An Unusual Presentation of Plasma Cells – Castleman Disease: A Case Report

MARIANA MIHĂILĂ, V. HERLEA, CAMELIA DOBREA, IOANA LUPESCU, GINA RUSU MUNTEANU,
GRETHI CHIRIAC, L. MICU, R. SERESCU, I. COPACI
1Department of Internal Medicine, Fundeni Clinical Institute, Bucharest, Romania
2Department of Pathology, Fundeni Clinical Institute, Bucharest, Romania
3Center of Hematology, Fundeni Clinical Institute, Bucharest, Romania
4Department of Radiology – Fundeni Clinical Institute, Bucharest, Romania

We present the case of a 76 year old female patient admitted in the Department of Cardiology for physical asthenia, profuse sweating and dyspnea for about one month. Clinical and paraclinical assessments performed at admission confirmed the diagnosis of cardiac tamponade. Surgical intervention was performed and 400 mL of clear effusion were drained. Post-operative evolution was marked by recurrence of symptoms, requiring after 3 weeks a new drainage of 600 mL of clear effusion, and biopsy of the pericardium was performed. Pathological exam described serous pericarditis with chronic inflammatory infiltrate, xanthogranulomatous reaction intricated in the pericardium and mesothelial hyperplasia. The patient was subsequently transferred to the Department of Internal Medicine for further investigations. Physical examination showed a patient with altered general status, pallor, vesicular murmur absent in both bases, presenting cutaneous hyperpigmentation at the level of the right hemi-abdomen and hip with posterior extension, and a peripheral indurated erythematous plaque. The patient presented nodular masses of 3 cm in the right latero-cervical and bilateral axillary regions, non-adherent to the superficial structures, as well as adenopathic blocks in both inguinal regions. CT scan of the thorax and abdomen showed moderate bilateral pleuresia, minimal pericardial effusion (15 mm) and multiple adenopathies on both sides of the diaphragm. Skin biopsy was performed, as well as bone marrow aspirate and excision of a right axillary lymph node. Pathological exams and immunohistochemistry tests confirmed the diagnosis of Plasma Cells Castleman disease.

Key words: Castleman disease, plasma cells, pericardial tamponade, lymph nodes, organomegaly.

INTRODUCTION

Castleman disease is a disease of the lymph nodes and of related tissues. Castleman disease is also known as giant lymph node hyperplasia and angiofollicular lymph node hyperplasia [1]. Evaluation of a reactive lymph node is essential for diagnosis and to exclude malignancy and other atypical lymph node hyperplasia. Interpretation of histopathology in Castleman disease should be performed in correlation with clinical manifestations and tests for proinflammatory cytokines (IL6), for HIV, human herpes virus 8 (HHV8), Epstein Barr virus and cytomegalovirus.

Keller, Hochholzer and Castleman distinguished two variants of Castleman disease: hyaline-vascular (HV) and plasma-cell (PC) [2]. HV-variant Castleman disease presents typical histological features: lymphoid proliferation, regression of follicles and expanded mantle zones with small lymphocytes arranged in an “onion-skin” fashion. The interfollicular zone is expanded with prominent hyalinized blood vessels, dendritic cells and small T-lymphocytes. Plasma cells and eosinophils are not abundant. The vascular proliferation in HV-Castleman disease is determined by increased vascular endothelial growth factor (VEGF) expression [3]. Deficiency of BCL-6 positive germinal center cells and follicular T cells (BCL-6 positive, CD 57 positive) had been demonstrated by immunohistochemistry [4].

The follicular mantle cells in HV-Castleman disease express CD5 and CD20 [5]. The lymphocytes are polyclonal, as shown by molecular analysis [6]. The proliferations of follicular dendritic cells (FDC) may generate a wide range of anomalies, from stromal rich variants to neoplasms [7]. FDCs in Castleman disease present strong expression of epidermal growth factor receptor (EGFR) [8].

