Aseptic Mesenteric Lymph Node Abscesses. In Search of an Answer. A New Entity?

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Rezumat

Abcese ganglionare mezenterice aseptice.
În căutarea unui răspuns. O nouă entitate?

Limfadenita mezenterică constituie o cauză frecventă de dureri abdominale și se poate manifesta prin simptomatologie de abdomen acut. Diagnosticul diferențial este adesea dificil, existând un mare număr de afecțiuni generatoare de limfadenopatie mezenterică. De multe ori, diagnosticul afecțiunii ce a determinat apariția limfadenopatiei mezenterice nu poate fi realizat nici măcar după intervenție chirurgicală cu biopsie. Eșecul stabilirii unei cauze precise pentru limfadenopatia mezenterică, ca și neresponsivitatea la terapiile conservatoare, îngreunează în mod deosebit managementul acestei afecțiuni. În acest articol am realizat un review detaliat la afecțiunile care pot genera limfadenita mezenterică, cu raportare la experiența noastră. Din cât putem cunoaște, reprezintă cel mai extensiv review pe această temă din literatura de profil. Cazul raportat de noi, cu un istoric de limfadenopatie mezenterică, abcese sterile ganglionare și splenice, noduli cutanați de vasculită și stenoză ileală pseudotumorală, cu un pattern de remisie și recurență pe parcursul a 25 de ani, a ridicat probleme deosebite de diagnostic diferențial. Considerarea sa ca fiind boala Crohn, vasculită sau sindrom al abceselor aseptice pare nesatisfăcătoare. Analiza datelor legate de acest caz poate ridica legitimitatea întrebării: ar trebui să recunoștem și să definim o nouă entitate?

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Cuvinte cheie: limfadenopatie mezenterică, masă mezenterică, abcese aseptice, vasculită, boala Crohn, masă retroperitoneală, obstrucție ileală, o nouă entitate de diagnosticat

Abstract

Mesenteric lymphadenitis constitutes a frequent cause for abdominal pain and may manifest acute abdominal symptoms. Very often, it is difficult to achieve a differential diagnosis as there are many diseases that can generate mesenteric lymphadenopathy. Many times, it is impossible to determine the diagnosis of the disease that has triggered mesenteric lymphadenopathy even after surgical intervention with biopsy. The failure in determining the precise cause of the mesenteric lymphadenoapathy, as well as its unresponsiveness to conservative treatments increases the difficulty in the management of this disease very much. In this paper we have reviewed the diseases that can trigger mesenteric lymphadenitis in detail, with reference to our experience. To the best of our knowledge, this is the most extensive review on this theme in current specific literature. The case reported by us, with a history of mesenteric adenitis, splenic and ganglionic abscesses, vasculitis skin nodules, pseudotumoral ileal stenosis and remission-recurrence pattern over 25 years, has raised extremely difficult problems of differential diagnosis. Its enlistment as a Crohn's disease, vasculitis or aseptic abscess syndrome seems unsatisfactory. The analysis of the data in this case can raise the legitimacy of the question: should we recognize and define a new entity?

Key words: mesenteric lymphadenopathy, mesenteric mass, aseptic abscesses, vasculitis, Crohn's disease, retroperitoneal mass, ileal obstruction, new entity to be defined

Introduction

The detection of mesenteric lymphadenitis in a patient raises a complex process of differential diagnosis and difficulties of treatment. Mesenteric adenitis represents a group of three or more mesenteric lymph nodes of at least 5 mm diameter (1). Primary adenitis is considered when there is a mesenteric lymphadenopathy unaccompanied by an identifiable intra-abdominal inflammatory or infectious process or that presents a less than 5 mm thickening of the terminal ileum. In these cases, an infectious terminal ileitis is considered to trigger the lympadenopathy. Instead, secondary adenitis appears in the context of an underlying inflammatory/infectious process. Enlarged mesenteric lymph nodes are associated with a large spectrum of diseases. Mesenteric lymphadenopathy is frequent in HIV-infected patients and in patients with cancer and its detection signifies an immuno-compromised person, a defective immunity (autoimmune diseases) or an underlying inflammatory/infectious condition. Sometimes, the imaging aspect and the clinical presentation of the patient suggest the cause, but in some circumstances, an accurate diagnosis is not possible even after surgery. The differentiation between the causes of mesenteric adenitis is essential, because the presence of primary mesenteric adenitis makes a surgical intervention unnecessary or some secondary causes can suggest a high risk of intestinal perforation (2). Mesenteric adenitis represents a frequent cause of right lower quadrant pain in adults (the second most common cause after appendicitis) (1). The presentation of many patients with acute abdominal symptoms and the unresponsiveness to conservative treatment makes the process of making a diagnosis and treating these patients even more complicated.

