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Case report

Globular amyloidosis of the colon

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ABSTRACT

Gastrointestinal involvement is frequent in systemic amyloidosis. However, amyloidosis can rarely be confined to the gastrointestinal tract or appear as a tumour mass. There have been few reports describing amyloid globular deposits in a variety of locations, as opposed to the usual linear ones. We herein report a rare case of globular amyloidosis involving the large bowel, which to the best of our knowledge is the second reported in the world literature.

A 74-year-old man consulted on anaemia. Endoscopy showed ulcerative lesions in the left colon, which were biopsied and diagnosed as ischemic colitis. Under light microscopy, we found globular discrete deposits in the lamina propria which were Congo red-positive and resistant to permanganate digestion. Histopathological diagnosis was globular amyloidosis with AL deposits. The patient underwent further studies, including a haematologic evaluation that discarded systemic involvement.

Globular amyloidosis seems to be a rare morphologic type of amyloidosis, but not a distinct entity. Its etiology, pathogenesis and relationship with patient prognosis and disease severity remain largely unknown. When amyloid deposits are confined to the gastrointestinal tract, systemic therapy can be avoided and patients should only be followed periodically. Immunohistochemical classification and clinical correlation are essential to rule out systemic amyloidosis.

Introduction

Amyloidosis is a heterogeneous disease characterized morphologically by deposition of protein fibrils which stain orange-red with Congo red and show green birefringence on polarizing microscopy due to their b-plate sheet configuration. Amyloidosis encompasses at least five different disorders with different types of protein deposits: light chains (AL), serum amyloid A (AA), transthyretin (ATTR), β2-microglobulin (Aβ2M) and senile amyloidosis [1,2]. The overall prevalence of amyloidosis ranges from 0.50% to 0.89%, and gastrointestinal (GI) tract is involved in 70%-100% of cases [3,4]. Diffuse deposition of amyloid in the GI tract occurs in many chronic systemic diseases, but localized deposits are uncommon [5,6]. Moreover, amyloid typically shows a linear pattern under light microscopy, and there have been only isolated reports of globular amyloidosis. Globular amyloid has been reported mainly in liver specimens, with 25 hepatic cases described to date [7]. Regarding GI tract involvement, only 4 case reports of globular GI amyloidosis have been published. These reports include 9 patients: 5 of them with systemic amyloidosis, 3 with localized amyloidosis of the GI tract, and a patient who was still being assessed at the time of reporting [1,5,8,9]. The clinical implications of this morphologic variant of amyloidosis are largely unknown [8].

Case report

A 74-year-old man consulted on anaemia. He had no medical history of chronic inflammatory disease, renal failure or familial amyloidosis. Several tests were performed to find the cause of anaemia, including upper and lower GI tract endoscopies. Lower endoscopy showed ulcerative lesions in the left colon, suspicious for ischemic colitis.

Microscopically, large bowel biopsies showed normal crypt architecture with no features of ischemic colitis or inflammatory bowel disease. The most relevant finding was the presence of globular amorphous discrete deposits in the lamina propria that were faintly stained with eosin (Fig. 1). These deposits were Congo red positive and permanganate-resistant (Fig. 2). AL amyloidosis was confirmed by immunohistochemistry. Final histopathological diagnosis was globular amyloidosis with AL deposits. The patient underwent further studies, including a haematologic and bone marrow evaluation that discarded systemic involvement. 12 months after biopsy, the patient is being followed-up with no evidence of disease.

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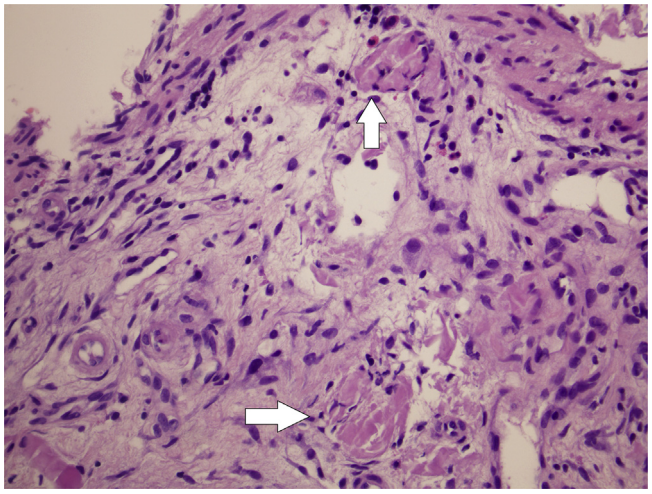

Fig. 1. Globular deposits of a faintly eosinophilic material in the large bowel wall (H-E x 200).