CASE REPORT

A 76 year old female patient was admitted in the Department of Internal Medicine – Fundeni Clinical Institute for investigations, after two episodes of cardiac tamponade of unknown etiology in the
previous month. The symptoms had started for one
month with fatigue, dyspnea, weight loss and
profuse sweating. Echocardiography exam at that
time confirmed the diagnosis of cardiac tamponade,
and surgical intervention was performed with drainage
of 400 mL of clear effusion. The symptoms reap-
peared soon after drainage, requiring after three
weeks surgical reintervention with drainage of 600 mL
of clear effusion, and biopsy of the pericardium
was performed. Pathological exam described serous
pericarditis with chronic inflammatory infiltrate,
xanthogranulomatous reaction intricated in the peri-
cardium and mesothelial hyperplasia. The patient
was referred to our department for evaluation. The
patient complained of weight loss of five kilograms
over the past month and a progressive cutaneous
pigmentation over the last ten years. At admission,
the axillary temperature was 36.8 Celsius degrees.
The patient was noted to be conscious, alert and
oriented but with altered general status. Physical
examination was significant for pallor and sweaty
skin, associated with cutaneous hyperpigmentation
at the level of the right hemi-abdomen and hip with
posterior extension, and a peripheral indurated
erythematous plaque (Figure 1).

Right laterocervical, bilateral axillary and
bilateral inguinal lymph nodes were detected,
measuring 3/3 centimeters (cm); these adeno-
megalies were non-adherent to the superficial
structures. Hepatomegaly and moderate spleno-
megaly were also remarked. Initial laboratory
testing included a complete blood count with
differential, chemistry and coagulation panels,
urinalysis, and computerized tomography (CT)
scans of the thorax, abdomen and pelvis. Blood
tests were unremarkable excepting leukocytosis of
11210/mm3 and moderate anemia with hemoglobin
levels of 8 g/dL. HIV test was negative. The CT
scan revealed widespread lymphadenopathies
involving the neck, axillae, chest/mediastinum,
abdomen and pelvis. CT also showed moderate
bilateral pleuresia and minimal pericardial effusion
(Figure 2).

Biopsy of the skin lesion was obtained from
the right hip. A mild infiltrate of lymphocytes and
plasma cells located around the vessels in the
superficial dermis and collagen fibrosis in the deep
dermis were noted (Figure 3).
Open biopsy of the right axillary lymph node was performed by the surgical service. The specimens from these biopsies were sent to pathology for histologic review, which revealed increased plasma cells infiltrate (Figure 4). The immunohistochemistry tests performed on the skin and lymph node biopsies showed plasma cells infiltrates with kappa and lambda light chain with a kappa/lambda (K/L) ratio of 4/1 (poly-clonal). The final pathology report concluded that the skin and lymph node lesions consisted in polyclonal lymphoid proliferation that was compatible with the plasma cell variant of Castleman disease. We also performed bone marrow aspirate. The marrow was hypercellular with very rich plasma cells infiltrates (20-25%) (Figure 5).

We initiated corticosteroid therapy consisting in dexamethasone, 16 mg daily. Initially we obtained a transient improvement of symptoms. Unfortunately after three weeks of treatment the general condition of the patient deteriorated, with high intensity abdominal pains. The repeated complete blood count revealed 68,670/mm³ white blood cells with an absolute neutrophil count of 60,160/mm³ and anemia (hemoglobin 8 g/dL). The patient presented cardiac arrest and died.

