Mesenteric panniculitis as a presentation of Whipple's disease : case report and review of the literature

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Abstract

***Background* : Whipple's disease is a rare, multi-organ disease caused by Tropheryma Whipplei. A classic presentation is characterized by arthropathy, diarrhea and weight loss but a broad spectrum of manifestations is possible. We present a case of a patient with mesenteric panniculitis as a manifestation of WD. A comprehensive review of the literature is provided.**

***Patient* : A 50 year old male presented at the outpatient clinic after an episode of fever and abdominal pain abroad. CT scan showed mesenteric infiltration with associated lymphadenopathies consistent with mesenteric panniculitis. After receiving 6 months of antibiotic therapy abdominal and joint pains improved.**

***Conclusion* : Clinicians should be aware of Whipple's disease. Mesenteric panniculitis is a rare presentation of this possible lethal infection. The golden standard for diagnosing WD is a PAS positive small bowel biopsy. Adequate antibiotic therapy is the cornerstone of treatment and usually leads to an amelioration of symptoms.** (Acta gastroenterol. belg., **2020**, 83, **666-668**).

Key words : infection, Whipple's disease, mesenteric, panniculitis, duodenal biopsy.

Introduction

Whipple's disease (WD) is a rare, multi-organ infection caused by Tropheryma Whipplei. A classic presentation is characterized by arthropathy, diarrhea and weight loss but a broad spectrum of manifestations is possible. In this case report, we present a rather unusual presentation of this possibly lethal infection.

Case history

A 50-year old patient presented at the outpatient clinic after an episode of fever and abdominal pain abroad (Moldovia) 3 weeks before presentation. Since then, he had excessive belching, fever disappeared but epigastric pain after eating persisted. He lost 8 kilograms in 2 months. Stool cultures were normal. Routine blood analysis at the time of the first control was normal (normal leucocytes, liver tests, lipase, creatinine, electrolytes and C-reactive protein). Gastroscopy showed no abnormalities and biopsies for Helicobacter pylori were negative. CT scan showed mesenteric infiltration around the pancreas with associated lymphadenopathies, consistent with mesenteric panniculitis (Figure 1). MRI of the pancreas and PET-CT confirmed the diagnosis of mesenteric panniculitis. Testing for anti-neutrophil cytoplasmic antibodies (ANCA), antinuclear antibodies (ANA), IgG4 and HIV was negative. Colonoscopy was normal. Therapy with traditional analgesics and amitriptyline was not successful. Control CT scan after 3 months did not show any signs of progression nor improvement. Endoscopic ultrasound of the pancreas confirmed the presence of mesenteric infiltration and lymphadenopathies though no biopsy could be taken. In the meantime the patient developed arthralgia. Methylprednisolone 32 milligrams a day was started and, as his general status worsened, this therapy was tapered after 12 weeks and Tamoxifen was associated. Twelve weeks of Tamoxifen use failed to induce clinical resolution. A surgical biopsy was then performed. Histology of the sample showed infiltration of the fat and lymph nodules by histiocytes, with positive Giemsa staining and negative PAS and Grocott staining. These histologic findings could be compatible with Histoplasmosis, but also Leishmaniasis or WD, although a positive PAS staining would be suspected with this last one. PCR on this biopsy for T. Whipplei was negative. Because of the clinical suspicion for WD we performed a PCR on duodenal biopsy and feces which were both positive for T. Whipplei. A diagnosis of WD was thus established. Therapy was started with Ceftriaxone 2 grams intravenous for 2 weeks, followed by 1 year of co-trimoxazol 800/160 milligrams twice daily. To date, after receiving 6 months of therapy abdominal and joint pains improved.

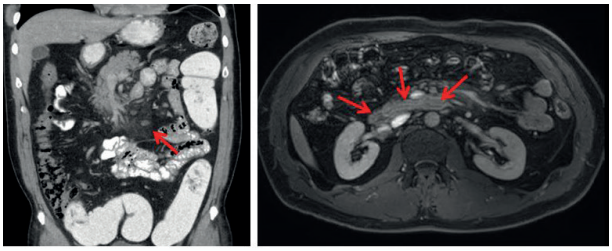

Figure 1. — Diffuse mesenteric infiltration around the pancreas and mesenteric lymphadenopathies on CT scan (left) and T1 mDixon in venous phase (right).

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Discussion

Whipple's disease is caused by T. Whipplei, a host-dependent gram positive, rod shaped bacterium (1). Epidemiological studies estimate the prevalence of WD in northern Italy at around 3 per 1 million with an annual incidence of 1 to 6 per 10 million inhabitants (2). There is a male to female predominance at a ratio of 8:1 and the mean age at diagnosis is 55 years (3). Exposure to T. Whipplei is assumed to result from food produced in contaminated soil and transmission occurs through respiratory and gastrointestinal routes (4). In most people an acute infection is followed by clearance by the immune system, nevertheless in certain individuals bacterial clearance seems to fail. The immune compromised host is particularly at risk for infection with T. Whipplei as demonstrated in a recent case by Lenfant et al. in this journal (5).

