Castleman's disease

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Abstract

We report two cases of Castleman's disease, a systemic and localized form. Diagnosis was based on the histological findings. Diagnosis was based on the histological findings. The great variability in symptoms and prognosis, according to the histological variant and presentation form is emphasized.

Key words: lymphadenopathy, lymphoproliferative disease, Castleman's disease, interleukin-6.

Introduction

Castleman's disease (CD), also known as angiofollicular lymphoid hyperplasia or giant cells lymph node hyperplasia, among other names (each reflecting an etiopathogenic hypothesis)[1,2,3,4] is a rare lymphoproliferative disorder of unknown cause and pathogenesis, but with characteristic histological changes. Classified as an atypical lymphoproliferative disorder, in conjunction with angioimmunoblastic lymphadenopathy, post-transplant lymphoproliferative disorders and polyclonal immunoblastic proliferation, it is mid-way between reactive adenopathies and lymphomas, conditions with which a differential diagnosis is made.5,6

Described in 1921 by Symmers, it was only recognized in 1954 by Castleman as an independent entity with its own characteristics and manifestations, according to the most frequent form of presentation, which the researcher called "mediastinal lymph node hyperplasia resembling thymoma". [1,3,5,7] It is a single tumor, intrathoracic in 70% of the cases, often in the anterior mediastinum, and of the hyaline-vascular type.[3] It is almost always asymptomatic, the main manifestations being conditioned by the mass effect. In 1956, analyzing thirteen cases, Castleman completed its description, including the systemic form of the disease. He found that it is much rarer than previously described (10 to 20% of cases), usually of the plasma cell type (80 to 90%) as a single lesion or a cluster of lesions confined in one region and in which extra-thoracic locations are more common (retroperitoneum, mesentery, superficial lymph node chains, muscle tissue), but not dominant.[9] An intermediate or mixed, multicentric form, with histological changes of both types, was associated with more severe multiorgan symptoms and worse prognosis, with a third of cases progressing to lymphoma or other neoplastic lesions.[2,3,4,7,8,10]

Several classifications have been proposed. The most commonly used are Keller's classification (1972), which considers two types - hyaline-vascular (HV) and plasma cells or plasmacytic (PC), and Flendrig's classification (1969), which divides the disease into type I and II, the former corresponding to Keller's PC form and the later corresponding to the HV form. Mixed type systemic disease is also accepted by these authors, as a third possibility, as mentioned above.

It can occur at any age, with no preference for gender or race. Peak incidence is observed between 10-40 years of age, with mixed forms usually occurring at more advanced ages.[1,3,4,7,8]

The systemic manifestations are characterized by their polymorphism, and the dominant symptoms can be very variable.[5,7,11] In the plasma cell type, fever, sweating, asthenia and weight loss are common, while in the mixed type, in addition to these symptoms,

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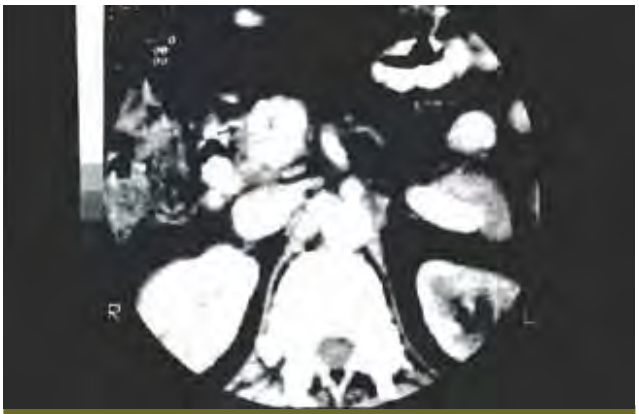


Abdominal CT scan – Case 1 – the perihepatic mass can be seen.

