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Distinguishing tropical sprue from celiac disease in returning travellers with chronic diarrhoea: A diagnostic challenge?

Marijke C.C. Langenberg [a,1], Pieter J. Wismans [b], Perry J.J. van Genderen [a,b,*]

[a] *Institute for Tropical Diseases, Department of Internal Medicine, Harbour Hospital Rotterdam, Haringvliet 2, 3011 TD Rotterdam, The Netherlands*
[b] *Travel Clinic Havenziekenhuis, Haringvliet 72, 3011 TD Rotterdam, The Netherlands*

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Summary *Background:* Within the present era of worldwide travel, it is important for all clinicians to consider the possibility of tropical sprue (TS) in returning patients with persistent diarrhoea after travel. The symptoms and histologic findings of TS can resemble but also be confused with celiac disease (CD).
Material and method: Patients at our institute diagnosed with CD or TS in the period January 2000–December 2010 were eligible for inclusion. Of all patients, demographic, clinical, laboratory and endoscopy data on admission and in follow-up were collected retrospectively.
Results: 28 CD and 7 TS patients were included. There were no differences in baseline clinical characteristics, duration of stay in a tropical region or in laboratory findings on admission. However, in the majority of CD patients antibodies against endomysium (EMA) or tissue transglutaminase (tTG) were present at presentation but absent in all TS patients at presentation.
Conclusions: In returning travellers with persistent diarrhoea, a diagnosis of CD is unlikely in case of absence of anti-EMA or anti-tTG antibodies but conversely increases the likelihood of TS. This distinct immunoserological profile may be of help in selecting the optimal treatment in returning travelers with chronic diarrhoea after staying in a tropical region.

* Corresponding author. Institute for Tropical Diseases, Department of Internal Medicine, Harbour Hospital Rotterdam, Haringvliet 2, 3011 TD Rotterdam, The Netherlands. Tel.: +31 10 4043305; fax: +31 10 4121645.
E-mail addresses: mcclangenberg@gmail.com (M.C.C. Langenberg), p.wismans@havenziekenhuis.nl (P.J. Wismans), p.van.genderen@havenziekenhuis.nl (P.J.J. van Genderen).
[1] Current address: LUMC, Albinusdreef 2, 2333 ZA Leiden, The Netherlands.

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1. Introduction

Tropical sprue (TS) is a rare chronic diarrhoeal disease of unknown aetiology, characterized by malabsorption due to abnormal flattening of the intestinal villi and inflammation of the mucosal lining of the small intestine. The illness usually starts with bouts of diarrhoea, fever and malaise. Thereafter a chronic phase of fatty diarrhoea, weight loss and malaise may ensue. The occurrence of TS is most prevalent in the indigenous population of South East Asia and South America [1] but may also affect expatriates, even after their return from tropical regions [2]. The resolution of symptoms after long-term antibiotic treatment with tetracycline or sulphamethoxazole/trimethoprim combined with vitamin supplementation suggests an infectious cause even though a causative micro-organism has never been demonstrated undisputedly [3—5]. Others suggest some overlap between TS and post-infectious irritable bowel syndrome (IBS), in particular of diarrhoea-predominant IBS [6].

Although being endemic in certain tropical regions of the world, TS is rarely seen in Europe and North America. Within the present era of globalization and worldwide travel, it is important for all clinicians to consider the possibility of TS in returning patients with persistent gastrointestinal complaints like diarrhoea and weight loss after travel, given its need for a specific treatment. The symptoms and histologic findings of TS, however, can resemble but also be confused with diseases that are more commonly seen in non-tropical climates like celiac disease (CD). CD is considered to reflect a systemic autoimmune disorder triggered by dietary gluten, a protein complex found in wheat, rye and barley, in genetically predisposed individuals of all ages from middle infancy onward. With a reported prevalence of up to 1% in West Europe [7], CD is probably one of the most likely diagnoses to consider in patients with chronic diarrhoea, regardless of any travel history.

However, if the usual causes of persistent diarrhoea are ruled out, keeping a high index of suspicion for TS in patients with a travel history to one of the endemic regions remains nevertheless important, given its need for a specific treatment. We wondered whether there are certain clinical or laboratory features more or less specific for TS, which may be of help for selecting the optimal treatment regimen in returning travellers with chronic diarrhoea. To allow a proper comparison, we compared the specificity of clinical and laboratory features of TS patients with a cohort of CD patients diagnosed in the same period at our institution.

2. Material and method

This retrospective cohort study was performed at the Harbour Hospital, Rotterdam, The Netherlands. The Harbour Hospital is a 161-bed general hospital near the Port of Rotterdam and also accommodates the Institute for Tropical Diseases, a national referral centre for tropical diseases in The Netherlands. All patients at our Institute aged above 18 years and diagnosed with either tropical sprue (TS) or celiac disease (CD) in the period January 2000—December 2010 were eligible for inclusion.

2.1. Definitions

The diseases TS and CD were diagnosed routinely based on clinical and laboratory data and the results of endoscopic evaluation of the upper gastrointestinal tract. CD and TS were diagnosed when patients had compatible histopathologic changes in small bowel biopsies (which included an increased number of intraepithelial lymphocytes, elongation of crypts and partial to total villous atrophy) in an appropriate epidemiological setting and an appropriate response to treatment. To that end, follow-up visits had to properly record the subsequent response to treatment and clinical course. All small bowel biopsies were graded according to the modified Marsh criteria [8]. Patients without histopathologically confirmed changes of small bowel mucosa were excluded, as were patients without evaluable clinical data or those lost to or without appropriate follow up. Of all patients, demographic, clinical, laboratory and endoscopy data on admission were collected retrospectively, with the use of a standardized data extraction form. All data was stored in an electronic database after de-identification of the individual patient data.

2.2. Statistical analysis

For comparisons between groups TS and CD, the Fisher's exact test was used for categorical variables. The unpaired *t*-test or Mann—Whitney test was used for continuous variables depending on their distribution. Categorical variables arranged in a natural order (*e.g.* duration of complaints and Marsh classification for villous atrophy) were compared between groups with the Chi squared test for linear trend. *P*-values <0.05 were considered statistically significant. The SPSS software package (version 17.0) or GraphPad InStat 3.0 was used for statistical analysis.

2.3. Ethical considerations

Given its retrospective observational (non-interventional) design and use of de-identified data, ethical approval of this study was not required, according to the Dutch Medical Research Involving Human Subjects Act.

3. Results

In the study period CD was diagnosed in 40 patients. Twelve patients with CD were excluded; in three cases clinical records were missing and in 9 patients there was no histopathologic confirmation of CD, leaving 28 patients fulfilling the inclusion criteria. TS was diagnosed in 8 patients. One TS patient was excluded because histopathologic documentation of villous abnormalities was lacking and clinical data were insufficient, leaving 7 eligible TS. As shown in Table 1, there were no differences in gender, age, duration of stay (including long-term stay) in a tropical region, duration of complaints and signs and symptoms between patients diagnosed with TS and CD. Of the general laboratory findings, patients with CD had significantly lower haemoglobin levels on admission as compared with TS