

Diffuse nodular lymphoid hyperplasia of the gastrointestinal tract in patient with selective immunoglobulin A deficiency and sarcoid-like syndrome – case report

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Abstract

Nodular lymphoid hyperplasia is uncommon in adult patients. Associated diseases are common variable immunodeficiency (CVI) and lymphoid tissue malignancies. In this case report we focus on clinical presentation and differential diagnosis of diffuse nodular lymphoid hyperplasia of the gastrointestinal tract coexisting with selective immunoglobulin A deficiency and sarcoid – like syndrome.

Key words: nodular lymphoid hyperplasia, IgA deficiency, sarcoid-like syndrome.

A forty-year-old man with the history of sarcoide-like syndrome in 1998 was admitted to Department of Gastroenterology because of unspecific symptoms including upper abdominal pain, bloating, loose stools (1-3 per day). He had not taken any medication during preceding months. The physical examination was unremarkable, except for slight abdominal tenderness on palpation.

Laboratory tests were normal, except for insignificant increase of CRP (5.8 mg/l, norm: 0-5 mg/l), alpha-1 globulin (0.35 g/dl, 4.7%, norm: 2-4.5%) and urine alpha-amylase (469 IU/l, norm: 0-380 IU/l). Gastrointestinal (GI) tract bacterial and parasitic infections were excluded. Abdominal ultrasonography and chest X-ray showed no abnormalities. CT of the lungs revealed nodular peribronchovascular interstitial thickening, small subpleural nodules and mild lymph node

enlargement (*Fig. 6*), observed morphological features suggest process with perilymphatic distribution, upper and mid lung zones predominance was typical for sarcoidosis although it did not exclude other diseases.

Endoscopic examinations including gastroduodenoscopy, colonoscopy and wireless capsule endoscopy revealed multiple pedunculated and sessile polyps, 2-10 mm in diameter located in the duodenum (*Fig. 1*), small bowel (*Fig. 2*) and on the ileocaecal valve; the mucosa was otherwise normal. The most involved segments of the GI tract were the proximal jejunum and distal ileum; no polyps were seen in the oesophagus, stomach and colon, however, the mucosa of the latter was granulated. The polyps were also seen on radiological examination as multiple round and oval filling defects, 1 to 5 mm in size (*Fig. 3*). Abdominal computed tomography demonstrated thickening of the small intestine wall particularly in the region of ileocaecal valve. In addition, multiple small (up to 11 mm) lymph nodes were detected in the small intestine and transverse colon mesentery and in the periaortal and pericaecal region (*Fig. 4*).

Histopathological examination of the polypectomy specimen from the duodenum and terminal ileum showed stimulated reactive lymphatic follicles covered with normal mucosa, a picture corresponding to lymphoid polyp (*Fig. 5*). Immunohistochemical staining (CD 20, CD 3, CD 43, cyclin D1, MIB1) excluded a lymphoproliferative process.

Immunological tests revealed significantly low serum IgA level (10 mg/dl, norm: 80-310), whereas total IgG, IgG 1-4 subclasses, IgM and IgE levels were normal.

The final diagnosis was diffuse nodular lymphoid hyperplasia of the GI tract in a patient with sarcoid-like syndrome as a rare manifestation of selective IgA deficiency.

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Discussion

Nodular lymphoid hyperplasia is a lymphoproliferative disease that cause still remains unknown [1]. The occurrence

Figure 1. a-b) Endoscopic picture of polyps (3-5 mm in diameter) in the duodenum. Similar abnormalities were found in the terminal part of the small intestine