FIG.1

lymphadenopathy, polyserositis, heart insufficiency, nephrotic syndrome, glomerulonephritis and rheumatic manifestations are prevalent.[5,11,12] A set of changes, known as POEMS syndrome (Polyneuropathy - Organomegaly - Endocrinopathy - Monoclonal protein - Skin changes) was recently described as part of the manifestations of mixed CD, and often occurs in an incomplete form.[3,5,7,13] In laboratory tests, anemia, thrombocytopenia, hypoalbuminaemia and changes in renal and hepatic functions are common.[1,2,3,9,11] In the PC and mixed types, elevated serum levels of immunoglobulins and IL-6 are frequent, but these parameters rarely change in the HV type. Characteristically, these changes are difficult to control through treatment, but disappear quickly and irreversibly after surgical removal of the main lesion. [1,3,12]

The histological findings are key to the diagnosis, and include the presence of a lymphoid follicle structure, with vascularised follicles, centered by a hyaline-walled vessel and surrounded by a crown of mature lymphocytes with a distinguishing "onion bulb" appearance',[1,4,8] surrounded by hypervascular tissue with multiple capillaries and arterioles with hyalinised vessels; among these vessels there are polyclonal plasma cells, usually IgG, IgM or IgA, and T lymphocytes, predominantly T-suppressors. The germinal centers contain histiocytes, grouped in bands or small clumps, with epithelioid appearance.[1,2] The two variants are distinguished by the prevalence of these changes; in the PC type, the presence of large hyperplastic follicles, a dense plasma cell infiltration of the stroma, small numbers of lymphocytes and poorly developed or absent follicular center-capillary network are characteristic; in the HV type, small hyaline-vascular follicles and scarcity or absence of plasma cell infiltration of the stroma that never has the typical towel appearance, and the presence of T lymphocytes in greater numbers; in the mixed form, there is co-prevalence of the two types of changes that are, on the whole, less abundant.[1,4,9] These findings are not specific, because some of them are found in Hodgkin's disease, in other lymphomas, and in the AIDS and AIDS-related complex and nonspecific immune response, among others.[2,5,10] In the differential diagnosis where these conditions occur, CD will be a diagnosis of exclusion.[5]

Despite the above, it is essentially a predominantly benign condition, the prognosis of which depends not only on the histological type, but in particular, on the form of presentation, with a spectrum ranging from benign and curable (localized forms capable of excision) to malignant and rapidly fatal (multisystemic forms or plasma cells where surgery is not possible).[5,7,14]

Case 1

F.S.M., male, 51 years of age, married, an industrial worker, born and resident in Aveiro, was admitted in the HUC on the 12th October 1993, to clarify a perihepatic formation with 10 years of evolution.

Besides constipation, the patient had no other complaints or changes. Ten years earlier, in a routine abdominal ultrasound, a perihepatic mass of homogeneous structure was detected, 5 cm in diameter, and three secondary adenopathies; in the laboratory tests, he only had high SR. The annual clinical, laboratory and imaging tests, including CT in 1987 (*Fig. 1*), found no other changes, and only high ESR was observed. No therapy was begun. In the patient's personal history, there was only a fracture of left knee in 1979, due to an accident at work; there was no relevant family history.

On objective examination, the patient was in excellent general condition and nutrition; deep abdominal palpation revealed a painful point in the epigastrium-right hypochondrium, with no palpable masses or other changes. The other tests were normal.

In the laboratory tests, the only changes were: ESR 111mm in the 1st hour, increased polyclonal IgG, positive HbsAb and HbcAb, other markers of hepatitis B

and C negative. Chest X-ray, ECG and bone marrow biopsy showed no changes. Hepatosplenic scintigraphy (Tc99m) revealed moderate hypoperfusion of the right hepatic lobe and splenomegaly with areas of hypofixation. Scintigraphy with Ga-67 showed an area of abnormal uptake in the abdominal midline just below the edge of the liver. A liver biopsy showed changes in the acinar zone 3, of the low grade hypoperfusion type. Laparotomy revealed multiple hard nodules, similar to adenopathies, the largest with 6 x 5 x 4 cm, adhering to the hepatic hilum, duodenal bulb, underside of the left lobe and caudate lobe of the liver; the left liver lobe was atrophied, with a few nodules, and hardened areas; splenomegaly was also observed. Liver biopsy showed mild sinusoidal dilatation and peri-centrolobular steatosis (20%). The larger mass corresponded to a clearly delimited tumor formation, with a thick fibrous capsule, similar to the normal lymph node; it showed marked follicular hyperplasia with large germinal centers with irregular borders; rare follicular-like structures with concentric distribution of lymphocytes, with blood vessel endothelial at the center, with cell proliferation and deposits of hyaline material - hyaline vascular lesion; in the interfollicular area, very intense plasma cell infiltration, in towel, with numerous Russell bodies, small lymphocytes and slight vascular hyperplasia. Polyclonal IgG expression was found in the plasma cells. Conclusion: intra-abdominal Castleman's disease, plasma cell type.

