Challenging case of Whipple’s disease: The contribution of radiology

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Abstract

Whipple’s disease is a rare chronic infectious disease, caused by Tropheryma whippelii. The disease can be challenging to diagnose due to the variable clinical manifestations and the nonspecific laboratory and imaging findings. We report the case of a 75-year-old man, complaining of weight loss and arthralgias with an insidious onset. A thoracic, abdominal and pelvic CT was performed, demonstrating features suggestive of Whipple’s disease. Although not specific, the imaging findings of fatty attenuation mesenteric and retroperitoneal enlarged lymph nodes are a common finding in Whipple’s disease. Esophagogastroduodenoscopy with duodenal biopsy confirmed the diagnosis through PCR analysis.

Keywords: Whipple disease, Tropheryma whippelii, Arthralgia, Weight loss, Lymph nodes

Introduction

Whipple’s disease (WD) is a rare and chronic infectious condition caused by Tropheryma whippelii, with very good response to antibiotic therapy if the diagnosis is made on time. It usually affects middle-age Caucasian men.

We describe a rare case of Whipple’s disease in a patient with insidious signs and symptoms, like arthralgias and anorexia, in which the imaging findings were the major clue to establish the diagnosis.

Clinical presentation

A 75-year-old Caucasian man was referred to the internal medicine consultation following a 6-month history of asthenia, anorexia and nausea associated with a 10 kg ponderal loss in the 3 months prior. He denied fever, night sweats, abdominal pain, other gastrointestinal or urinary symptoms.

Regarding the past medical history, the patient reported a chronic inflammatory process in the left ankle and oedema in the right first finger’s metacarpophalangeal joint for the last ten years.

The patient was being followed in the haematology consultation due to a Monoclonal Gammopathy of Undetermined

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Significance diagnosed 6 years ago. He developed an iron deficiency anaemia in the last 2 years without identifiable cause.

Physical examination showed cachexia, pale and hydrated mucous membranes. Also, a left supraclavicular mass with roughly 2 cm diameter was noted. The remaining physical examination was normal. Vital signs were within the normal range.

The laboratory data showed microcytic and normochromic anaemia, vitamin B12 and iron deficiency, with normal ferritin; slightly increase in C-reactive protein and erythrocyte sedimentation rate; and hypoalbuminemia. The remaining laboratory workup including coagulation tests, renal and liver function, and thyroid hormones was unremarkable.

Thoracic, abdominal and pelvic CT scan was performed and a left supraclavicular and several retrocrural, retroperitoneal and mesenteric nodules of adipose density (-45HU) were observed (Fig. 1).

The left supraclavicular mass was imaged by ultrasound (Fig. 2) and samples were obtained by ultrasound-guided biopsy. The histopathological analysis revealed them to be non-necrotizing granulomas with giant cells and moderate plasmacytosis. The Periodic Acid-Schiff (PAS) highlights positive granules in macrophages cytoplasm (Fig. 3). Afterwards the esophagogastroduodenoscopy (EGD) was performed to obtain fragments from the duodenum (Fig. 4).

The histopathological examination of the duodenal biopsies showed a diffuse foamy macrophage infiltration of the lamina propria under the intestinal epithelium along with lymphatic enlargement. The macrophage’s cytoplasm also stained positively for PAS (Fig. 5). In the polymerase chain reaction (PCR) analysis performed, 16S rRNA sequence analysis confirmed that the causative microorganism was Tropheryma whippelii.

After the diagnosis of WD has been made, the patient was prescribed with 2 mg/day IV ceftriaxone therapy for 2 weeks, followed by twice daily trimethoprim-sulfamethoxazole (160 mg TMP-800mg SMX) for 12 months. Clinical improvement was observed within days, shown by the recovery of appetite and weight gain (10 kg over 6 months), along with the normalization of all laboratory findings within months.

