

Severe malnutrition with Whipple's disease

Whipple Disease (WD) is a rare, chronic and multisystem infection caused by *Tropheryma Whipplei* (TW). The bacterium was isolated and characterized less than 20 years ago by sequencing its ribosomal RNA (rRNA). The TW bacterium is transmitted amongst humans, via the oro-oral and the feco-oral routes. It is an opportunistic bacterium and can be found in the stool in asymptomatic carriers.¹ Recent studies have shown an increased incidence in middle-aged Caucasian populations, especially if exposed to animals or soil. The infection is endemic in some African developing countries.

WD most often affects the gastrointestinal system, interfering with normal digestion and absorption of nutrients.² WD can involve the whole body, but the most common symptoms are weight loss, diarrhea, vomiting, joint pain and swelling of the legs. Intestinal biopsy and histopathology demonstrating the presence of foamy, PAS-positive macrophages is highly suggestive of WD, which is confirmed by PCR of bacterial DNA.³

The disease, if not correctly identified and treated, can be fatal.

The type and duration of therapy for WD is still under discussion and different treatment protocols are currently followed in different countries.

Case Report

The present case is that of a 66 year old Caucasian woman from Terracina (LT), Italy, who had no significant past medical history and hadn't been hospitalized for any reason previously. The patient denied drinking alcohol or smoking, or recent travel. She did not report any significant family history.

The patient presented to the Emergency Department (ED) of "Policlinico Gemelli" Hospital in Rome. She complained of asthenia, decreased appetite and weight loss (35 kg) for 2 years, and vomiting and diarrhea for 1 year. The patient was under-weight, with skin noted to be dry and of greyish discolouration (**Figures 1 and 2**).

Infectious etiology as the cause of GI disease



Figure 1: Deformed hands with signs of arthritis and muscle atrophy.



Figure 2: Dry and greyish skin.

had been excluded previously by negative stool cultures for parasites, *Shigella*, *Salmonella*, *Campylobacter*, *Giardia* and *Clostridium difficile* toxin, confirmed with our tests. Six months previously, the patient underwent a colonoscopy, which was negative for colonic pathology, and upper GI endoscopy with evidence of hyperemia of the gastric antrum and scalloped folds in the duodenum. Biopsies were taken, which excluded *H. pylori* infection, but demonstrated villous atrophy, compatible with celiac disease. However, the lab results were negative for, anti endomysium IgA and anti-transglutaminase IgG and IgA. The patient also provided a history of intermittent joint pain, with morning stiffness in both ankles. She was prescribed steroid therapy (prednisolone, 16 mg daily), and NSAIDs, without any evidence of response.

Our laboratory blood tests showed anemia (9.8 g/dl), high C-RP value (31 mg/l, reference range 0-5 mg/l), high procalcitonin (0.74 ng/ml, reference value <0.15 ng/ml) and a low albumin (2.5 g/dl, reference range 3.5-5.5 g/dl). With the suspicion of Whipple Disease, we performed an upper GI endoscopy with biopsies. The endoscopy revealed a diffuse whitish stippling, suggestive of lymphoid hyperplasia, a diffuse pattern of mucosal involvement with breaks, villous atrophy and disarranged mucosa. Scalloping of the small bowel folds were also noted. Biopsies of the duodenal wall revealed a rich population of macrophages in the lamina propria of the mucosa, with characteristic PAS-diastase positive cytoplasmic inclusions, in agreement with the clinical suspicion (**Figures 3 and 4**).

Following the treatment suggested by Fenollar et al., we treated the patient with a combination of doxycycline (100 mg BD) and hydroxychloroquine (200 mg TID).⁴ We periodically followed the patient and after 6 weeks of treatment, she gained 4 kg in weight with normalizations of her bowel habits. Most of her symptoms dramatically improved. In particular, the patient did not complain of joint pain, asthenia and vomiting anymore. After six months, the medical examination showed an increased in weight of 14 kg, and stable bowel habits since previous check. The patient underwent an endoscopic capsule control, with the PillCam capsule endoscopy (Given Imaging, Yoqneam, Israel), according to the standard protocols. The capsule endoscopy documented a persistent villous atrophy, but an improvement in disarranged mucosa and breaks. Laboratory tests showed hemoglobin of 10.7 g/dl, calcium of 8.6 mg/dl, C-RP 7.98 mg/l and albumin of 3.3 g/dl.

