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Original article

Kikuchi-Fujimoto disease: Report of 4 cases and review of the literature

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ABSTRACT

Introduction: Kikuchi-Fujimoto disease or histiocytic necrotizing lymphadenitis is a benign disease of unknown origin predominantly affecting young women and presenting in the form of cervical lymphadenopathy and/or prolonged fever.
Material and methods: The authors report 4 cases of Kikuchi-Fujimoto disease diagnosed in the Internal Medicine Department of Ibn Sina university hospital in Rabat between 2009 and 2010.
Results: These 4 women with a mean age of 27 ± 8.6 years [16–37] were admitted with febrile syndrome and cervical lymphadenopathy. The diagnosis was based on histological examination of a lymph node biopsy. The disease was associated with systemic lupus erythematosus in one case and actinomycosis in another case. A favourable course was observed in response to corticosteroid therapy in two patients, antibiotic therapy in one patient and antipyretic treatment alone in the fourth patient.
Conclusion: In the light of these four cases, the authors discuss the diagnostic difficulties, the modalities of treatment of Kikuchi-Fujimoto disease and its clinical course.

1. Introduction

Kikuchi-Fujimoto disease or histiocytic necrotizing lymphadenitis is a rare, benign disease presenting in the form of cervical lymphadenopathy, frequently associated with a series of systemic manifestations. The pathophysiology of this disease remains unclear and may be associated with autoimmune diseases, especially systemic lupus erythematosus and certain infectious agents. We report the cases of four women with Kikuchi-Fujimoto disease.

2. Material and methods

This retrospective study was based on 4 cases of Kikuchi-Fujimoto disease observed in the Internal Medicine Department of Rabat University Hospital between 2009 and 2010. The diagnosis was established on the basis of a complete clinical, laboratory and radiological assessment, as well as histological examination of a lymph node biopsy.

3. Results

The mean age of the patients was 27 years (range: 16 to 37 years). Epidemiological, clinical, laboratory and radiological characteristics are summarized in Tables 1–4, respectively.

Cervical lymph nodes, confirmed by ultrasound, were firm, measuring about 2 cm in diameter, mobile, painless and not associated with any local inflammatory signs.

Histological examination of a cervical lymph node biopsy in all four patients revealed lymphoid tissue with perfectly conserved architecture. The presence of clear zones composed of histiocytes surrounding apoptotic cells comprising nuclei with dense chromatin or fragmented nuclei was observed in paracortical zones of the lymph node. No pathogens, tuberculoid granuloma, or caseous necrosis were observed. Immunolabelling with anti-CD20 and anti-CD3 antibodies demonstrated a homogeneous distribution of B and T lymphocyte populations (Fig. 1) and a large population of CD68+ histiocytes (Fig. 2), an appearance suggestive of Kikuchi-Fujimoto histiocytic necrotizing lymphadenitis.

Laryngoscopy, performed in one patient due to the presence of an enlarged parotid gland, demonstrated a non-bleeding granulating appearance. Histological examination of a nasopharyngeal biopsy demonstrated chronic inflammatory changes with the presence of *Actinomyces*.

In one patient, Kikuchi-Fujimoto disease was associated with systemic lupus erythematosus (SLE), a diagnosis based on the presence of suggestive clinical features as well as a positive

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Table 1
Epidemiological characteristics.

	Case 1	Case 2	Case 3	Case 4
Age	37 years	16 years	28 years	26 years
Gender	Female	Female	Female	Female
Ethnic origin	Moroccan	Moroccan	Moroccan	Moroccan
History	Nil	Tonsillectomy 4 years ago	Nil	Penicillin allergy

Table 2
Clinical characteristics.

	Case 1	Case 2	Case 3	Case 4
History of the present illness	Fever General malaise For 3 months	Fever General malaise For 3 months	Inflammatory polyarthralgia Face rash Fever, general malaise 2 months postpartum	Bilateral parotid and neck swelling Fever, general malaise For 4 months
Physical examination	T° = 38.5 °C Bilateral cervical and axillary lymph nodes	T° = 40 °C Bilateral cervical and axillary lymph nodes	T° = 39 °C Malar rash Bilateral cervical lymph nodes	T° = 38 °C Parotid hypertrophy Bilateral cervical lymph nodes

Table 3
Laboratory characteristics.

Laboratory parameter	Case 1	Case 2	Case 3	Case 4
CBC: Hb (g/dL)	11	11.6	10.5	12.5
WBC (/mm^3)	4000	2800	2900	5300
Lymphocytes (/mm^3)	1000	896	900	2100
Platelets (/mm^3)	250,000	147,000	155,000	260,000
ESR (mm)	40	49	70	12
CRP (mg/L)	6	8	60	4
PE	Normal	Normal	Polyclonal hypergammaglobulinaemia	Normal
IDR + AFB	Negative	Negative	Negative	Negative
Serology[a]	Negative	Negative	Negative	Negative
24-hour proteinuria	Negative	Negative	Negative	Negative
ANA	Negative	Negative	1/1280 (homogeneous fluorescence)	Negative
Anti-DNA			1/40	
SA + bone marrow biopsy	Normal	Normal		Normal

CBC: complete blood count; PE: protein electrophoresis; Hb: haemoglobin; IDR: tuberculin skin test; WBC: white blood cell; AFB: test for acid-fast bacillus in sputum; ESR: erythrocyte sedimentation rate ; ANA: antinuclear antibody; CRP: C reactive protein; SA: sternal aspiration.
[a] Rubella, hepatitis B-C, HIV, Cytomegalovirus, Toxoplasmosis.

immunological work-up. In another patient, Kikuchi-Fujimoto disease was associated with actinomycosis.

Treatments and clinical course are reported in Table 5. Patient follow-up was based on physical examination and ultrasound.

4. Discussion

Kikuchi-Fujimoto disease was described for the first time in 1972 in Japan simultaneously by two pathologists, Kikuchi and Fujimoto [1,2]. It has been subsequently reported sporadically in various countries, predominantly in Japan (80% of cases) [3,4]. It can occur at all ages (range: 5 to 75 years), but predominantly affects young adults with a mean age of 25 to 30 years with a female predominance in the majority of series [3–8]. The mean age of the patients in this series was 27 ± 8.6 years, in accordance with the epidemiological data concerning this disease.

Clinical features are dominated by the presence of cervical lymphadenopathy in more than 80% of cases, usually located in the trapezius or jugular and carotid lymph node chains, as observed in our patients [8]. Lymph nodes are firm, sometimes very large measuring 2 to 6 cm in diameter, mobile, but rarely painful and never ulcerating [3–5,8]. Systemic signs, predominantly fever, were also present in our patients and have been reported in 30 to 50% of cases [8]. They often constitute the predominant clinical features, wrongly suggesting an infectious cause or a haematological malignancy. A pseudo-urticarial rash, hepatosplenomegaly, arthralgia, weight loss or deep lymph nodes (mediastinal, retroperitoneal) may also be present [8].

Table 4
Radiological characteristics.

	Case 1	Case 2	Case 3	Case 4
Chest X-ray	Normal	Normal	Normal	Normal
Abdominal ultrasound	Normal	Normal	Normal	Normal
Neck CT scan	Bilateral cervical lymph nodes	Bilateral cervical lymph nodes	Bilateral cervical lymph nodes	Homogeneous parotidomegaly + lateral cervical lymph nodes
Chest, abdomen, pelvis CT scan	Normal	Normal	Normal	Normal
Laryngoscopy				Granulating appearance