

Unusual Causes of Adenopathy in a Tropical Environment: About 3 Observations

Nafy Ndiaye^{1,2*}, Abdoulaye Leye^{1,2}, Ngone Diaba Diack^{1,2}, Yakham Mouhamed Leye^{1,2}, Michel Assane Ndour^{1,2}

¹Department of Internal Medicine/Endocrinology, National Pikine Hospital Center, Dakar, Senegal

²Faculty of Medicine, Cheikh Anta Diop University of Dakar, Dakar, Senegal

Email: *fyfyname@yahoo.fr, ablayeye@hotmail.com, diackngone@gmail.com, leyeyakham@yahoo.fr, michelassanendour@yahoo.fr

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Abstract

Introduction: The discovery of peripheral lymphadenopathy is a frequent reason for consultation and hospitalization in Internal Medicine. The aim of this article is to review through three cases the etiologies of chronic lymphadenopathy rarely reported in a tropical environment. **Observations:** The first patient is a 62-year-old man who has been infected with HIV-1 for 14 years and who had a multicenter form of Castleman disease. The diagnosis was confirmed after 3 histological lymph nodes. The progression was favorable under Etoposide-based chemotherapy. The second observation is about a 38-year-old woman with a 2-month chronic febrile adenopathy without improvement after anti-tuberculosis treatment. The diagnosis of Kikuchi Fujimoto disease, in its necrotizing form, was confirmed in histology. The evolution was made favorable by the corticosteroid therapy. The third observation is about a 63-year-old woman with an enlargement of groups of lymph nodes, liver, and spleen. This tumoral syndrome was associated to an exudative ascites and a Systemic Inflammatory Response Syndrome (SIRS). The initial diagnosis was a multifocal tuberculosis based on a set of evidence (exudative lymphocytic ascites, epidemiological context and a positive Quantiferon TB test). The first ganglionic histology was not contributory. It was the second ganglionic histology that indicated the diagnosis of lymph node plasmocytoma revealing a myeloma. The patient died of septic shock. **Conclusion:** In tropical environment, the etiologies of chronic lymphadenopathy are not limited to tuberculosis and malignant haemopathies. Carrying out ganglionic histology is an absolute necessity.

Keywords

Adenopathy, Kikuchi Disease, Castleman Disease, Lymph Node Plasmocytoma

1. Introduction

Peripheral adenopathies is a frequent reason for consultation in Internal Medicine. In tropical environments the etiologies of cervical lymphadenopathies are dominated by tuberculosis and lymphomas [1] [2]. However, some rare causes such as Kikuchi disease, Castleman disease or lymph node plasmocytoma should be mentioned in some situations. We report 3 cases of patients initially treated for lymph node tuberculosis and for whom the diagnosis after histological study, with immunohistochemistry, were these rare causes cited above.

2. Observations

2.1. Observation 1

It concerned a 62-year-old man admitted for NYHA dyspnea of stage III, without orthopnea, associated with a dry cough, in a context of permanent fever and an impairment of the general health.

The patient had been under treatment for an HIV-1 infection, for 14 years, with an antiretroviral tritherapy combining: ABC, 3TC, EFV. His medical history also informed about a hospitalisation one year earlier for a tubulo-interstitial nephropathy attributed to a previous TDF intake. He was also under TB treatment for 3 months due to a suspicion of lymph node and multifocal tuberculosis undocumented.

At the entrance, the patient's blood pressure was at 110/70 millimetres of mercury (mmHg); his temperature at 40°C for a heart rate at 125 beats/min; his pulse rate was 28 cycles/min and oxygen saturation at 98% in ambient air. The physical exploration revealed firm, mobile, non-inflammatory cervical and axial adenopathies with a skin of normal aspect. The examination also revealed the presence of bilateral crepitant rattles predominantly on the left pulmonary base, and anhepatosplenomegaly. The liver was of firm consistency with an anterior smooth surface with a hepatic arrow at 19 cm. The splenomegaly was of stage 3 according to the classification of Hackett. There was no abdominal collateral venous circulation or ascites.