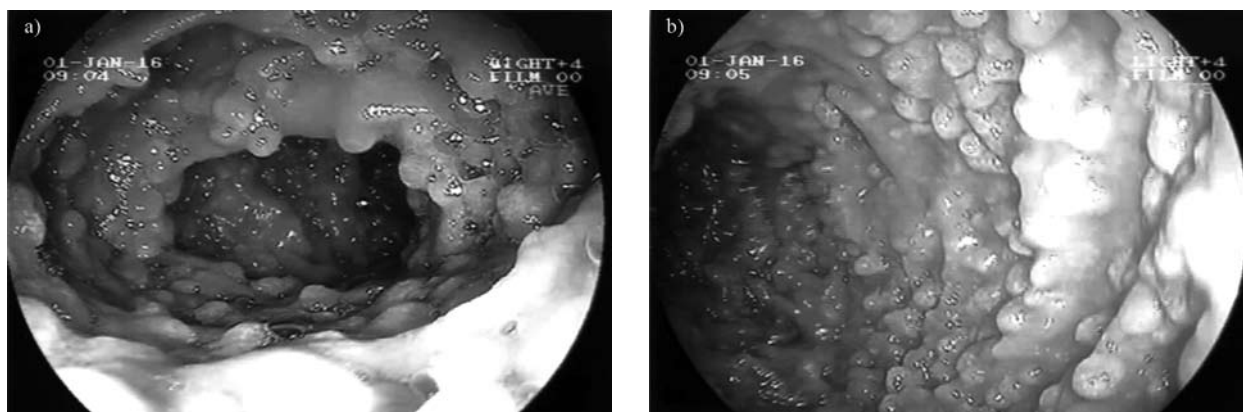
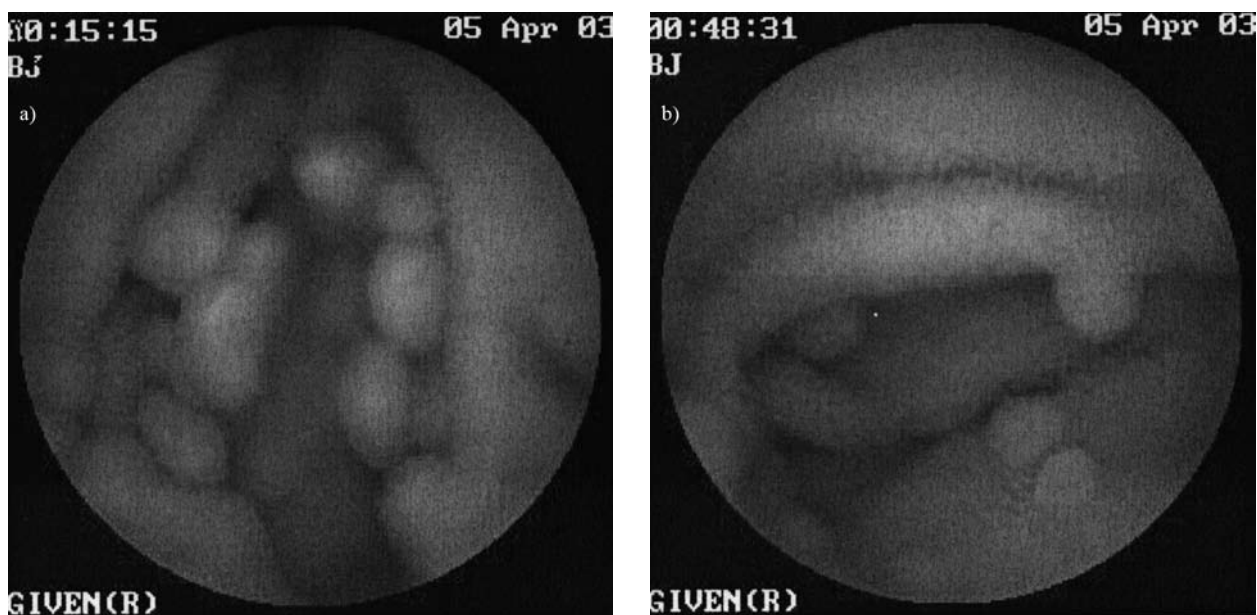


Figure 2. a-b) Wireless capsule endoscopy revealed multiple, small polyps in the small bowel, located mainly in the proximal jejunum and distal ileum



of nodular lymphoid hyperplasia is rather rare. It has been reported to appear in about 20% of patients with common variable immunodeficiency syndrome [1-7]. In some cases it was observed to associate with intestinal lymphoma [8-11]. Nodular lymphoid hyperplasia was also reported in adult patient without any kind of immunodeficiency [12-13]. In some cases the infection with *Giardia lamblia* was found [14]. There is a theory of the local immune response to the antigens as a stimulators in GI tract, but still no antigen is defined.