In this paper we present the case of a patient with a very prolonged suffering caused by an aggressive, unresponsive to treatment, chronic aseptic abscessed mesenteric lymphadenitis that required multiple surgical interventions. Despite an evolution over more than 25 years and the trial of different forms of therapies to prevent the frequent recurrences of acute abdomen in this patient, this case remains partially unclear. We consider that it is important to make such a case known, bringing information regarding this challenging disease or even creating the premises to define a completely new condition, unrecognised until now.

Case report

In 1984, a 39-years old, underweight female patient was admitted emergently with manifestations of subacute intestinal obstruction: nausea, slow intestinal transit, intense periumbilical pain, fever and clapotage. The patient declared herself to be the carrier of a genital candidosis, resistant to antibiotic treatment. Laboratory tests indicated a mild leucocytosis and increased ESR (73 mm/h). There were no hydroaerial levels. Treatment with ampicillin and kanamycin had no effect, but instead, the manifestations of a clear intestinal obstruction became prominent. Therefore, the patient was operated on. There was a moderate distension of the intestinal loops and a ring-like ileal stenosis, located 1.5 m from the ileocecal valve, of a sclerotic-inflammatory aspect. At the level of the ileal stenosis there was a voluminous mesenteric confluent lymph node mass, extending retroperitoneally, into the root of the mesentery. It did not have the aspect of a determination of Crohn's disease, but instead, it suggested an ileal neoplasm with a massive ganglionic dissemination. Other suspicions were: an intestinal carcinoid or an ileal tuberculosis with adenopathy. All the other intraperitoneal organs were normal. A mesenteric ganglion was prelevated and its examination revealed that it was suppurated and the intraoperative histopathologic exam showed a sinus histiocytosis with purulent necrosis. In terms of oncologic surgery, an entero-mesenteric radical excision was clearly impossible to achieve and therefore, a laterolateral ileo-ileal derivation was created. The postoperative evolution of the patient was simple. The result of the parafine histopathologic examination was: chronic unspecific inflammation with areas of necrosis. No bacteria, amoeba or fungi were identified in the ganglionic pus.

A silent period of eight years followed, in which the patient had no complaints and gained weight. In 1992, the patient came back to the hospital with a clear picture of intestinal occlusion: periumbilical colicative pain, intestinal clapotage, but no palpable abdominal tumor and no peritoneal irritation, with hydroaerial levels at small intestine level on the X-ray; laboratory tests: mild anaemia and leucocytosis, increased ESR (90 mm/h). Intraoperatively, besides a normal process of inframesocolic perivisceritis, a remarkable discovery was made: the ileal stenosis discovered at the first operation had vanished, the anastomosis of the intestinal derivation was permeable and there was an enormous mesenteric adenopathy, with confluent, suppurated ganglionic masses. The adenopathy spread, like a 5-cm wide belt, to the root of the mesentery and the inferior margin of the pancreas. A 2/2 cm suppurated ganglionic block was excised and the intra-operative histopathologic examination result was sinus histiocytosis. Despite all attempts, no bacteria or fungi were identified by examination or culture. Again, a complete resection of the entire ganglionic mass, with the risk of devascularizing the entire small intestine, was not possible and the intervention was limited to biopsy. Postoperatively, intense abdominal pain, febricity, increased ESR, leucocytosis and anaemia persisted. A consultation by a team of specialists in infectious diseases suggested the possibility of an intestinal and mesenteric ganglionic tuberculosis and a trial tuberculostatic treatment was started. The response was very good, with remission of pain and febricity. The tuberculostatic treatment was taken by the patient for 6 months, until August, 1992. Then, the intestinal subocclusion phenomenona recurred. Laboratory tests confuted a possible histoplasmosis. Suspecting an ileal candidosis or a Crohn's disease, a trial fungistatic and Crohn's disease treatment was started with Fungizone and Salasopirin. None of these had any effect, the patient continuing to present intermittent episodes of intestinal transit alteration, with diarrhea and abdominal pain. For one year, the patient continued an intermittent treatment with Nystatin, with an apparently favourable effect. After one year, in 1993, the acute