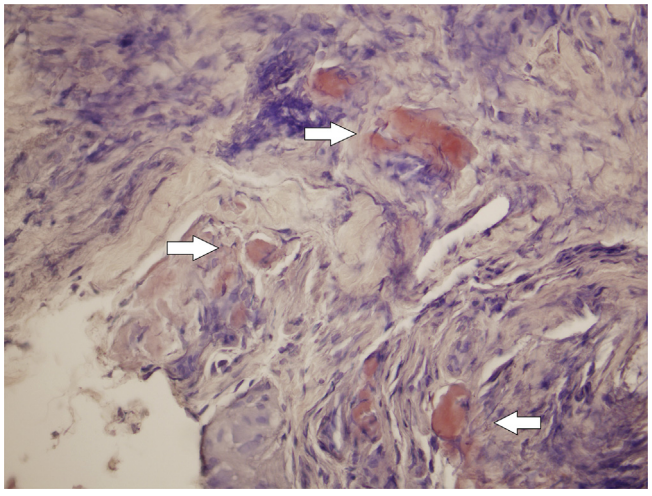

Fig. 2. Congo red staining of the globular deposits, corresponding to light chains. Note the cauterization artifacts in the surrounding tissue (Congo red after permanganate digestion, ×200).

Discussion

Amyloidosis is a heterogeneous group of disorders associated with extracellular deposition of non-branching linear fibrils, with a mean diameter of 10 nm and a β-pleated sheet configuration on x-ray diffraction analysis. This configuration leads to the typical Congo Red staining and apple-green birefringence under polarized light. There have been identified 27 nonstructural amyloid precursors associated with human disease, and amyloid deposits also contain nonfibrillary proteins (glycosaminoglycans, Apo E and amyloid P component) [2].

Amyloidosis can be localized or systemic. Systemic amyloidosis can be subdivided into five types: AL amyloidosis (related to plasma cell dyscrasias); AA amyloidosis (mainly associated with chronic inflammatory diseases or malignancies); hereditary systemic amyloidosis (autosomal dominant disorders with mutations of some plasma protein genes); dialysis-related amyloidosis (characterized by deposition of fibrillary β2-microglobulin, mainly in musculoskeletal structures); and senile systemic amyloidosis (deposition of normal transthyretin) [1].

Localized amyloidosis (LA) is limited to one or a few organs. The amyloid fibrils are usually composed of monoclonal light chains, but patients show neither circulating monoclonal protein in serum or urine nor bone marrow clonal plasmacytosis. LA usually involves the genitourinary or respiratory tract and skin, and GI involvement is rare [1]. Patients with localized GI amyloidosis should be identified, because in contrast to patients with systemic amyloidosis they will not develop systemic disease and they can remain asymptomatic for long periods of time without requiring systemic therapy [6].

Amyloid usually shows a linear pattern of deposition under light microscopy, and the globular pattern is uncommon [9]. It consists of round, oval or irregular globules of homogeneous dense eosinophilic material with occasional perivascular involvement. It has been described to be frequently associated with linear deposits. Larger globules can be concentrically laminated. Globular amyloidosis has been mainly reported in the liver [7], but it can also occur in the breast, uterine cervix, pituitary, thyroid, pancreatic islets and bone [10–13].

To the best of our knowledge, only 4 case reports of globular amyloid deposits in the GI tract have been published to date [1,5,8,9]. These reports include 9 patients, 5 of them with systemic amyloidosis and 3 with localized disease. One patient was still being assessed at the time of reporting and therefore systemic involvement cannot be excluded. The type of protein deposited was AA amyloid in 7 patients and AL amyloid in 2 patients. The most frequent location of amyloid deposits was the stomach (5 patients, all of them with systemic involvement), followed by the small bowel (in 3 patients, with localized disease) and sigmoid colon (in 1 patient, with localized disease). Table 1 summarizes the main clinical features of these patients.

Hemmer et al. [1] reported a case of globular amyloidosis of the small bowel with a striking endoscopic image, corresponding to numerous filiform polyps up to 3 cm extending from the duodenal bulb to the jejunum. Acebo et al. [5] reported a case of globular amyloidosis occurring as a 0.5 cm pedunculated polyp in the jejunum. Martín-Arranz et al. [8] described a soft, rounded lesion 1 cm in size, with reddish and friable surface, involving the sigmoid colon. Demirhan et al. [9] reported erosions of the gastric and duodenal mucosa which did not respond to anti-H2 treatment. In 2007, Tada et al. [4]described significant differences between the endoscopic appearance of AL and AA amyloidosis of the small bowel. AA amyloidosis was associated with granular mucosa, erosions, mucosal friability and shallow ulcers. Multiple polypoid protrusions and thickening of the mucosal folds were seen only in patients with AL amyloidosis. The protrusions were considered to be secondary to a more intense and circumscribed amyloid deposition. In 8 of the 9 reported cases of globular GI amyloidosis, the AA and AL types were associated with mucosal erosions and excrescent nodules, respectively. However, deposition of amyloid in globular amyloidosis is usually denser and more extensive than in linear amyloidosis, so we suggest that the relationship described by Tada et al. may not be completely applicable to globular amyloidosis.

Microscopically, in 7 of 9 patients globular amyloid deposits were reported to be associated with linear perivascular or interstitial deposits, and in two cases this feature was not described. 5 patients with GI amyloid deposits were diagnosed with systemic amyloidosis and showed extra-GI deposits. These non-GI deposits showed a conventional linear perivascular or interstitial configuration.

In globular amyloidosis of the GI tract, the size of the globules ranged from 5 to 40 μm, although this feature was not specified in two cases. In our case, they measured about 30 μm. In previous reports of globular amyloidosis of the liver, globules showed sizes between 5 and 40 μm too, but they were generally smaller than those found in the GI tract [14]. The amyloid globules in pituitary adenomas have been reported to have larger sizes [12].

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