Discussion

Regarding clinical and imaging data, the differential diagnosis was liposarcoma, lymphoma, atypical granulomatous infection and WD, the latter confirmed with PCR analysis.

WD was first described by the pathologist George Hoyt Whipple in 1907, and it is a rare multisystemic inflammatory condition resulting from infection by the Gram-positive bacterium Tropheryma whippelii [1].

WD is more prevalent in Caucasian men, and although it may occur at any age, the diagnosis is most frequently made in patients between 50 and 60 years of age. Its reported annual prevalence is 3/1000000 and the annual incidence is approximately 0.1–0.6/1000000 new cases in Western countries [2,3].

Classically, the disease has an insidious onset, often taking several years until definitive diagnosis is made. The manifestations are variable, being weight loss, diarrhoea/malabsorption, polyarthritis (typically palindromic, mi-
Fig. 2 – Ultrasound image showing left supraclavicular solid nodule, homogeneous hyperechoic, with circumscribed margins and 26 mm of diameter.

Fig. 3 – Supraclavicular sample. Twenty times magnification, PAS staining. Non-necrotizing granulomatous lymphadenitis: macrophages with intracytoplasmic granules PAS-positive are readily apparent.
Pericarditis with negative blood culture is the most frequent cardiac manifestation [4].

Although, laboratory features are variable and nonspecific, anaemia, hypalbuminaemia and nutrient malabsorption (eg, iron) are the most common findings. Most patients present with increased inflammatory parameters, like an elevated erythrocyte sedimentation rate, C-reactive protein and thrombocytosis [2,6].

The imaging findings are also nonspecific and the literature on this topic is scarce. US findings of diffusely hyperechoic lymphadenopathies in the retroperitoneum and mesenteric fat are the most typical changes in the WD; a thickening of the small bowel’s wall with moderate dilatation and disappearance of normal wall stratification are also common [7–10].

The CT features include thickening of small bowel folds sometimes with a nodular appearance, together with enlarged abdominal lymph nodes with very low attenuation [10,11].

Gastrointestinal WD has a wide spectrum of endoscopic appearance. The endoscopic examination reveals pale yellow and shaggy mucosa alternated with eroded, erythematous, or mildly friable mucosa in the duodenum and/or jejunum, suggesting infectious or inflammatory small bowel pathology [4,12,13].

The most distinguished pathophysiologic characteristic of WD is massive infiltration of PAS-positive granules in foamy macrophages in the lamina propria of the small intestine, namely duodenum. After suspecting WD on the pathological evaluation of biopsy samples, PCR analysis to detect the specific 16S rRNA sequence of the bacterium is mandatory for a definitive diagnosis [14,15].

Without treatment, WD is invariably fatal. Currently, the recommendation is to initiate therapy with an intravenous
cephalosporin (eg, ceftriaxone) or β-lactam (eg, meropenem),
followed by long-term trimethoprim-sulfamethoxazole (160 mg
TMP-800 SMX twice daily) for at least 12 months [16,17].
The patient was treated with 2 mg/day IV ceftriaxone ther-
apy for 2 weeks, followed by twice daily trimethoprim-
sulfamethoxazole (160 mg TMP-800 SMX) for 12 months.
Response to treatment is generally good and it should be
monitored by clinical examination. PCR analysis should be
considered if there are new symptoms [2,4,10].

Conclusions

Diagnosing WD remains challenging since there are no spe-
cific clinical, laboratorial or imaging findings. However, the de-
gree of suspicion of the condition can be heightened when the
set of all those findings are correlated together.
This case shows that the imaging features seen on CT
scan, such as enlarged and hypoattenuating (adipose tissue
density) cervical, retrocrural, retroperitoneal and mesenteric
adenopathies, which also correspond to hyperechoic lymph-
adenopathies on US, were pivotal to suggest and establish
this diagnosis.

Patient consent

An informed consent was obtained from the patient.

Declaration of Competing Interest

The authors declare no conflict of interest.

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