After the biological examination the hemogram revealed a bi-cytopenia with a normochromic normocytic anemia at 6.4 /dl (14 - 17 g/dl) and also a thrombocytopenia at 48,000/mm³ (150,000 - 400,000/mm³). There was an inflammatory biological syndrome with a C-reactive protein (CRP) at 384 mg / l (N < 6 mg/L), an initial rate of sedimentation (SV) at 145 mm (<10 mm/h), an hyperfibrinemia at 729 mg/dl (175 - 400 mg/dl), and a ferritinemia at 5 times the normal rate (10 - 250 ng/ml).

The renal function was impaired with serum creatinine at 22.85 mg/l (8 - 14 mg/l), urea at 1.28 g/l (0.15 - 0.45 g/L) and a glomerular filtration rate at 37.34 ml/min according to MDRD (90 - 125 mL/min). The 24-hour proteinuria was negative and the Addissediment count found abnormal leukocyturia at 128,125 cells/mm³ (N < 10000/mm³). The serum protein electrophoresis showed a hypo-albuminemia at 28 mg/l (35 - 45 g/L) and polyclonal hypergammaglobulinemia. There was no

cytolysis or cholestasis in our patient and the triglyceride level was normal.

Both the Quantiferon-TB® test and Acid-Fast Bacilli (AFB) in sputum smears test by direct examination, PCR, and culture were negative. The other infectious specimens (blood cultures, uroculture, thick blood film and blood smear) were negative. Concerning the HIV infection, the CD4 lymphocyte rate was 950/mm³ (500 - 1200/mm³) and the HIV viral load was negative.

The X-ray chest revealed a coarse symmetrical bilateral reticulo-nodular infiltrate which is more visible at the bases. Thoracic CT scanned frosted glass nodules, 1 pleural nodule and several parietal pseudo-nodules in the lower lobes. The abdominal ultrasound revealed a homogeneous hepatosplenomegaly associated with a deep abdominal lymphadenopathy.

In the myelogram, there was 8% non-dysmorphic plasmacytosis without images of hemophagocytosis.

Two ganglion biopsies were performed on the patient showed the presence of a reactional adenitis. A third biopsy performed three months later, following several episodes of relapse/remission of the health state, found an atrophy of the germinating clear centers with a cell population made up of small lymphocytes, polyclonal matrix plasmocytes kappa+, lambda+. The CD20 marking showed the persistence of a paracortex mainly constituted by a zone of the residual mantle. The search for HHV8 was positive. Therefore, we retained the diagnosis of CD in its hyaline vascular form.

An etoposide-based chemotherapy (VP16) at 150 mg/m² every 15 days was successfully initiated, despite the intermittent occurrence of transient influenza syndrome after treatment.

2.2. Observation 2

Madame D 38 years was admitted for unstable chronic cervical poly-adenopathies and an impairment of the general health.

Her health state has been evolving for 2 months before her hospitalisation marked with the appearance of multiple cervical and axial adenopathies together with a constant fever with thrill but no sweats. There was no dysphagia, or a dyspnea, neither a coughing. Her health state motivated a tuberculosis treatment in a hospital of level 1 despite a normal initial health check (hemogram, CRP, search for AFB, X-ray chest). With a persistent fever and the appearance of a general rash, she had been taken in our health structure.

The clinical exploration revealed cervical and axillary macro-polyadenopathies. The adenopathies were firm, sensitive, fixed compared to the deep aspect, free compared to the superficial aspect, with a healthy skin. In addition, she had generalized pruritic erythematous squamous lesions with facial involvement where the lesions were associated with palpebral edema; a SRIS with a 38°C fever and a worsening of the general health with a weight loss of 8 kg, an asthenia and a non-selective anorexia.

With this syndromic grouping, drug eruptions on lymphadenopathy tubercu-

losis or lymphoma or lymph node metastasis were the diagnostic hypotheses. Waiting for the results of the histology, we stopped the anti-tuberculosis treatment.

The biological assessment revealed a moderate inflammatory syndrome with CRP at 25.8 g/l and thrombocytosis at 498,000 elements/mm³. Hemoglobin and white blood cell count were normal. Renal function and transaminases were normal. Lactate Dehydrogenase (LDH) and ferritinemia were not measured.