Classic WD is characterized by a triad of symptoms : gastrointestinal complaints, arthralgia and weight loss. During the course of the disease, two stages are distinguished which can seldom be followed by a tertiary stage. The prodromal stage is predominated by non-specific symptoms including fever, fatigue and arthralgia. During the second stage involvement of the gastrointestinal tract and weight loss become apparent (6). Gastrointestinal symptoms range from mild abdominal pain to severe diarrhea with a wasting syndrome (7). A late stage of classic WD is characterized by neurological involvement and is generally linked to a more complicated course (6). A rather uncommon presentation of WD is mesenteric panniculitis, as described in our patient. An inflammatory reaction of the abdominal mesentery was already linked to infections with T. Whipplei in the late 1940's but cases have been scarce since then (8). Other etiologies of mesenteric panniculitis are thrombosis, mesenteric arteriopathy, thermal or chemical injuries, vasculitis, avitaminosis, autoimmune disease, retained suture material, pancreatitis, bile or urine leakage, hypersensitivity reactions and recent abdominal surgery (9). The inflammation primarily affects the adipose tissue of the mesentery of the small intestine and colon. A range of abdominal symptoms like vague abdominal pain, bloating, constipation, nausea and vomiting but also weight loss and fever dominate the clinical picture. Lymphadenopathies are not seldom seen in combination with mesenteric panniculitis and were also apparent in our patient. Differential diagnosis of mesenteric panniculitis comprises mostly malignancy (Table 1) (10).

As T. Whipplei resides in the gastrointestinal mucosa, an upper gastroscopy with duodenal biopsies is the preferred method to confirm the diagnosis of WD. There are no macroscopically pathognomonic lesions but a pale yellow color of the mucosa with dilated villi is frequently observed (1). When evaluating samples of mucosa infected by T. Whipplei, a PAS staining is used to unveil foamy macrophages in the lamina propria (Figure 2). The macrophages own their diastase resistant inclusion bodies in the cytoplasm to the remains of degraded parts of T. Whipplei. When eradicated successfully, the remains of T. Whipplei can reside inside macrophages and can be responsible for positive PAS stainings for years after infection (1).

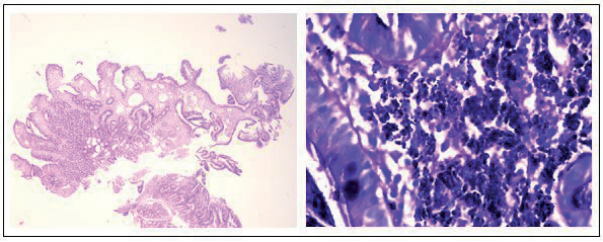

Figure 2. — Left : duodenal biopsy with broadened villi, expanded lymph vessels and macrophages within the lamina propria. Right : PAS positive foamy macrophages concentrated in the lamina propria.

Table 1. — **Differential diagnosis of mesenteric panniculitis**

Differential diagnosis of mesenteric panniculitis
– Lymphomas – Lymphosarcomas – Carcinoid tumors – Desmoid tumors – Infectious diseases (tuberculosis and histoplasmosis) – Peritoneal mesothelioma – Amyloidosis – Desmoplastic carcinoma metastases – Reaction to an adjacent cancer or chronic abscess – Retroperitoneal sarcoma

PCR is the latest of techniques to detect microorganisms and is of great value at diagnosing WD given the high specificity (100%) and sensitivity (96%) (11). This method is particularly useful in patients with clinical suspicion of WD and negative duodenal biopsies, as was the case in our patient. Negative duodenal biopsies are more frequently seen in patients treated with antibiotics on forehand.

Specific antibodies against T. Whipplei antigen can be used to detect its presence in a sample before foamy macrophages are visualized with PAS staining in early stages of WD (12). One should be aware that antibodies against T. Whipplei are also common in asymptomatic carriers and therefore a positive immunohistochemistry does not necessarily indicate a symptomatic infection. A western blot technique can help to differentiate between these two states (13).

Adequate antibiotic therapy has become the cornerstone of treatment and usually leads to an amelioration of symptoms in a few weeks. Multiple regimens have been proposed but the current standard treatment comprises Ceftriaxone 2 grams a day or meropenem 3 grams a day during 14 days, followed by a long term treatment of co-trimoxazol 160/800 milligrams twice daily. Doxycyclin 200 milligrams a day accounts as the most adequate alternative when intolerance to co-trimoxazol is observed (14). The use of corticosteroids and anti-TNF agents is associated with an earlier onset of gastrointestinal symptoms, exacerbations during

therapy and a more complicated course overall (15). Immune reconstitution inflammatory syndrome (IRIS) is the most feared complication when treating a patient with WD. It can be observed in 10% of cases and is the result of a non-specific activation of CD4+ cells. IRIS is characterized by fever, arthritis and pleurisy and can be fatal when adequate therapy, usually oral corticosteroids, is not started within time (12). One should also be aware of the Jarisch–Herxheimer reaction, an exacerbation of skin rashes and fever within 24 hours after antibiotic treatment of spirochetal infections. Recommendations are to arrange a six monthly follow-up with duodenal biopsies as long as T. Whipplei can be detected in invasive samples. Particularly in the first 3 years after diagnosis, when a high suspicion for relapses is needed, follow-up visits should be warranted (6). The use of PCR on non-invasive samples for follow-up is not standardized at the moment (7).

Conclusion

Clinicians should be aware of Whipple's disease and should consider diagnosis in patients with vague symptoms most certainly when accompanied by arthropathy, diarrhea or weight loss. Mesenteric panniculitis is a rare presentation of this possible lethal infection. The golden standard for diagnosing WD is a PAS positive small bowel biopsy but immunohistochemistry and PCR are valuable alternatives and are becoming broad available. Adequate antibiotic therapy is the cornerstone of treatment and usually leads to a rapid amelioration of symptoms. Caution should be taken for IRIS when treating a patient with WD.

Conflict of interest

There was no conflict of interest.

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