manifestations of incomplete intestinal occlusion and febricity reappeared. The coproparasitological exam revealed giardia cysts, but the treatment with Fasigyn (Tinidazole) proved to be inefficient. This time, due to the new technical endowment of the hospital, a CT examination was taken (*Fig. 1 A,B*): mesenteric adenopathy with diameters of 2-3 cm, some ganglionic masses having a central necrosis, others being abscessed, starting from the root of the mesentery; mesenteric fibrosis; important hepatomegaly. The CT aspect was compatible with Crohn's disease or intestinal and ganglionic tuberculosis. Another surgical intervention was necessary. Intraoperatively, an enteromesenteric block constituted of agglutinated intestinal loops and mesentery was noticed, with voluminous confluent ganglionic masses in the entire mesentery, extending to its root, giving it a thickness of approximately 4 cm. The intestinal derivation was permeable and there were no ileal tumours. 4 ganglia were excised, with the same result: aseptic pus, histiocytosis. The remaining ganglia were punctured and emptied of pus. The microscopic examination of the pus revealed frequent degraded neutrophils, fibrin filaments, absence of germs. The aerobic and anaerobic cultures remained sterile. Also, no antibodies to Yersinia in the serum of the patient were found. Postoperatively, a treatment with Prednisone for three weeks was administered with a favourable response and a prolonged period free of any symptom, characterised by normal blood tests. After 13 years, the patient came again with a prolonged febrile syndrome and abdominal pain. Besides the precedent aspect of mesenteric adenopathy, splenic abscesses were diagnosed. A splenectomy was performed, the spleen presenting a 6/5 cm, 3/2 cm and several other small abscesses, with ulcerated walls and central necrosis. Microscopic examination showed cellular debris, a polymorphic inflammatory infiltrate with eosinophils, granulomas with giant cells and rare epitheloid cells, fibrous reaction, suggesting a parasitic infestation. The PAS coloration revealed the presence of splenic amyloidosis. The histopathologic examination of the ganglia revealed subacute lymphadenitis with histiocytosis and rare eosinophils, suggesting a parasitic infection with Entamoeba hystolitica; the histopathologic examination of other fragments of splenic tissue revealed multiple abscessed granulomas composed of mononuclear cells, epithelioid and rare gigantic cells, with central necrosis and multiple altered neutrophils (*Fig. 2, 3, 4, 5, 6*); the histopathological examination together with the Ziehl-Neelsen coloration raised the suspicion of splenic tuberculosis with atypical myocobacteria. However, postoperatively, the presence of mycobacteria, parasites or an infection with fungi could not be confirmed. We remarked on the legs of the patient the presence of erithema nodosum-like cutaneous nodules, suggesting a vasculitis. In this context, the patient was sent for further exploration to an internal medicine clinic. The medical diagnostic was that of drug-induced lupus erythematosus without identifying the drug that induced the lesions and the histopathological diagnostic was that of unspecific vasculitis. The patient followed a specific treatment for vasculitis with no further recurrences. After another 6 years free of disease, we heard that the patient had died of myocardial infarction.
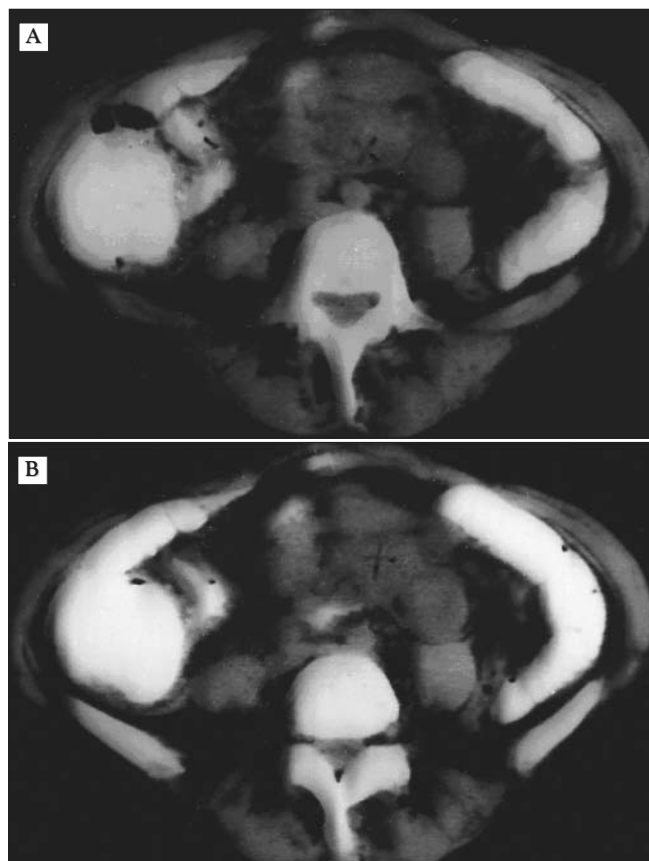

***Figure 1 (A,B).*** *CT aspects of the mesenteric adenopathy*
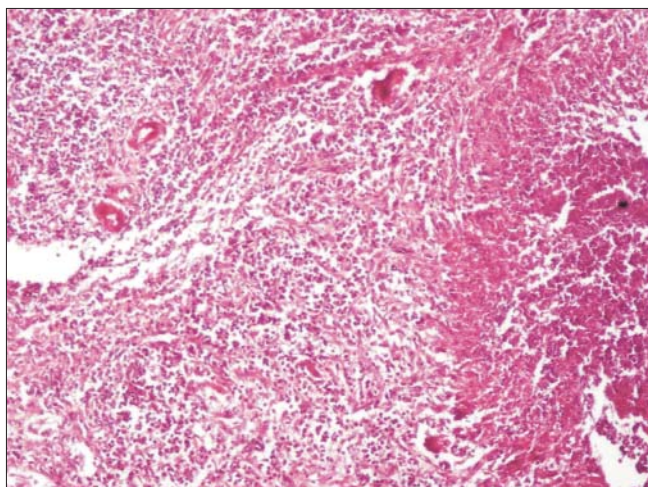
Figure 2. *Splenic tissue with widespread areas of necrosis, bordered by granulation tissue. Small arterioles with marked lesions of the vascular wall. Hematoxylin Eosin stain x40*

