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A juvenile, misdiagnosed case of Whipple's disease

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Dear Editor,

Whipple's disease (WD) is a rare syndrome which generally occurs in patients aged more than 50 years, especially in farmers, carpenters, and gardeners (1). WD may present with different and not specific symptoms, so that diagnosis is frequently a challenge for physicians. An appropriate, long-term antibiotic therapy is effective, and untreated disease is lethal (2). Therefore, a prompt diagnosis is mandatory.

A 37-year-old male baker, with a compensated hypothyroidism, complained of migrant polyarthralgias in 2005, and a diagnosis of seronegative joint disease was performed. Patient received a therapy with ibuprofen (400 mg b.i.d) for 6 months, and a steroid therapy (prednisone 16 mg/day) was added due to persistence of symptoms. A methotrexate (100 mg/die) therapy was started after 6 months, tapering steroid therapy. Five months later, patient complained of severe diarrhoea (10-15 bowel movements/day), vomiting, anorexia, low-grade fever, and progressive, severe weight loss (22 kg), and he was admitted to our Unit on May 2007. At entry, sideropenic anaemia (haemoglobin 10 g/dl; ferritin 17 ng/dl), increased ESR to 25 mm/h, and increased leucocytes count with $15,2 \times 10^9/L$ (neutrophils: 78%). A small bowel follow-through (x-RAY) and a pancolonscopy were unrewarding. A contrast-enhanced computed tomography showed thickness of the mesenterial adipose tissue with several perigastric, para-aortic, and para-oesophageal lymphnodes enlargement. Upper endoscopy revealed several intraepithelial haemorrhages and red spots on enlarged duodenal folds (Figure 1). The histological assessment on the duodenal biopsies showed intestinal villi filled with white material, and clear signs of lymphangiectasia. In the lamina propria, we observed a severe infiltration by foamy macrophages with a coarse granular cytoplasm which stained strongly with the period acid-Schiff reagent (Figure 2), and WD disease diagnosis was performed. Real-time PCR on paraffin-embedded duodenal biopsy specimens confirmed the infection by

Tropheryma whipplei. A trimethoprim/sulfamethoxazole therapy (160/800 mg b.i.d) was administered for 1 year. In June 2008, the patient was totally asymptomatic and a 10 kg increased body weight was registered.

WD was firstly described in 1907, but only in 1992 *Tropheryma whipplei*, a rod shaped bacterium, was identified in culture as aetiological agent of the disease (1). Although WD has traditionally been regarded as a gastrointestinal disease, most cases begins insidiously with arthropathy. Indeed, in a large series, a seronegative joint disease was the first symptom in 63% of patients, preceding gastrointestinal symptoms by some years (1). Those subjects which are in contact with soil (farmers, carpenters, gardeners) are at increased risk of WD, and a distinctly higher prevalence in males (M/F = 8:1) has been reported (1). WD in our patient, which was young and without professional risk, started with a seronegative joint disease, requiring methotrexate therapy. Gastrointestinal symptoms occurred 11 months following immunosuppressive therapy (6 months steroid plus 5 months methotrexate therapy), however he was referred to our Gastroenterology Unit only 5 months later with an important weight loss. Since WD is a lifethreatening and potentially lethal disease (1), we would emphasize that the onset gastrointestinal symptoms in a patient with a seronegative joint disease, especially during immunosuppressive treatment (3), should prompt the suspect of WD. Indeed, although methotrexate does not alter Th1/Th2 balance, it reduces cytokine production by T-helper cells (4) and it has been reported that low activity of Th1-helper cells could favour clinical manifestations of WD after systemic dissemination (1).

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Figure legends.

Fig. 1. Endoscopic features of the duodenal mucosa.

Fig. 2. PAS positive macrophages diffuse infiltration of duodenal mucosa.