DISCUSSION

In our case we excluded autoimmune disorders, connective tissue diseases, as well as HIV, EBV and cytomegalovirus infections. In plasma cells – Castleman disease, present in our patient, the lymph nodes have hyperplastic follicles with preserved architecture. The FDS network is not expanded [9]. The characteristic feature is represented by increased interfollicular plasma cells which are usually polyclonal, but may be monotype (frequently lambda light chain) in PC-Castleman disease associated with osteosclerotic myeloma or polyneuropathy, organomegaly, endocrinopathy, monoclonal gammopathy and/or skin changes (POEMS syndrome) [10]. Castleman disease has a great variation of symptoms and signs. It may be unicentric (affects one lymph node station) or multicentric (affects more than one lymph node), as in our case. 30% of patients with multicentric disease have HV and 70% PC histology [11]. Multicentric Castleman disease has many manifestations: fever, night
sweats, severe fatigue, anorexia, weakness, weight loss. Night sweats may be the manifestation of exaggerated IL6 secretion. Anemia is explained by reduced production of hepcidin in the liver under the influence of IL6, reducing iron absorption and utilization. IL6 inhibits albumin production, causing a reduction of oncotic pressure, which together with increased vascular permeability by VEGF leads to edema, ascites, pleural effusion. Our patient presented cardiac tamponade and the pathological exam described chronic inflammatory infiltrate with xanthogranulomatous reaction. Three similar cases have been described in the literature [12-14]. These cases are the PC variant of Castleman disease. The development of effusion may be due to an inflammatory syndrome. Excess IL6 impairs dendritic cell maturation and promotes a Th2 immune profile, expansion of CD5-b lymphocytes producing autoantibodies. Our patient presented another atypical feature: the large skin lesions resembling Kaposi sarcoma, caused by infiltrates of lymphocytes and plasma cells in the dermis, a characteristic feature of the POEMS syndrome. The severe abdominal pain may be secondary to a debilitating polyneuropathy also seen in patients with POEMS syndrome. Therefore, we believe that this patient might have had a Castleman disease variant of POEMS syndrome that is not associated with clonal plasma cell disorder and should be distinguished from POEMS syndrome which diagnosis is made with the major criteria, two of which must include polyradiculopathy and monoclonal plasma cell disorder and at least one minor criteria (organomegaly, endocrinopathy, characteristic skin changes, papilledema, extravascular volume overload and thrombocytosis).

Overexpression of inflammatory cytokines has been incriminated in the pathogenesis of POEMS syndrome. In a case presented by Shikama N et al. [15] a patient with cardiac tamponade had high levels of IL6 in the pericardial fluid compared with serum levels (1760 vs. 6.57pg/mL). There are no published randomized clinical trials for the treatment of Castleman disease. Corticosteroids are administered to manage acute exacerbation of multicentric Castleman disease. High-dose steroids improve symptoms and lymphadenopathy [16]. Most patients require excessive doses of steroids. Steroids are therefore associated with rituximab or alkylating agents. Steroid therapy is associated with an increased risk of infection and death due to sepsis. In some case reports there were described other agents with activity in plasma cells-Castleman disease including: interferon-α, bortezomib, thalidomide, suramin (interferes with the binding of IL6 to its receptor), anakinra (an IL1-R antagonist), siltuximab (mAb anti IL6).

**CONCLUSION**

The clinical manifestations in our patient were atypical, such as cardiac tamponade and large skin lesions that were not Kaposi sarcoma. Castleman disease is a rare disease and it is important to make a differential diagnosis with lymphoma and serositis with an absolute necessity of a histopathological examination in order to have a diagnosis. The diagnosis in this case was made by lymph node and skin biopsy. Symptomatic, multicentric HIV negative Castleman disease responds poorly to corticosteroid treatment. New drugs will find their place in the management of Castleman disease.

Correspondence to: Ionel Copaci, Center of Internal Medicine, Fundeni Clinical Institute Șos. Fundeni 258, sector 2, Bucharest, Romania, Phone: + 40722300250, Fax: + 40213119190 E-mail: ionel.copaci@gmail.com
Mariana Mihăilă, Center of Internal Medicine, Fundeni Clinical Institute Șos. Fundeni 258, sector 2, Bucharest, Romania, Phone: + 40722207281, Fax: + 40213119190 E-mail: m.mihaila@yahoo.com

REFERENCES


Received July 30, 2015