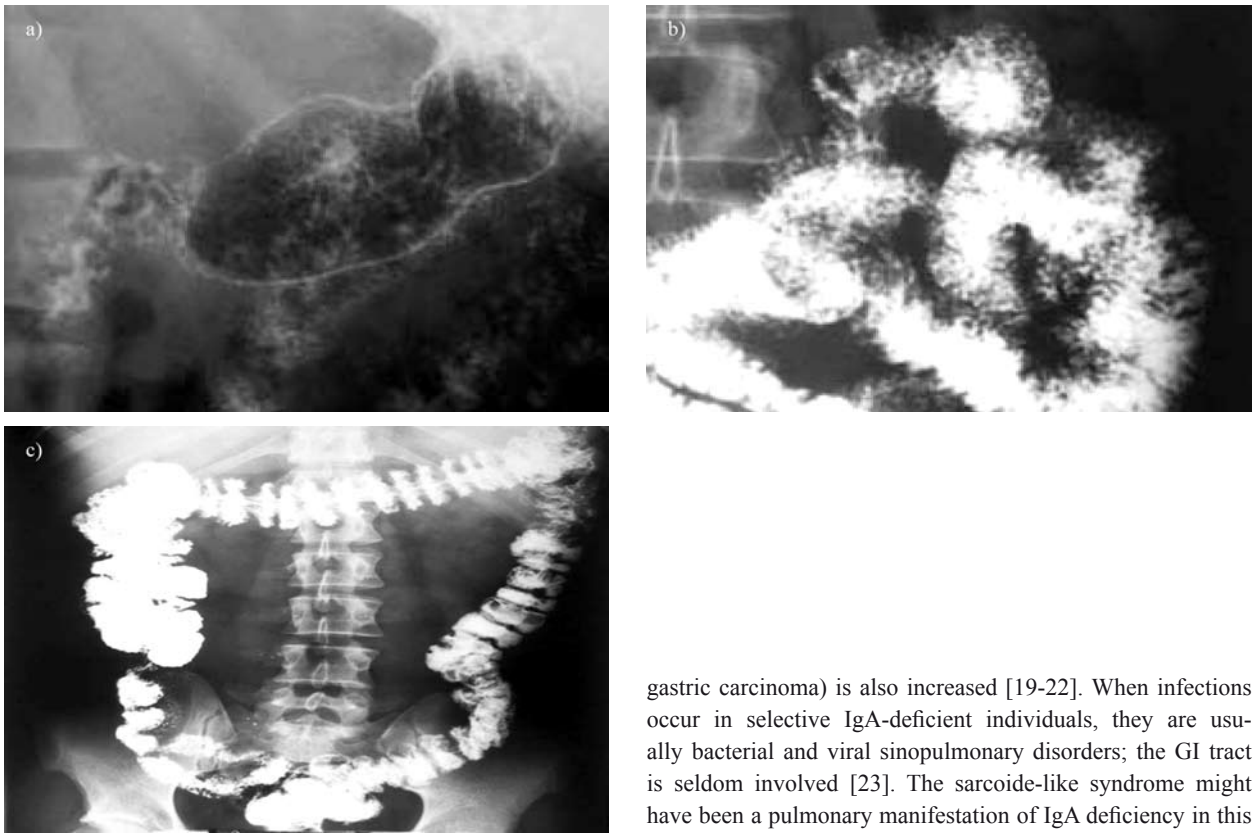
Nodular lymphoid hyperplasia always requires precise differential diagnosis from the other polyposis conditions, especially malignant lymphoma and familial adenomatous polyposis. The most often localisation of hyperplastic lymphoid nodules usually described as innumerable polypoid lesions, is the small bowel, especially the terminal ileum, but they can occur in the stomach and in the colon as well. In some rare cases the polypoid lesions themselves can cause bleeding or intestinal obstruction [15], but if these polyps are small they typically themselves do not cause any clinically significant

symptoms. The frequent gastrointestinal symptoms described by patients usually result from underlying conditions like malabsorption syndrome or coexisting diseases like immunodeficiencies and infections, so it is always important to define them and to undertake the appropriate therapy.

Nodular lymphoid hyperplasia in cases with no complications does not require any special treatment, however, the patients should undergo the prophylactic examinations. Nodular lymphoid hyperplasia is a benign disorder and usually the evolution of the disease is benign but in some cases lymphomatous association and transformation was documented [16]. The risk of malignancy in patient with coexisting hypogammaglobulinemia, especially the risk of lymphoma and gastric carcinoma is higher [17].

