Letters to the Editor

A case of Whipple disease with pleural effusion diagnosed by means of PCR

Sirs,

Whipple disease (WD) is an uncommon entity, and it is probably diagnosed only late in its disease course. Exact data regarding incidence and prevalence of this condition are not available (1, 2). Most patients have intestinal involvement when the physician in charge of the patient considers a diagnosis of WD. At present the diagnosis of WD is based on the documentation in biopsies of involved tissues, not exclusively in the gut, of *Tropheryma whippelii* (1). T-cell defects in WD patients have been observed in several studies (3). It is supposed that this defect is not acquired but rather inherited as indicated by the detection of HLA-B27 in approximately 40% of the affected patients. However, Olivieri *et al.* reported a lack of association with spondyloarthritis and HLA-B27 in Italian patients with Whipple's disease (4).

We report a recently diagnosed case of WD in our Division, who presented with articular involvement, diarrhea and constitutional symptoms and developed serohematic pleural effusion during admission.

A 44-year-old man was admitted to hospital because of arthritis and diarrhea. He complained of a 2-year-history of episodes of intermittent migratory arthralgias and arthritis involving the knees, wrists and ankles of generally less than a week of duration for each episode. He had been treated with NSAIDs and low doses of prednisone with partial and transient improvement. One month before admission, he began with a new episode of frank arthritis in the wrists along with diarrhea. He lost 5 kg since the onset of diarrhea. On physical examination only arthritis in both wrists was found. The ESR was 45 mm/1h and the C reactive protein 122 mg/L. Chest and hands radiographs, routine biochemistry profile, including renal and hepatic function tests, ANA, anti-native DNA, C3, C4 and anticardiolipin antibodies were normal or negative. HLA-B27 test was positive. Upper gastrointestinal endoscopy showed whitish-yellow plaques alternating with erythematous and mildly friable mucosa in the post-bulbar region of the duodenum. During his stay in the hospital and while he was waiting for the duodenal biopsy, he developed dyspnea and pleuritic chest pain. Chest radiograph showed right pleural effusion (Fig. 1). A thoracocentesis yielded a serohematic fluid. Pleural effusion analysis showed glucose 89 mg/dl, proteins 2.65 mg/dl, LDH 203 IU/1, 6.600.000 erythrocytes/mm^3, leucocyte/mm^3 (with 62% polymorphonuclear cells) and adenosine deaminase 18 U/1. Cultures and cytology analyses were negative. An angio-computed tomography scan excluded the presence of pulmonary embolism.

A duodenal biopsy showed widened villi with dilated lacteals with normal crypt-to-villus ratio. The lamina propria was expanded by numerous histiocytes with granular cytoplasm. Also, PAS-positive material (rod-shape) in the histiocytes of the lamina propria was found (Fig. 2). Polymerase chain reaction (PCR) detection identified *Tropheryma Whippelii* (Fig. 3). A diagnosis of WD was established and treatment with cotrimoxazole 160 mg trimethoprim/800 g sulphamethoxazole twice daily was begun. Following this therapy the patient improved with total resolution of arthritis, diarrhea and pleural effusion. Also, his body weight got back to the normality. A new PCR performed 3 months after the onset of therapy disclosed a less intense band that supported the clinical improvement (Fig. 3). The patient was treated for 1 year. At that time the patient was free of symptoms and a new upper gastrointestinal endoscopy was normal. Most organs can be involved in WD (5). About 60% of the cases had peripheral arthritis preceding the diagnosis by a mean of 6 years. Our case had peripheral arthritis involving wrists, knees and ankles that preceded the diagnosis approximately by 2 years. Only when he developed gastrointestinal symptoms a diagnosis of WD was suspected.

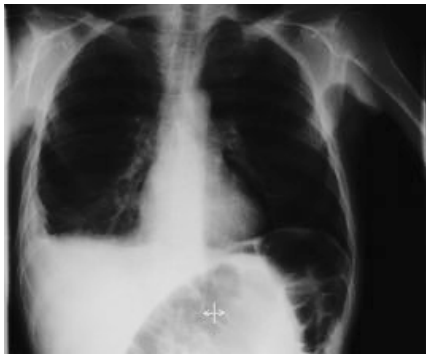

Fig. 1. Chest radiograph showing right pleural effusion in the setting of WD.

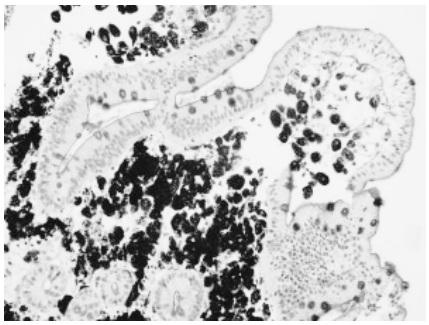

Fig. 2. Duodenal biopsy showing numerous PAS-positive diastase-resistant rods in the histiocytes of the lamina propria.

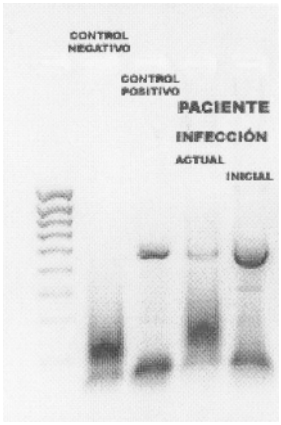

Fig. 3. PCR results for specific bacterial 16SrRNA gene of *Tropheryma Whippelii* performed on duodenal tissue sample.
"Control negativo" means negative control.
"Control positivo" means positive control.
"Inicial" means band obtained from duodenal tissue sample obtained at the time of diagnosis.
"Actual" means band obtained from duodenal tissue sample obtained from a new upper gastrointestinal endoscopy performed 3 months after the onset of treatment.

Of note, our patient suffered a serohematic pleural effusion but pulmonary manifestations are rarely observed in patients with WD. To the best of our knowledge, serohematic effusion has not been previously reported in patients with this disease. Although we could not bring about PCR techniques in the pleural effusion, the presence of this manifestation in the context of the disease suggests that it may be also related to WD.

Major advances made recently in the techniques for detecting and isolating the causative agent of WD may show that this condition is more common than previously considered. Also, the presence of serohematic pleural effusion in our case suggests that WD may be associated with a broader clinical spectrum than previously reported.

A routine use of PCR techniques in the synovial fluid might be useful in making a more precise and early diagnosis of patients with arthritis without obvious etiology.

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References

1. LANGE U, TEICHMANN J: Whipple arthritis: diagnosis by molecular analysis of synovial fluid—current status of diagnosis and therapy. *Rheumatology* 2003; 42: 473-80.
2. PUECHAL X: Whipple disease and arthritis. *Curr Opin Rheumatol* 2001; 13: 74-9.
3. MARTH T, RAOULT D: Whipple's disease. *Lancet* 2003; 18:239-46.
4. OLIVIERI I, BRANDI G, PADULA A *et al.*: Lack of association with spondyloarthritis and HLA-B27 in Italian patients with Whipple's disease. *J Rheumatol* 2001; 28: 1294-7.
5. MAHNEL R, MARTH T: Progress, problems, and perspectives in diagnosis and treatment of Whipple's disease. *Clin Exp Med* 2004; 4: 39-43.