No other therapy was administered. The patient continued to be monitored periodically and remained asymptomatic. His condition was the same three months after surgery.

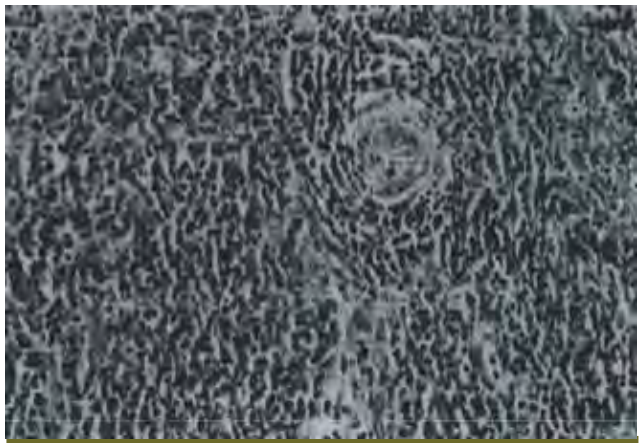
Case 2

J.A.C.M., male, 39 years of age, single, a construction worker, born and living in Covilhã, was hospitalized in Coimbra University Hospitals on the 17th August 1994, due to an undetermined febrile syndrome. Two months before admission, the patient had high fever (38°C - 39°C) with sudden onset, which remained irregular, accompanied by chills and sweats; asthenia and easy fatigability that worsened progressively until hospitalization; inflammatory myalgia and arthralgia, symmetrically affecting large and small self-limiting joints within a few days and, later, inconsistent, bilateral lower back pain mild but persistent, with periods of exacerbation suggestive of renal colic. By day 3 after onset, the patient was monitored in Covilhã District Hospital and treated with co-trimoxazole, without improvement, and hospitalized 1.5 months later due to worsening of symptoms and deterioration of his general condition. The findings of anemia, bilateral pleural effusion and elevated alkaline phosphatase, with ESR of 100 mm in the 1st hour, led to his transfer to Coimbra University Hospitals. At that time, Widal reaction had already been performed, revealing anti-O of 1/80, and Ag HBs and HIV 1 and 2 were negative. There was no reference to other symptoms. There was nothing relevant in the personal and family history.

On objective examination, the patient was anxious, in a poor general condition, thin, pale, with cyanosis, anicteric, and afebrile, with decreased hair growth, respiratory rate of 32 breaths/min, pulse 108 bpm, BP 130/80 mmHg, with movable and painless adenopathy in all the peripheral chains (0.5 to 2 cm in diameter) of hard-elastic consistency, a large number of dental caries, and oropharynx unchanged. Edema of the chest wall and abdomen was observed, as well as free bilateral pleural effusion in the lower 1/3, and tachycardia; abdominal examination showed no other changes and a brief neurological test was normal.