The cases of diffuse nodular lymphoid hyperplasia connected with hypogammaglobulinemia, usually coexist with common variable immunodeficiency syndrome, but in the case of our patient we found only selective immunoglobulin A deficiency and no other immunological defects.

Figure 3. Radiological examination shows innumerable nodules suggesting nodular lymphoid hyperplasia: a) in the stomach and duodenum; b) duodenum and small bowel; c) colon. The lesions are round or oval, 1-5 mm in diameter



Selective IgA deficiency is defined as the total absence or severe deficiency of the IgA class of immunoglobulins in blood serum and secretions. Other immunoglobulins, such as IgM and IgG are present in normal or increased levels. This disorder is the most common primary immunodeficiency. The specific function of IgA is to protect the body's mucosal surfaces from infection. Although about 50% of the people with IgA selective deficiency are asymptomatic and free of complications [18], in some cases severe IgA deficiency can cause recurrent infections of mucosal tissues, allergies, celiac-like enteropathy or autoimmune disorders. The risk of malignant disorders (lymphoma,

gastric carcinoma) is also increased [19-22]. When infections occur in selective IgA-deficient individuals, they are usually bacterial and viral sinopulmonary disorders; the GI tract is seldom involved [23]. The sarcoide-like syndrome might have been a pulmonary manifestation of IgA deficiency in this patient. The diseases and genetic disorders reported to be associated with selective IgA deficiency and GI tract are as follows: Crohn's disease, celiac disease, intestinal nodular hyperplasia and recurrent giardiasis. There is no treatment for selective IgA immunodeficiency syndrome.

In this article we would like to put an emphasis on the extremely extensive range of changes in the GI tract and their coexistence with only selective IgA deficiency and with sarcoid-like syndrome as a pulmonary manifestation of the disease. At present the patient receives symptomatic treatment (antibiotics and probiotics) for recurrent GI infections. He undergoes prophylactic examinations in order to exclude a malignant process every year.

Figure 4. a-b) Abdominal computed tomography demonstrates lymph nodes (up to 11 mm) enlargement (small arrows) and thickening within colonic wall (big arrows)

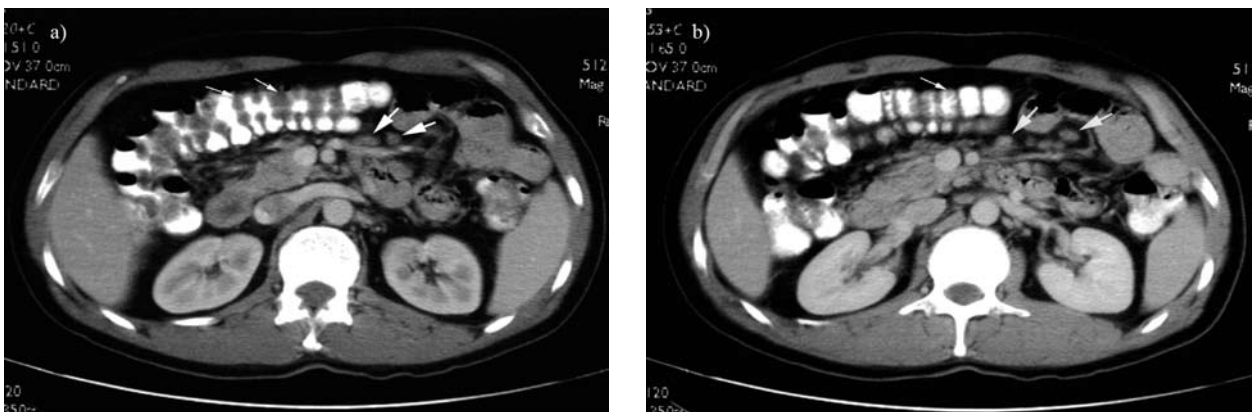


Figure 5. A biopsy specimen from the terminal ileum polyp: a the lesion is covered by intact epithelium (hematoxylin-eosin, magification x 120); b lymphoid infiltrates (hematoxylin-eosin, magification x 280); c focal lymphoid hyperplasia and large lymphoid follicles with prominent germinal centres (hematoxylin-eosin, magification x 280)