Blood cultures, uroculture; thick blood film and HIV serology were negative. There was no pulmonary focus or enlargement of the mediastinum on chest X-ray. The abdomino-pelvic ultrasound did not detect deep adenopathies.

Ganglionic histology with immunohistochemistry showed signs of necrotizing lymphadenitis with scattered diffuse eosinophilic necrosis plaques of varying size, made of apoptotic cells, in which nuclear debris could be perceived with foamy histiocytes on contact. At the periphery of the foci of necrosis and in the inter-follicular zones, there was the presence of numerous immunoblastic cells with large nuclei and an abundant lymphoid population. Some lymphoid follicles with clear germinal centers persisted, particularly under the capsule. In immunohistochemistry, a CD5(+) and CD4(+) T lymphocyte hyperplasia was observed at the periphery of necroses and inter follicular areas. There was a CD20-labeled B lymphocyte population represented by residual lymphoid follicles and immunoblasts that accounted for the majority of the Ki67 labeled cyclic cells.

The patient was then treated with corticosteroids at 0.5 mg/kg of prednisone equivalent. The evolution was marked by a disappearance of the fever with stable apyrexia in 3 days. We also observed a rapid and spontaneous desquamation of the cutaneous lesions that had completely regressed after 7 days. The lymphadenitis disappeared completely after 2 months. A weight gain of 5 kg was also observed.

2.3. Observation 3

She was a 63-year-old female patient who has been followed for one year for an enlargement of groups of lymph nodes, liver and spleen, an exudative ascites and a systemic inflammatory response syndrome. Her medical history revealed a hospitalization at the nephrology department for acute functional renal failure with undocumented etiology 4 months before the onset of her symptomatology.

She presented a tumor syndrome including symptoms described as: diffuse, chronic, non-inflammatory, firm, mobile, asymmetric and non-compressive poly adenopathies with a skin visibly normal, a stage III splenomegaly of the Hackett classification without collateral venous circulation, and of a regular painless hepatomegaly with a lower moss edge without hepato-jugular reflux. She also presented a well-tolerated free ascites with average abundance, a left basal pulmonary condensation syndrome, and a clinical anemia without externalized bleeding. These symptoms occurred in a context of deterioration of general state and a permanent fever. The ascites aspiration brought back a macroscopically hematic exudative lymphocyte. There was an inflammatory syndrome: the vs was 97 mm for

the first hour (<20 mm), CRP = 268 mg/L, a hypoalbuminemia at 15.8 g/L associated with a polyclonal hypergammaglobulinemia at 35.98 g/L (9.1 - 17 g/L) in the electrophoresis of serum proteins and a 3-fold hyperferritinemia. The hemogram revealed a lymphocytosis at 4600/mm³ (1500 - 4000/mm³) and normochromic normocytic anemia at 8.6 g/dl. The liver function test showed a prothrombin level of 50%, a 2-fold hepatic cytolysis and leukocyte alkaline phosphatase of 1.5 times the normal rate. The creatinine serum was 10.5 mg/l with a DFG of 68 ml/min (MDRD), the urea = 0.45 g/l. The AFB smear was negative but the Quantiferon-TB® test was positive. The rest of the infectious test (blood cultures, uroculture, thick blood film and HIV serology) was negative. On the front thoracic X-ray, we could see non-systemic reticulo-nodular infiltrates at the level of the pulmonary bases. On the abdominal ultrasound, we could see a homogeneous hepatosplenomegaly with free trunk and coelio-mesenteric adenopathies. The thoraco-abdomino-pelvic CT scan showed multiple mediastinal, coelio-mesenteric, latero-aortic, and non-necrotic inguinal adenopathies, a hepato-splenomegaly with no abnormalities in focus, pleural effusion of small abundance, and ascites of medium abundance. The node fine needle aspiration and the ganglionic histology were non-contributory with an aspect of inflammatory adenitis. The search for malignant cells in the ascites fluid was negative. In our context of tuberculous endemic disease, febrile tumor syndrome, exudative lymphocytic ascites, and positivity of Quantiferon, an empiric anti-tuberculosis treatment was initiated. Under TB treatment, there was persistent tumor syndrome, ascites, and fever. There was no weight gain. The inflammatory syndrome had partially regressed but with a CRP always higher than 100 mg/l. This led to a second lymph node biopsy with immunohistochemistry study, which concluded a medullary plasmocytoma with a lambda IgG phenotype. There were neither emperipolesis nor Hodgkin cells nor Sternberg cells. The pelvis skull, rachis and costal grating X-rays showed no osteolytic lesions or osteocondensation. The medullogram found dysmorphic plasma cells greater than 10%. The patient died of septic shock before immunofixation was performed in the blood and the urine.

