk of complications and recurrence. Differential diagnosis should be made excluding other causes of adenopathy, such as lymphoma, tuberculosis and viral infections that cause enlarged lymph nodes. The association between Kikuchi-Fujimoto’s disease and autoimmune disorders such as systemic lupus erythematosus is commonly found in the literature.

This paper presents the case of a 12-year-old female patient who developed weight loss and later neck lymphadenopathy, diagnosed with necrotizing lymphadenitis and later progressed with Type 1 Diabetes Mellitus (DM1).

CASE REPORT

R.N.S, 12 years old, previously healthy, with reports that during the year of 2016 developed significant weight loss of six kilograms, two kilos in the month of October, not associated with restrictive diet or increased physical activity. In October, she also noticed lymph node enlargement in the right cervical region, with painless lymph nodes, with little mobility, without fever signs, firm and hardened, one lymph node was large, approximately 3cmx3cm.

She complained of “facial heat” associated with pulsatile holocranial headache, in addition to pain and weakness in the lower limbs. The patient had no night sweats, fever or prostration during this period. The mother sought the emergency service, where she was instructed to perform warm compresses on the cervical region. The next day, the teenager developed lipotimia, not accompanied by syncope, which led them to the health service again.

A laboratory study showed elevated lactate dehydrogenase (LDH) of 630 U/L (reference value up to 247 U/L), without change in CBC or leukogram. The main hypothesis was lymphoma, which led to the transfer of the patient to the Santa Casa de Belo Horizonte for better assessment. Upon admission, she was in good general health, afebrile, with no new symptoms other than those already reported.

We ordered a chest radiography, the result showed no alterations, no signs of mediastinal enlargement. A new laboratory test was performed, which also showed no alterations, and a new LDH test with a value of 253 U/L, an improvement. An excisional lymph node biopsy was performed, and it revealed necrotizing lymphadenitis.

The report described findings suggestive of Kikuchi-Fujimoto disease, although it is not possible to rule out infectious processes or lymphoproliferative diseases. The material sent for immunohistochemistry showed an immunohistochemical profile and morphological findings confirming the KFD hypothesis. R.N.S. was discharged for outpatient follow-up after seven days of hospitalization.

The patient progressed well, with total lymph node enlargement regression in three months. Seven months after discharge from the hospital, in May 2017, she developed polydipsia, polyuria, adynamia and weight loss. She was then taken to the ER, where a capillary glycemia test of 385mg/dL was performed, without any suggestive signs of diabetic ketoacidosis.

Venous hydration and correction of glycemia with regular bolus insulin (2U) were initiated. The patient was hospitalized again for adequacy of glycemic control and adaptation to the use of a regular and NPH insulin scheme. She was discharged with adequate glycemic control and remained in outpatient follow-up with a pediatric endocrinologist.

DISCUSSION

The Kikuchi-Fujimoto disease was first described in Japan in 1972 as lymphadenitis associated with focal proliferation of reticular cells, accompanied by numerous histiocytes and extensive nuclear debris. The disease is usually found in young adults under 40 years of age. The higher prevalence in women has been frequently reported in the literature, however, recent studies show a 1:1 ratio when both genders are compared.

Although it affects mainly Asian patients, there are literature reports of this pathology in several continents. It can present either acute or subacute onset, taking two to three weeks on average to develop. The most frequently found signs and symptoms are: cervical lymphadenopathy (56 to 98%), followed by persistent low fever for about one week (30 to 50% of patients).

Duy Vu et al (2016) presented a rare case of KFD in a 48-year-old patient with lymph node enlargement in the upper and retroperitoneal abdomen, without cervical involvement, in which the biopsy was definitive for diagnosis. In the case reported, the patient had painless cervical lymphadenopathy, not associated with fever.

Although the pathogenesis remains unknown, the clinical presentation and the histological changes suggest that the immune response of T cells and histiocytes to an infectious agent occurs. Papers suggest viral infections, such as those caused by Epstein Barr, HIV and Herpes Virus 6 and 8, as precursors of KFD onset. Both these infections and KFD present similar manifestations, such as atypical lymphocytosis, respiratory symptoms and no response to antibiotic therapy. However, this hypothesis has not yet been confirmed.

The diagnosis is made through biopsy and histopathological study, where alterations in lymph node structure are compared. However, recent studies show a 1:1 ratio when both genders are compared.
histological patterns in clinical practice: proliferative, necrotic and xanthomatous.

Several histiocytes and lymphoid cells containing nuclear fragments and eosinophilic apoptotic debris characterize the proliferative pattern, with predominance of inflammatory infiltrates. This pattern corresponds to approximately one third of the cases. The necrotizing pattern shows a degree of coagulative necrosis and is seen in 50% of the cases. On the other hand, the xanthomatous pattern is rare and develops a buildup of foamy histiocytes.

Immunohistochemistry, as in the case of our patient, can be used to complement the histology test. The main differential diagnosis is made with lymphoma. Infectious diseases such as mononucleosis and tuberculosis should be excluded, as well as systemic lupus erythematosus (SLE). Several authors report an association between KFD and the later development of SLE. That is why it is so important to follow these patients. After the lymphadenopathy resolution, our patient developed type 1 Diabetes Mellitus, which, like SLE, is also characterized as an autoimmune disease. No other cases were found in which such association occurred in the literature we reviewed.

KFD is often described as benign and self-limiting, within resolution in months. The propaedeutic is based on the treatment of symptoms with antipyretic and anti-inflammatory drugs when necessary. The use of glucocorticoids is only suggested in cases that develop with severe symptoms.

Our patient presented a benign and self-limiting course of the disease, with not too many symptoms. After 3 months of the lymph node enlargement resolution, she was diagnosed with type 1 DM and remained in outpatient follow-up.

REFERENCES