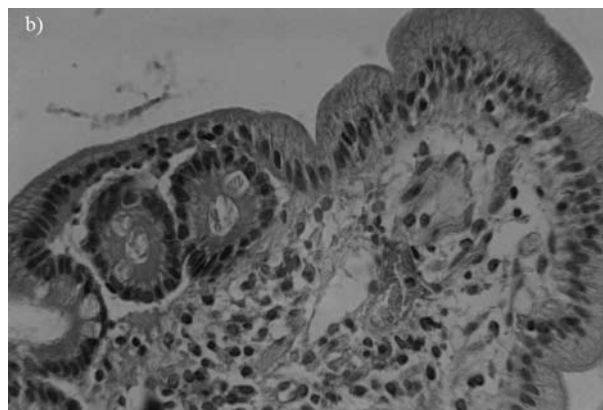
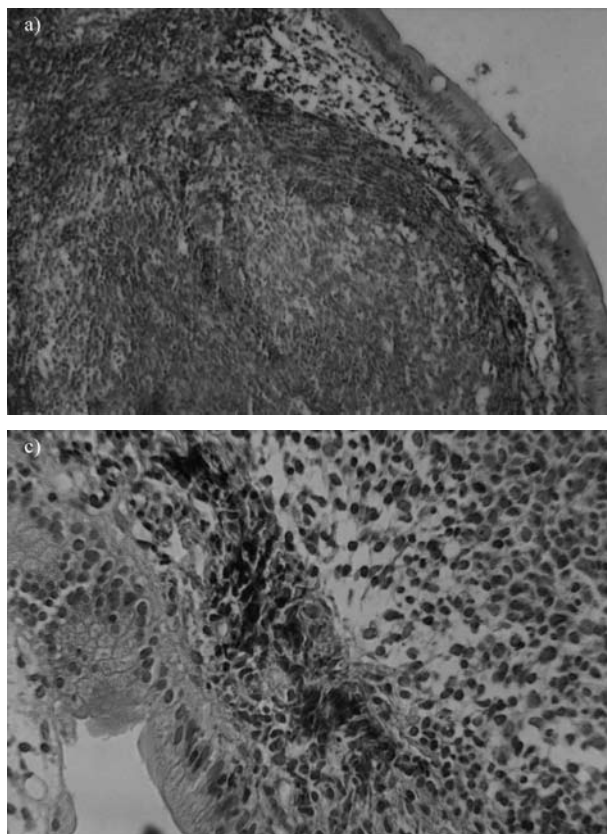
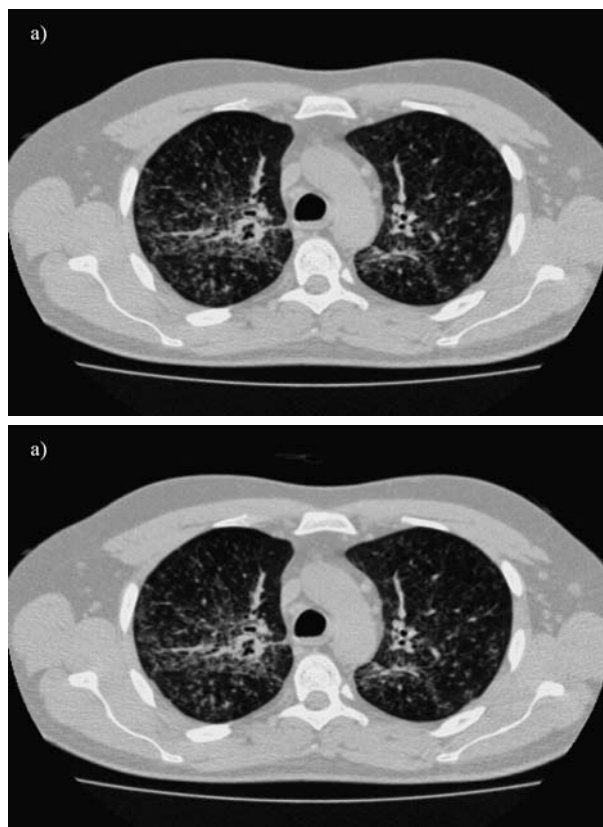


Figure 6. a-b Computed tomography of the lungs revealed: nodular peribronchovascular interstitial thickening, small subpleural nodules and mild lymph node enlargement



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