Discussion

We have followed-up a patient with abscessed mesenteric lymphadenitis associating recurrent manifestations of intestinal obstruction that required repeated surgical interventions over a period of 25 years. The initial presentation of the patient in 1984, when the imaging, laboratory testing and other
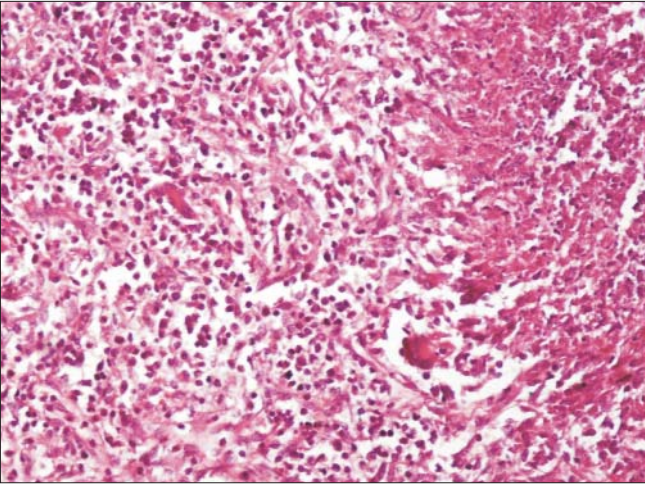
Figure 3. *Rare multinucleated giant cells, frequent histiocytes, some having abundant cytoplasm and epithelioid aspect in the granulation tissue of the spleen. Hematoxylin Eosin x100*
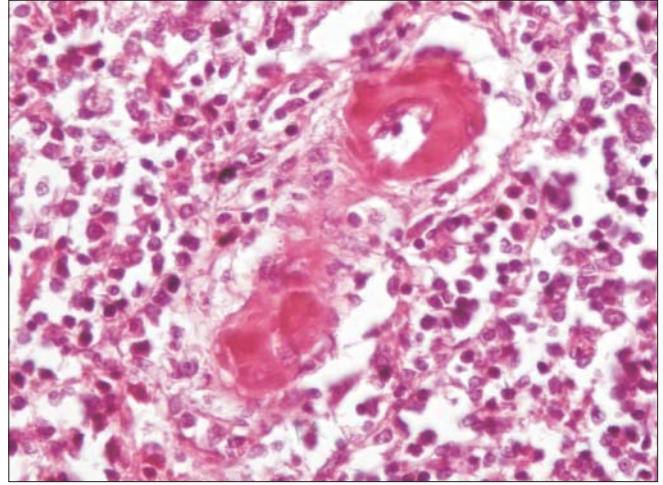
Figure 4. *In the perilesional area, small calibre arteries with the replacement of tunica muscularis by eosinophilic material with tinctorial characteristics that are compatible with fibrinoid necrosis (Congo red-, PAS+). Hematoxylin Eosin x100.*
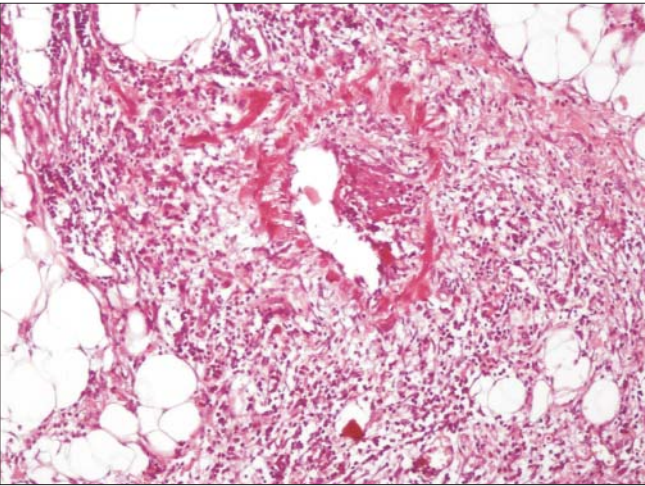
Figure 5. *In the adipose tissue of the splenic hilum a small blood vessel with fibrinoid necrosis of the wall; endoluminally, a recent thrombus, partially occluding the vascular lumen. Hematoxylin Eosin x400*
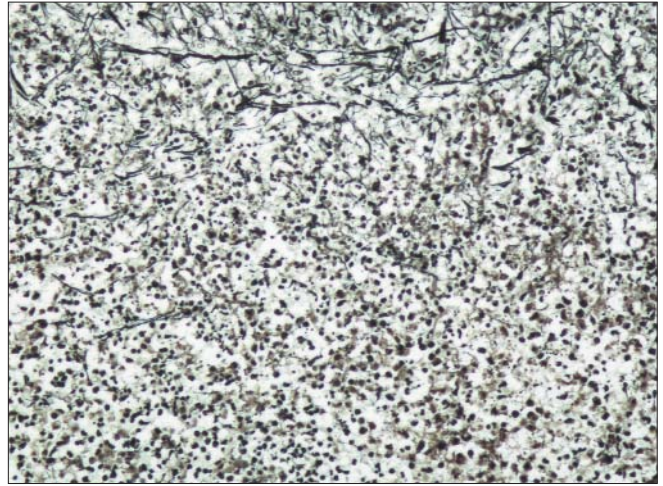
Figure 6. *A reticulin network in the necrotic mass, confuting the suspicion of tuberculosis (Gomori stain x100)*