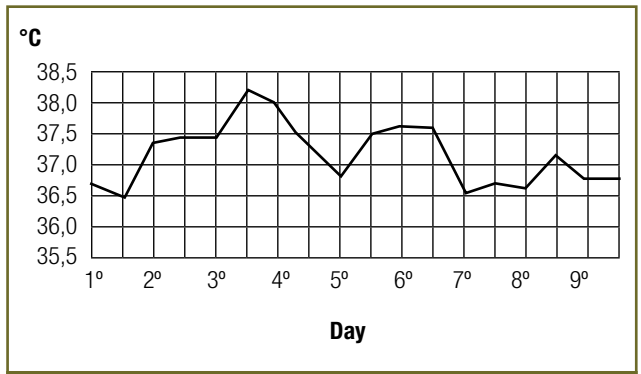
The complementary tests revealed: inflammatory anemia (Hb 10.2 g/dL), leukocytosis 12.5 WBC/L with normal leukocyte formula; hypoprothrombinaemia 62%; decreased serum iron with elevated ferritin; ESR 72 mm in the 1st hour; C-reactive protein 22; creatinine 2.1 mg/dL, urea nitrogen 27 mg/dL; hypoalbuminaemia 1.6 g/dL with normal globulin; g-GT and alkaline phosphatase 3xN, with normal transaminase and bilirubin; hypoxia (PO_2 42 mmHg) with hypocapnia (PCO_2 28 mmHg), pH 7.43. The following were negative or normal: Direct and indirect Coomb's test, test for lymphocyte populations, complement test, intradermal reaction to tuberculin, blood cultures, hepatitis B and C markers, SACE, VDRL, several serology including HIV1 and 2, autoantibodies and tumor markers. Serology for hepatitis A, cytomegalovirus, Epstein-Barr virus, herpes 1 and 2, rubella and toxoplasmosis were positive for IgG and negative for IgM. A brief urine analysis was normal; urine culture, stool cultures and parasitological examination of the faeces were negative.

Chest X-ray showed bilateral pleural effusion, occupying the lower 1/3 of both hemithorax; ECG was normal, abdominal ultrasound revealed peritoneal effusion in the ileal loops, and CT scan of the chest



Axillary node histology - Case 2. Image of a follicle with "epithelioid" germinal center, surrounded by concentric layers of small lymphocytes and intense plasmacytosis

FIG. 2



Temperature graph – Case 2

FIG. 3

and abdomen revealed no other changes.

The bone marrow biopsy showed marked changes to the stroma with enhanced reticulin, vascular ectasia and interstitial hemorrhage; cellularity of 50%; maturation changes of three series with a predominance of mature forms, and plasmacytosis of 10%. Biopsy of axillary nodes (*Fig. 2*) found preserved pulp, with intense plasmacytosis with cytoplasmic IgG in the interfascicular region, marked vascular proliferation and Castleman type images of the follicles — hyalinised germinal centers or "epithelioid" aspects, with frequent small lymphocytes around them arranged in concentric layers, giving an onion bulb appearance. In sparse, scattered, interfollicular and follicular center cells, there was also IgM - k expression. Conclusion: lymph node with Castleman type images in the plasma cell type.

At first, therapy with imipenem, oxygen, serum, human albumin, lysine acetylsalicylate and multivitamins was administered, but the patient remained febrile (*Fig. 3*), prostrated, and anxious, and his condition was progressively worsening. After introduction of naproxen, by day 6, the patient was afebrile (*Fig. 3*), but the anemia and leukocytosis worsened (*Table 1*); thrombocytopenia, hypofibrinogenaemia, increase of fibrin degradation products, oligoanuric renal failure, anasarca and congestive respiratory distress appeared, requiring assisted ventilation, continuous bilateral chest drainage and haemodialysis with ultrafiltration. After diagnosis of CD and introduction of corticosteroid therapy, there was good progress, with removal of the assisted ventilation, normalization of renal function and a gradual recovery of independence. All the parameters gradually returned to normal (*Table 1*), except for the thrombocytopenia and the onset of purpura. Two urinary infections were intercurrent - one by Candida tropicalis and the other by Enterococcus faecalis - which responded to the therapy given. On day 27, CHOP (cyclophosphamide, vincristine, EPI doxorubicin, prednisolone) chemotherapy was begun; the patient showed good tolerance, but no significant improvement. The patient remained independent, but weak and thin, with the same peripheral adenopathy, petechiae of the limbs, left pleural effusion, thrombocytopenia and changes in hepatic tests. He was discharged on day 45 after admission, treated with 32 mg of methylprednisolone and continued on a program of chemotherapy.