Discussion

Signs and symptoms of WD are variable and polymorphic, and about 15% of patients do not have the classic abdominal and joint manifestations. On the other hand, etiological diagnosis is crucial due the potential mortality of WD, if untreated. Our patient, after only 6 weeks of treatment, showed marked improvement of her clinical condition with progressive weight gain. Clinical improvement was associated with a normalization of

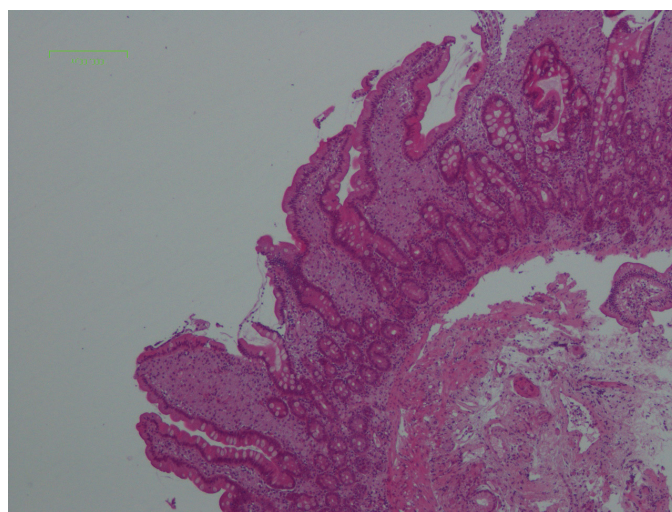


Figure 3: Duodenal mucosa section showing villi distorted by macrophage collections in the lamina propria (Hematoxylin-eosin 4x).

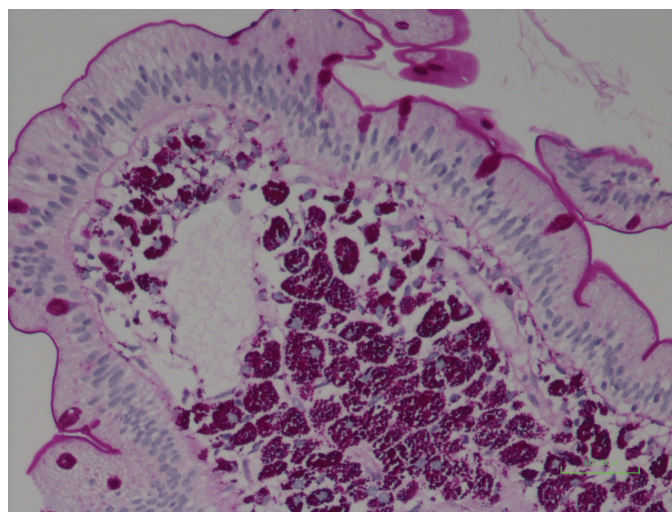


Figure 4: Higher magnification of the infiltrate stained with PAS stain (40X) showing multiple rounded PAS-positive, diastase-resistant inclusions present in the macrophages in the lamina propria.

laboratory tests with progressive increase in hemoglobin, calcium and albumin values. Regular follow up of these patients is essential, with a complete physical examination along with periodic duodenal biopsies and PCR study. The alteration in villous mucosa may persist for many years despite the clinical improvement.

One interesting point to note in our report is that our patient visited multiple specialists over many years

and was thought to have a malabsorption syndrome. However, her condition was not definitively diagnosed and she progressed to become malnourished and severely emaciated. Due to the rarity of WD, the specific PAS staining was never performed, which led to the delay in her diagnosis.

A recently published paper described a case of WD diagnosed by the capsule endoscopy [5], this non-invasive and innovative technique could be utilized in future to follow-up these patients and to verify the resolution of macroscopic findings. We decided to follow up our patient using capsule endoscopy rather than perform endoscopic procedures, which are very uncomfortable and alternatively requires sedation. Capsule endoscopy allowed us to document easily the progressive improvement of lesions and villous regrowth, which are two very important prognostic parameters.

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A rare cause of obstructive jaundice - VHL syndrome

Von Hippel-Lindau syndrome (VHL), is a rare genetic disorder characterized by visceral cysts and benign tumors in multiple organ systems. It is an autosomal dominant condition associated with hemangioblastomas of the central nervous system and retina, renal cysts, renal cancer, pheochromocytoma, pancreatic cysts, tumours of the endolymphatic sac in the ear and epididymal cystadenomas. Pancreatic involvement, especially as isolated organ involvement, is not common in patients with VHL.^{1,2} Most pancreatic lesions are simple cysts and rarely cause symptoms or develop into malignant tumors. Extrahepatic biliary obstruction secondary to pancreatic cysts is a rare occurrence in VHL syndrome.^{3,4} We describe a patient with VHL who had biliary obstruction due to pancreatic cysts.

Case Report

A 30 year old female patient presented with jaundice for 25 days, gradual onset and progressive, with generalised pruritus and pale coloured stools. There was no history of fever, vomiting, abdominal pain, abdominal distension, melena, hematemesis, pedal oedema, night blindness, bleeding gums or diarrhoea. The patient gave a history of having undergone brain surgery, the details not available. There was history of visceral cystic lesions in her elder sister. On physical examination, scratch marks were present all over the body. The right kidney was palpable. A cystic lesion was palpable in epigastrium.