diagnostic techniques were limited and some diseases were just being described, made the interpretation of this case so complex. Even with our actual diagnostic possibilities and with the current knowledge on diseases and syndromes, this case retains some elusive aspects. The difficulty in differential diagnosis was at its apex in this case, as many diseases had similarities with it, but a certifying factor for any of them was absent.

It is known that the second most common cause for abdominal lymphadenopathy and pain with acute symptoms leading to laparotomies is nonspecific mesenteric lymphadenopathy, where histopathological examination usually shows sinus histiocytosis or follicular hyperplasia and a primary pathology cannot be identified surgically or by other methods of exploration (3). In these cases, patients complain of

abdominal pain, periods of acute intestinal obstruction alternating with diarrhea, nausea and vomiting. Primary, unspecific mesenteric lymphadenitis is considered to be initially caused by an infectious terminal ileitis, a thickened terminal ileum being observed in many cases (1). Due to the high density of the lymph nodes and to the physiologic stasis at that level, there is an extensive exposure of the intestinal wall to several antigens and substances, that can also penetrate the wall, be lymphatically or haematologically spread and induce an immune process in the mesenteric lymph nodes. Many diseases can be responsible for a terminal ileitis and mesenteric lymphadenopathy: infectious, inflammatory, autoimmune diseases, neoplasm, amyloidoses. Infections associated with ileitis and mesenteric lymphadenopathy are tuberculosis (Mycobacterium tuberculosis), infection with Mycobacterium avium intracelullare in AIDS patients, Yersinia pseudotubercu-

losis, Yersinia enterocolitica, Staphyloccocus aureus, beta-haemolytic Streptococcus, E. coli, Salmonella typhi, non-typhoidal Salmonella, Bacteroides, Clostridia, Enterococci, Whipple disease; viral infections: lymphadenopathy syndrome associated to AIDS, Epstein-Barr virus, Parvovirus, chronic hepatitis C and B; parasitic infections, especially in immuno-compromised, AIDS patients: Strongiloides stercoralis; fungal infections, also usually found in AIDS patients: cryptococcosis (Cryptococcus neoformans), gastrointestinal candidosis, histo-plasmosis (4-7). Mesenteric lymphadenopathy is common in patients infected with HIV (1,7-9). From the non-infectious inflammatory bowel diseases associated with mesenteric adenitis there have been described: Crohn's disease, ulcerative colitis, celiac disease, appendicitis, diverticulitis. Also, auto-immune diseases, such as several types of vasculitis, can present gatrointestinal manifestations and mesenteric lymphadeno-pathy: systemic lupus erythematosus, Wegener granulomatosis, Behçet's syndrome, ANCA-associated vasculitis, Henoch-Schonlein purpura (10-14). Very rarely, amyloidal deposits in the lymph nodes (15) or chronic inflammatory diseases of the mesentery, such as sclerosing mesenteritis, have been described (4).

Even more, associations of several of these diseases can be encountered, for example those of systemic lupus erythematosus and Crohn's disease or bacterial infection and Crohn's disease (9,16), celiac sprue and intestinal lymphoma (4). An association between appendicitis and mesenteric lymphadenopathy has been described, but in our patient, the appendix was normal (17).

Along with the diagnostic incertitude that persists in this case, we can also remark that, as already described, the exten-sion/localization of a mass (neoplasm, adenopathic masses) in the retroperitoneal space, as happened in this case (the root of the mesentery), adds to the surgical complexity, inaccessibility and to the difficulty in achieving complete resections (18-20).