Less than a month later, the patient was readmitted in a state of cachexia, with bilateral pneumonia and severe respiratory insufficiency. All the previous symptoms recurred, particularly the blood dyscrasia (*Table 1*) with thrombocytopenia — 9,000 platelets, prolonged prothrombin time, hypofibrinogenaemia and high FDP, with a deterioration of renal function. Following the administration of antibiotics, and an increase in the methylprednisolone dose, further clinical and laboratory improvement was observed, with resolution of the pneumonia, progressive recovery of the general condition and improvement of the renal function. Complaints of diplopia and decreased visual acuity led to the diagnosis of bilateral macular

TABLE I

Changes in the laboratory results – Case 2

	H.D.C.*	Med. III	ICU Cortic.	Chemo		Readmiss 3rd Nov	Deflazac 30th Nov	Discharge 18th Jan 95
				Disch	6th Oct			
Days hosp.		2º	21º	43º	50º			
Hb	14.6	10.2	8.2	9.8	11.2	7.7	11.0	13.8
Leukoc.	8.9	12.5	20.7	3.0	7.0	7.9	7.1	9.1
Platelets	195.	223.	33.	63.	29.	9.	99.	260.
ESR	30	—	72	9	—	—	26	19
CRP	—	—	22	Neg	—	5.8	Neg	Neg
Prothr. T.	—	+1.9"	+2.9"	+1.2"	+0.7"	+1.4"	-0.3"	-0.3"
Fibrinog.	—	3.6	2.6	1.3	2.1	0.9	3.3	3.6
FDP	—	20	40	10	5	20	Neg	Neg
Creat.	—	2.1	5.8	0.6	0.7	2.7	1.0	1.1
Ur. Nit.	—	27	171	15	14	70	31	22
Tot. prot.	N	4.7	5.6	5.9	6.0	5.1	6.8	7.2
Album.	N	1.6	3.2	3.9	3.9	2.7	4.5	5.1
gGt	N	188	60	80	67	57	46	59
Alk. Phosp.	360	435	161	155	127	78	73	70
T Cholest.	—	90	80	108	116	127	132	243
Triglyc.	—	242	290	98	120	223	100	194

* Covilhã District Hospital

hemorrhage, likely to be a result of the changes in coagulation and high blood pressure (HBP), which were observed after the increase in corticosteroid administration. The replacement of methylprednisolone by an equivalent dose of deflazacort showed excellent results, with resolution of the HBP, glucose intolerance and fluid retention; the chemotherapy regimen was suspended and the patient was discharged in an improved condition on day 23. Three months after discharge (nine months since the onset of symptoms), the patient was recovering, with improved general condition, ocular complaints resolved, adenopathy disappeared, blood pressure and all laboratory parameters returned to normal.

Discussion

In the first case, in which a retroperitoneal mass was observed, the diagnostic hypotheses considered did not include CD, due to its rarity. The long evolution and the excellent condition of the patient led the doctors to consider a case of a benign lesion such as accessory liver, or low malignancy lesion such as low-degree lymphoma, tumor of the mesenchymal tissue, sympathetic nerves and lymph nodes. Neoplasms of the pancreas and adrenal glands were also considered. In the second case, with sudden onset, deterioration of the general condition and polyadenopathies, the hypotheses on admission were low-degree lymphoma or other lymphoproliferative malignancy, disseminated mycobacterial or fungal infection (possibly associated with AIDS) and also connective tissue diseases; hypothesis of angioimmunoblastic lymphadenopathy and CD were considered only after establishing similarities with two previously known cases.

In the first case, the lesion was, as is common, found in a routine examination, and remained stable over several years;[3,5,9] in the second case, a marked systemic condition was predominant, with inflammation and rapid evolution. In neither case did the tests performed allow a definitive diagnosis, and histopathological examination was necessary for its confirmation; it is noted that lymphoproliferative diseases are dependent on this test for confirmation of diagnosis and clinical suspicion is a valuable guidance in interpreting the results, since a third of ganglionary biopsies do not enable a definite diagnosis.[15]

In our two cases, the PC type of CD was found, but only in the second case the disease was considered a diagnostic hypothesis. According to the above, one would expect that in the first case, the disease would occur in the HV type, as the PC type, especially in the abdomen, is usually accompanied by relatively abundant systemic symptoms; in the second case, the severity of the condition, with multicentric lesion, made it more likely to be the mixed form of the disease, a hypothesis that was later confirmed by a review of the histological material.

