Eosinophilic vasculitis: A rare presentation of Whipple’s disease

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Whipple’s disease is a multisystem infectious disease caused by the bacterium Tropheryma whippelii. A case with an unusual presentation is reported. A 66-year-old man presented with a febrile vasculitic rash on his forearms. An extensive rheumatological, hematological and infectious workup gave negative results, apart from mild anemia and eosinophilia. An abdominal computed tomography revealed a retroperitoneal lymphadenopathy, and a skin biopsy revealed an eosinophilic vasculitis. This diverted the work toward ruling out a lymphoma or a vasculitic process. A lymph node biopsy was then performed which revealed a diffuse neutrophilic inflammation with abundant foamy macrophages, fat necrosis and lipogranuloma formation. These findings were considered to be nonspecific, and no further pathological investigation was carried out. After a course of corticosteroids, diarrhea and weight loss predominated and subsequently a diagnosis of Whipple’s disease was confirmed on a small-bowel biopsy. Lymph node involvement was then confirmed on re-evaluation using the appropriate stains.

Key Words: Eosinophilic vasculitis; Lymphadenopathy; Whipple’s disease

Vascularite éosinophilique : Manifestation rare de la maladie de Whipple

La maladie de Whipple est une maladie infectieuse plurisystémique causée par la bactérie Tropheryma whippelii. On fait ici état d’un cas inhabituel : un homme de 66 ans s’est présenté avec une éruption fébrile de type vasculaire aux avant-bras. Des analyses complètes, rhumatologiques, hématologiques et bactériologiques ont donné des résultats négatifs, sauf une anémie et une éosinophilie légères. La tomographie abdominale a révélé une lymphadénopathie rétropéritonéale et la biopsie cutanée a révélé la présence d’une vascularite éosinophilique. Cela a permis de réorienter les démarches afin d’écarter un diagnostic de lymphome ou de vasculaire. Une biopsie d’un ganglion lymphatique a ensuite été réalisée et a révélé une inflammation neutrophilique diffuse, accompagnée de macrophages spumeux abondants, de nécrose graissuse et de formation de lipogranulomes. Ces observations ont été considérées non spécifiques et aucune autre analyse anatomopathologique n’a été effectuée. Après une corticothérapie, la diarrhée et la perte de poids ont prédominé et, par la suite, un diagnostic de maladie de Whipple a pu être confirmé grâce à une biopsie du grêle. La atteinte des ganglions lymphatiques a ensuite été confirmée lors d’une réévaluation au moyen des colorants appropriés.
sedimentation rate of 37 mm/h. His serum albumin level was 20 g/L but his liver profile was otherwise normal. His serum tissue transglutaminase antibody level was normal. He underwent a gastroscopy, and duodenal biopsies were obtained that revealed subtotal effacement of the intestinal villi with blunting as well as diffuse infiltration of the lamina propria by foamy macrophages (Figure 2). This histology was consistent with Whipple’s disease and the diagnosis was confirmed by periodic acid-Schiff (PAS) staining which coarsely dyed the intracytoplasmic granules. At this time, the pathology of the abdominal lymph node was reinvestigated and the diagnosis of Whipple’s disease involving the lymph node was made (Figure 3). It was confirmed by the PAS-positive reaction of the infiltrating macrophages in a fashion similar to the intestinal biopsy (Figure 4).

The patient was treated with a two-week course of intravenous ceftriaxone and later, trimethoprim and sulfamethoxazole (one double-strength tablet taken twice a day) were administered, with a plan to continue the treatment for one year. Within the first few weeks of treatment, his diarrhea resolved and he started gaining weight.

**DISCUSSION**

The typical clinical manifestations of Whipple’s disease, namely diarrhea, weight loss and malabsorption, are present in the majority of patients at the time of diagnosis (3). However, these symptoms are usually preceded by a wide range of symptoms such as arthralgias and abdominal pain, and general systemic features such as fever and weight loss. Neurological and cardiovascular manifestations occur typically late in the course but have been described at the initial presentation in the absence of significant gastrointestinal complaints, making the diagnosis of this rare disease further challenging.

In the current case, the presentation was a vasculitic skin rash, fever and eosinophilia. Rarely has cutaneous manifestations been an early feature in this disease, and apart from five documented cases (6-10) in the literature of direct Whipple’s involvement, cutaneous manifestations are generally
nonspecific and related to malnutrition – hyperpigmentation, urticaria, erythrodtema and subcutaneous nodules. In the present case, cutaneous involvement with Whipple’s disease was ruled out by re-examining the skin biopsy with PAS staining after Whipple’s disease had been diagnosed.

We consider eosinophilic vasculitis to be a secondary manifestation of Whipple’s disease. This is based on the temporal relationship between the appearance of the eosinophilic rash and the gastrointestinal symptoms, as well as the presence of eosinophils in the skin, small bowel and lymph nodes.

The diagnosis in the present case was delayed because of the unusual initial presentation leading to the workup directed toward a vasculitic process or a lymphoma. The correct diagnosis of Whipple’s disease could have been reached earlier if it had been included in the differential diagnosis of abdominal lymphadenopathy and diarrhea.

Recently noninvasive testing using the polymerase chain reaction test for \textit{T. whipplei} has been introduced, and probably explains the increased incidence of this disease (2). Similarly, the presence of foamy macrophages has been described in many organs in patients with Whipple’s disease. Such extraintestinal involvement is not well characterized and can be missed if the appropriate stains are not used, as in the present case.

**CONCLUSION**

Although rare, Whipple’s disease should still be in the differential diagnosis of any unexplained digestive disease associated with intra-abdominal lymphadenopathy or systemic manifestations (Table 1). It is not uncommon that Whipple’s disease has extraintestinal involvement (lymph nodes, liver, spleen, etc), so diagnostic suspicion should be heightened when an abundance of histiocytes accompanied by inflammatory infiltrates are seen. In such cases, a PAS stain or \textit{T. whipplei} polymerase chain reaction test should be considered.

**Eosinophilic vasculitis: A presentation of Whipple’s disease**

**TABLE 1**

<table>
<thead>
<tr>
<th>Differential diagnoses of abdominal lymphadenopathy and recurrent diarrhea</th>
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<tbody>
<tr>
<td>• Lymphoma</td>
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<td>• Celiac disease</td>
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<td>• Crohn’s disease</td>
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<tr>
<td>Tuberculosis</td>
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<tr>
<td>Clostridium difficile</td>
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<td>Histoplasma capsulatum</td>
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**REFERENCES**