The differential diagnosis in the reported case

The initial consideration of the case as being an ileal neoplasm (benign tumor or malignancy-adenocarcinomas, intestinal carcinoids, lymphoma, metastatic diseases of colon carcinoma, breast, ovarian and lung cancer) with massive adenopathy, based on the intraoperative aspect and aseptic characteristic of the biopsy specimens, proved to be wrong, as in only one year, the tumor-like area of ileal stenosis completely disappeared, as if it never existed. Also, the prolonged survival of the patient makes such a diagnosis impossible. Lymphoma, usually non-Hodgkin lymphoma, is the most frequent cause of mesenteric ganglionic masses, directly spreading to the small bowel or having a mass effect on the intestine (4). However, usually, ileal cancers are benign tumors, with a very small percent of malignant processes, but the accompanying adenopathy is not so massive and no cases of spontaneous resolution without radical surgical excisions and complementary treatments have been ever reported (7). Also, small bowel neoplasms rapidly invade the intestinal wall, producing haemorrhage, perforation and widespread disease (21).

At the initial presentation of the patient, in 1984, HIV-infection was not suspected, due to its recent definition, the little knowledge on the disease and its unknown prevalence in our country at that point. Many of the features of presentation and evolution of the patient could have clearly been linked and explained by a HIV-infection: persistent mesenteric lymphadenopathy, chronic resistant genital candidosis, a temporary positive result to the tuberculostatic treatment, suggesting an intestinal and ganglionic tuberculosis or infection with other Mycobacterium opportunistic species (difficult to evidence by examination and cultures), a favorable temporary effect of the fungistatic treatment (suggesting gastrointestinal candidosis), the histopathologic aspect of parasitic infections in the splenic abscesses, liver lesions, spleen abscesses, the prolonged febrile syndrome, skin nodules and the vasculitis. Also, the periods of remission-recurrence of the disease could have been interpreted as an immune reconstitution inflammatory syndrome that develops after anti-retroviral therapy (2). However, the patient presented in this case was eventually tested and she was HIV-negative; also, her survival over more than 25 years from the initial presentation to our clinic makes such a diagnosis impossible.

Kaposi sarcoma, in or outside an AIDS, can associate enlarged mesenteric lymph nodes, that have a tendency to coalesce, forming conglomerates, small bowel nodules and skin nodules (22). However, the histopathologic examination and the evolution of the patient did not confirm such a diagnosis.

Another frequent cause for mesenteric adenitis with intestinal stenosis is tuberculosis or atypical mycobacterial infections. In these infections, terminal ileum and cecum can be thickened, lymph nodes have a multiloculated aspect with central caseating areas of necrosis and frequently associate liver and spleen lesions. The intestinal lesions can be ulcerative, hypertrophic or ulcero-hypertrophic; with chronic inflamma-tion the intestinal wall can present tuberculomas, strictures or fibrosis with intestinal stenosis, obstruction and perforation. It is accepted that sometimes, there is clearly a mycobacterial infection, even if it can not be proved by laboratory examina-tion. Also, in 70% of cases the chest radiograph is normal (7). The presence of all these characteristics, the disappearing of the initial intestinal tumor-like stenosis, the symptoms (prolonged febricity, weight loss, leucocytosis), the short response to the tuberculostatic treatment were in favour of a mycobacterial infection. Even the vasculitis could have been explained, as a mycobacterial-associated vasculitis has been described. Also, the skin nodules could have been determina-tions of tuberculosis. However, the recurrence of the disease and the final remission under Prednisone treatment makes this diagnosis improbable.

Lymphoma is another frequent cause for mesenteric lymphadenitis and mass effect on the small bowel. Lymphoma adenopathies usually coalesce, by contrast with inflammatory adenopathy (4) and can be homogenous or have necrotic areas (23). However, the repeated histopathologic examination showed no features of lymphoma and the survival of the patient was long.

The constant aseptic aspect of the pus from the lymph

nodes and splenic abscesses, the absence of specific agglutinins in the serum of the patient, as well as the final resolution of the symptoms under vasculitis-specific treatment makes an infectious cause unlikely. However, it cannot be entirely excluded, as the diversity of the germs/fungi that can induce lymph node and splenic aseptic abscesses, as well as a stenotic ileitis, can never be entirely explored. It is possible that, initially, a bacterial/mycotic component had a role in the terminal ileitis. The persistent genital candidosis of the patient induced at a certain point a suspicion of gastrointestinal candidosis with lymphadenopathy. Candida organisms are known resident microbiota of the gastrointestinal tract and may promote, in certain people, inflammatory lesions or even gastrointestinal candidiasis (24,25). It is accepted that the type of intestinal mycrobiota, host-microbiome interactions and microbial antigens can drive inflammatory bowel disease, which is another possible cause for ileal stenosis and mesenteric adenopathy (26).