The clinical, laboratory and imaging diversity found are consistent with the previously described cases, and has been the subject of multiple considerations and interpretations. For some authors, despite the histological similarity, the two types represent different manifestations, depending on the host response, and are unrelated to each other. But for other authors, they are just different phases of the same disease, which with an onset as the PC type or the "active form" with clinical and laboratory signs of systemic inflammation and massive lymph nodes infiltrated with plasma cells, in which areas of normal structure can be identified, evolves over time to atrophy of the follicles, vascular proliferation and fibrosis to the HV type, the "inactive form", in which the absence of inflammatory signs and completely altered lymph nodes is predominant, without any trace of its normal structure. The mixed type would be merely an intermediate stage of the disease[1,3,8,16] and the diagnosis at any stage depends on the clinical manifestations, which vary widely from individual to individual, as it can be seen.

The possibility that CD is not an autonomous entity, but rather, an unusual manifestation of a more frequent condition, led to an attempt to associate with other diseases that have been identified, preceding, coexisting or emerging later during the evolution of the disease. The most frequently accepted associations are monoclonal gammopathy, associated with increased incidence of lymphoma,[3] scleroderma, amyloidosis, primary or acquired immunodeficiency, Castleman-like changes present in about 60% of patients with AIDS, Kaposi's sarcoma, lymphomas and other neoplasms or diseases affecting the immune system.[4,10,13] The autoimmune cytopenia, with positive Coomb's test and antiplatelet Ab and anti-neutrophils, are also known, as well as other situations described, in isolation or in small series.[7,13]

The etiopathogenesis has been under investigation, and several theories have been proposed, but none are proven or universally accepted. It is seen that the localized forms are more common in young people, and the multisystemic forms at more advanced ages, and this may mean different etiologies, despite similarities in their manifestations. In the localized forms, a local response to an antigen or hamartomatous growth of the lymph node tissue,[1,5] as a result of local changes[9] in immunoregulatory mechanisms, may be the root cause of the changes found. The multicentric form would be, rather, a response to a general immunoregulation disorder, a fact supported by the frequent association with immunodeficiency, severe infections and Kaposi's sarcoma.[3,4] The hamartomatous theory is based on the irregular structure of the lymph node and the finding of areas with an appearance suggestive of this type of lesion, but there is no evidence that the situation is congenital or inherited.[1] The chronic inflammatory response to nonspecific stimuli (infectious, immunologic or neoplastic)[9,10,12] is supported by changes in the acute phase proteins, the polyclonal nature of the immunological changes found, and the histological findings characteristic of these situations (capillary proliferation and cell infiltrate with polyclonal plasma cells, lymphocytes and eosinophils); however, no stimulus was definitively identified. Some systemic manifestations support the immune nature of the disease; however, in the case of altered immune response,[5,11] it would be expected that all lymph nodes, not just some, would have their structure modified, leading to some authors draw attention to the fact that the lesions found do not always correspond to the lymph nodes (some lesions occur on sites where the lymph nodes are not frequent, as in the muscle tissue[3,11]). The cases of monoclonal plasma cell proliferation may correspond to a more advanced stage of the disease, considering that the initial hyperplasia predisposes to the proliferation of neoplastic clones; however, no significant changes were found in the form of presentation and clinical manifestations in both situations, maintaining its course with the same relative benignity.[3,14]