3. Discussion

The formal diagnosis of tuberculosis is based on the detection of Koch bacillus (BK) on direct examination or after culture [3]. In extra pulmonary tuberculosis (EPTB), pathological products are generally paucibacillar. The absence of evidence of KB does not eliminate EPTB. Approximately 10% to 50% of EPTB is associated with pulmonary infection. The sensitivity of tuberculous lymphadenitis culture is 14% [4]. The diagnosis of EPTB will be based on a set of epidemiological, clinical, biological and histological arguments [4]. This may explain why tuberculosis is one of the leading causes of chronic adenopathy in our practice [1] [2]. For our 3 observations, the diagnosis was established by the lymph node histology with immunohistochemistry analysis done in France. The fact that this technique is not available in our country could explain the scarcity of publica-

tions on these affections and the delay in diagnosis for patients 1 and 3 Castleman Disease (CD) is a predominant polyclonal and vascular lymphoplasmocytic proliferation within lymphoid structures [5].

Its clinical presentation is heterogeneous ranging from discrete asymptomatic adenopathies to recurrent diffuse adenopathy episodes associated with severe systemic symptoms which explains the multicentric form of the disease [6]. This form, which is often associated with HIV infection [7], raises a differential diagnosis problem especially in tropical areas with tuberculosis and/or lymphoma, which are the main causes of chronic adenopathy in our regions [1] [2]. In the case of our patient, the diagnosis was difficult as in many cases reported in the literature [8] [9] [10].

Kikuchi-Fujimoto disease (KFD) is a rare necrotizing lymphadenitis of unknown cause described for the first time in 1972 simultaneously by two Japanese authors: Kikuchi and Fujimoto [11]. More common among Asians (Japanese, Koreans and Taiwanese) [11], Kikuchi necrotizing lymphadenitis has rarely been reported in Sub-Saharan Africa [12] [13] [14]. The diagnosis is based primarily on the anatomopathological analysis of a biopsy excision of an adenopathy. Histologically, Kikuchi disease can occur in 3 different aspects: the necrotizing aspect, which is the most frequent one (>50%), the proliferative aspect (30%) and xanthogranulomatous aspect (<20%). Our patient presented the necrotizing form of the disease. Among the different diagnoses of this form, there is the lymph node tuberculosis [15].

The plasmacytoma is a monoclonal proliferation of malignant plasmocytes that can develop in isolation, corresponding to the solitary plasmacytoma (medullary or extramedullary) or enter into multiple myeloma. Extramedullary solitary plasmacytomas represent 3% to 5% of all plasmacytomas [16]. In the case of our patient the lymph node plasmacytoma has enabled the discovery of myeloma. The lymph node plasmacytomas are rarely reported [17] [18] [19]. There have been no case reports as yet in Senegal. Before retaining a lymph node plasmacytoma, a lymphoma must be eliminated [19]. In the case of our patient, there was no histological argument for a lymphoma.

4. Conclusion

Determining the etiology of chronic adenopathy is not always easy. The lymph node biopsy with immunohistochemistry is essential in the etiological investigation. The etiologies of lymphadenopathy in tropical environments remain dominated by granulomatosis and haemopathies. Kikuchi necrotizing lymphadenitis and Castleman disease must also be evoked when dealing with chronic cervical adenopathy, whether or not they develop in a febrile context. Before retaining a lymph node plasmacytoma, a lymphoma must be eliminated.

Consent

Informed consent for the publication of these observations was obtained.

Conflict of Interest

The authors declare to have no conflict of interest.

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