Many types of vasculitis can initially present with intestinal determination, associating mesenteric lymphadeno-pathy and can display cutaneous nodules with the progression of the disease (systemic lupus erythematosus, Henoch-Schonlein purpura, Wegener granulomatosis) (22,27). Their normal pattern is of remission-recurrence, even under specific anti-inflammatory and immunomodulatory treatment. Gastrointestinal manifestations, like intestinal pseudo-obstruction can be the initial event in the history of the vasculitis in some cases (14). The histopathologic examination of the cutaneous nodules showed a process of vasculitis in the case of this patient. Also, the laboratory tests suggested a drug-induced lupus erythematous, without identifying the drug responsible for triggering the lesions. More than 80 drugs can trigger lupus erythematosus (28). From the initial complaints, along several years, the patient received multiple medications that could have induced subcutaneous manifestations of lupus erythematosus (e.g. antihypertensive, antifungal and tuberculostatic medication). Drug-induced lupus erythematosus is usually milder than the other forms of lupus erythmatosus and is responsive to the discontinuation of the causal drug and to glucocorticoids (28,29). However, a drug-induced lupus erythematosus caused by antifungal or tuberculostatic medication would be subsequent to the mesenteric lymphadenopathy and ileal obstruction and not an explanation for the mysterious disease of the patient. Even more, other diseases can associate vasculitis as well, such as tuberculosis and Crohn's disease (16,30). Primary or secondary intestinal vasculitis associate mesenteric lymphadenitis and can lead to a transmural involvement, intestinal obstruction, protein-losing enteropathy, intussusception, perforation (7). Also, due to the immunological defects associated to vasculitis, the patients have an increased risk of infection, that represents the most significant cause of disease in these cases (6). This would be compatible with the transitory response of the patient to tuberculostatic or antifungal medication and also with patient death due to myocardial infarction, knowing that vasculitis can associate thrombotic cardiovascular events (13). Patients with intestinal vasculitis complain of abdominal pain, nausea and vomiting,

intestinal bleeding, intestinal transit alteration. Still, vasculitis displays determinations on other organs too and is usually associated with intestinal perforation and less frequently with obstruction. The diagnosis of vasculitis is based on the evidence of disease activity in other parts of the organism and mesenteric lymphadenopathy is extremely rare an isolated manifestation in such diseases (22). In our patient, despite 23 years of disease before the presumed diagnostic of vasculitis, no other organ was affected by a process of vasculitis.

Amyloid deposits in the mucosa and muscle layer of the small bowel, with intestinal dysmotility, adenocarcinoma-like amyloidosis, ulcerations with mucosal bleeding, wall thickening have been described. Primary amyloidoses (immunoglobulin light chains) presents with constipation, digestive chronic pseudo-obstruction or obstruction (31). Also, amyloidosis may present with lymph node involvement (15). In the case of our patient, there were amyloidal deposits in the splenic abscesses, along with an inflammatory infiltrate, but they were not found in the lymph node specimens. The presence of the amyloidotic deposits can be the result of a chronic inflammatory reaction.

Systemic and chronic hypereosinophilia is associated with gastrointestinal lesions, enlargement of the mesenteric lymph nodes and spleen, hepatic fibrosis, aortitis, cardiac lesions of thrombotic nature due to inflammatory infiltration with eospinophils (32). In the reported case, there was an inflammatory infiltration with eosinophils in the splenic abscesses that suggested a parasitic disease, the patient died due to myocardial infarction, but there was no associated eosinophilia or elevated levels of IgE.

Mesenteric panniculitis/sclerosing mesenteritis, an inflammatory and fibrotic disease of the mesentery of unknown aetiology can associate mesenteric lymphadenopathy and symptoms like abdominal pain, fever, weight loss, nausea and vomiting. However, in our patient, the mesentery was normal, which also excludes Castleman disease associated mesenteric lymphadenopathy (22,33).

In the group of bowel inflammatory diseases that usually associate mesenteric adenopathy, we can exclude ulcerative colitis. Ulcerative colitis is characterised by a continuous inflammation limited to the intestinal mucosa and is not associated with granulomas or stenotic lesions, as seen in the current case (34).

Mesenteric lymphadenopathy can be caused by appendicitis, diverticulitis, cholecystitis, pancreatitis (22). None of these was found in the case reported by us.

Mesenteric lymph node cavitation syndrome is a disease that can complicate the evolution of celiac disease. It is characterised by central cavities in the mesenteric lymph nodes with a hyaline-like material, fibrous tissue and lymph node remnants content and by hyposplenism (35). However, our patient did not present a persistent diarrhea associated to gluten-intolerance as seen in this disease.

From the multitude of potential causes, we consider that this case could be classified as a Crohn's disease and/or aseptic abscesses syndrome/disseminated aseptic abscesses. Many times, disseminated aseptic abscesses can be found in association with