More recent theories are based on the presence of plasma cells that are incapable of recirculating, and high levels of interleukin-6 (IL-6).[14] There may be a primary disorder of plasma cells which, unable to recirculate, differentiate by producing abnormal amounts of IL-6; or a proliferative response to an

antigenic stimulus, altered from normal in intensity and plasma cell differentiation;[17] or even an initial deregulation in the synthesis of IL-6 that, produced in the germinal centers in large quantities,[5,7] promotes the maturation of plasma cells, mesangial cell proliferation and synthesis of acute phase proteins.[10,11,17,18] What is undeniable is that the administration of IL-6 in humans causes fever, asthenia, anorexia, myalgia, edema, anemia, thrombocytosis, increase on acute phase proteins, creatinine, aminotransferases and alkaline phosphatase, hyperglycemia, hypoalbuminaemia, proteinuria and auricular fibrillation.[5] These symptoms, which are often found in the PC type of the CD, are in line with the high levels of IL-6 present in this type, and regress after the administration of anti-IL-6 antibody.[18] According to these hypotheses, a study in congenitally anemic mice found that after the administration of a retrovirus inducing the synthesis of IL-6, a multicentre syndrome with polyadenopathies, splenomegaly and polyclonal hypergammaglobulinaemia would develop. Investigation of the lymph nodes revealed vascular hyperplasia and plasma cell infiltration of the stroma, as found in the mixed-type CD.[13] It should be noted that IL-6 is rarely found in the HV type, which is usually asymptomatic.

Further studies are still needed. The important role played by IL-6 in the systemic manifestations of the CD is clear,[18] but it is still unclear whether the abnormal plasma cells are producing high quantities of this substance, or whether some other nonspecific stimulation is causing the increase in its production, resulting in a change in plasma cell function, or even if these findings may be another satellite manifestation of the true aetiology.

In the cases presented, we observed, in the first, the existence of high ESR and increased polyclonal IgG in the serum; the plasma cells observed in the histological examination were also polyclonal, but autoimmune manifestations were not found; in the second case, the inflammation condition was strong, with fever, arthralgia, polyserositis and a higher number of acute phase proteins, and cytopenia and increased creatinine were found; no hypergammaglobulinaemia was observed, but the plasma cells, on histological examination, were also polyclonal. In neither case was stimulation of inflammatory reaction observed, nor was it possible to determine the levels of IL-6. We did not identify any association with any other pathological condition.

The therapy, always nonspecific, depends on the type and form of presentation of the disease. [11] In localized forms, with or without systemic manifestations, surgical excision of the mass is curative, recurrence is not known, and prognosis, in these cases, is excellent. In multifocal disease, particularly when associated with systemic manifestations, various therapies have been proposed and tried, [5,16,18,19] the most accepted ones being corticosteroid therapy alone,[12,16,18] chemotherapy (similar to that used in high-degree lymphomas) or an association of the two.[5] Radiation for single or localized, non-operable lesion was performed with satisfactory results in the PC type, but showed no results in the HV type.[16] More recent studies used anti-IL-6 antibodies as a specific therapy, with contradictory results.[18]

In the first case presented, surgical removal was performed only on the main lesion, which was well delimited and encapsulated, as usual[1,3,8], since the periganglionar reaction, common in these situations, prevented the removal of satellite adenopathies (these are almost always hyperplastic nodes, in which a small amount of plasma cells and hyalinised follicles can be found[16] and is not associated with the persistence of disease recurrence).[2,8] In the second case, the lesion was multicentric and curative surgery was impossible. A response to high doses of methylprednisolone was observed, although incomplete, and side effects made its replacement with deflazacort necessary, with excellent results. Chemotherapy (CHOP) was initially associated with corticosteroids, without any additional benefit being observed; on the contrary, it seemed to contribute to the patient's weakened condition, predisposing to severe lung infection. The prognosis for this patient remains reserved, but relapse and resistance to corticosteroids may be expected. For some authors, the life expectancy of this group does not exceed 2.5 years on average,[7] and the mixed type is more severe than the PC type; other authors consider a protracted course of the disease (10 to 20 years) with acute and remission periods.[3,5] The causes of death include sepsis, lymphoma, Kaposi's sarcoma and other malignant neoplasms.[3,5,7]

In conclusion: we observed two patients with CD, one with the PC type, with localized, intra-abdominal lesions, scarce symptoms and minimal changes to additional tests, and the other with the mixed, multisystemic form, and severe clinical and laboratory changes. In the first case, the surgery was curative

and the prognosis excellent; in the second case, the patient was dependent on corticosteroid, and relapses are always expected, therefore the prognosis remains reserved. ■

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