inflammatory bowel disease and are located in the abdominal lymph nodes, spleen and liver (2). Many diseases are associated with mesenteric adenopathy, but only a few display aseptic abscesses. Crohn's disease is characterised by transmural granulomatous thickening of the gastrointestinal tract, hyper-vascularity and fibrous and fat tissue proliferation, adenopathy, abscesses in the mesentery. It is an autoimmune disease or a disease of immune deficiency, in which environmental, bacterial and immunological factors interact, inducing the disease in genetically susceptible individuals. It usually affects the terminal ileum and cecum, but it may involve any segment of the gastrointestinal tract from mouth to anus, causing a large variety of symptoms (36). Crohn's disease may display a small intestine-only pattern in 11 to 48% of cases. Mesenteric lymphadenopathy can persist even in the absence of an active Crohn's disease. Crohn's disease can present in a stricturing, penetrating or inflammatory form. The stricturing form leads to bowel narrowing, obstruction and fistulae. Primary Crohn's disease granulomas are composed of histiocytes, with no giant cells (37). Crohn's disease may present with different forms of skin manifestations as: metastatic Crohn's disease, erythema nodosum, erythema multiforme, pyoderma gangrenosum, epydermolysis bullosa acquisita, skin rashes, skin changes due to malnutrition in the context of the digestive disease. From the extradigestive manifestations, mucocutaneous changes are the most frequent (in 22 to 44% of the patients (37). Metastatic Crohn's disease is characterised by sterile, non-caseating skin granulomas. Also, in the aetiopathophysiology of Crohn's disease, vasculitis is known to be a component (36). In addition, Crohn's disease presents many similarities or even coexists with various forms of vasculitis, responding to the same treatment, including corticosteroids, immunomodulators and biological agents such as infliximab or etanercept (17). This might explain why our patient had a positive response to the vasculitis treatment, with a prolonged remission of the symptoms. Crohn's disease is characterised by recurrences after surgical treatment, despite medical treatment, due to digestive complications. Also, the altered immunological pattern in Crohn's disease can explain a tendency to associated infections and the temporary response to antibiotics and antifungal medication seen in our patient. In Crohn's disease there is a mesenteric fat hyperplasia as a source of C reactive protein that contributes to the inflammatory process of the disease (38). Differentiating between Crohn's disease and tuberculosis is a complex process and the difficulty in identifying atypical mycobacteria makes a differential diagnosis even more complicated (39). In the reported case, the only finding that is not superimposable on Crohn's disease is the massive character of the adenopathy, that is rarer in Crohn's disease and more frequent in tuberculosis (22).

Aseptic abscess syndrome is a rare disease, of unknown cause, first described in 1995 (40). This diagnosis is considered when a patient presents sterile abscesses, with no identified pathogen, that do not respond to antibiotics and are sensitive to corticosteroid therapy (41). Aseptic abscesses affect with decreasing frequency: the spleen, abdominal lymph nodes, liver and pancreas, but may affect other organs as well. It may have cutaneous manifestations: Sweet's syndrome, pyoderma gangrenosum, neutrophilic dermatosis. It coexists, precedes or is subsequent to inflammtory bowel disease in a significant percent of cases (42). The symptomatology consists of abdominal pain, low-grade fever, diarrhea and weight loss and patients present leucocytosis with neutrophilia, anemia, increased ESR and C reactive protein. Our patient displayed all these features, but did not have marked leucocytosis as described in this syndrome (up to 48.000 leucocytes/mm^3) (40).

Abscesses of the spleen are rarely described in literature (reported frequency of 0.14-0.7%), being usually related to an infectious process in the context of alterations in the immune system, having a high mortality rate, that many times require splenectomy (43,44). Aseptic abscesses of the spleen is an even more rare entity. We have found only one case reported in literature (45).

The failure in identifying a cause for the mesenteric lymphadenitis should be classified as a primary mesenteric lymphadenitis. All data, including typical histopathological description with sinus histiocytosis in the lymph nodes, sustain this diagnosis. However, in our case, there was not a mild terminal ileal thickening, as described in the primary forms, but a severe stenosis, mimicking a neoplasm. We consider that there is a question whether primary mesenteric adenitis truly exists or in such cases the primary cause for a reactive lymphadenopathy is escaping the diagnosis.

Ever since 1936, in literature, there were cases of unusual inflammatory lesions in the ileocecal region with mesenteric adenitis (46). Even now, despite the progress in imaging and laboratory diagnosis, in the absence of a clear infectious or neoplastic cause, these cases remain little understood. Many of the features of presentation and evolution of the patient are superimposable on Crohn's disease associating a sterile abscesses syndrome. Still, a doubt persists, and the presentation of the patient in 1984, when diagnostic possibilities were limited, adds to the uncertainty of this case.

Conclusions

Briefly, we presented a patient with a long evolution, of over 25 years, of mesenteric lymphadenitis, with sterile abscesses in the lymph nodes and spleen, skin vasculitic nodules and an initial ileal tumor-like stenosis, with a remission-recurrence pattern of obstructive digestive manifestations, that required multiple surgical interventions and responded favourably to a treatment addressed to vasculitis. This case raised a compli-cated differential diagnosis over more than 25 years. Whether it represented a Crohn's disease, sterile abscesses syndrome, vasculitis having only intestinal and skin manifestations, an undiagnosed infection or a completely new entity, that would require recognition, definition and reporting from other centers remains to be solved by future experience. We only reported the case and raised the question.

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