Systemic Amyloidosis in a Teenage Boy With Inflammatory Bowel Disease

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Abstract- Systemic amyloidosis is a very rare complication of inflammatory bowel disease (IBD). The reported cases of secondary amyloidosis in children with IBD are much fewer than those reported in adults. Herein, a teenage boy with Crohn’s disease is presented who developed nephrotic syndrome due to renal involvement secondary to amyloidosis, whereas the patient was under treatment with corticosteroid and 6-mercaptopurine. To our best knowledge, this is the first reported case of secondary amyloidosis in a teenage Iranian boy with Crohn’s disease.

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Introduction

Crohn’s disease is an inflammatory bowel disease (IBD), in which inflammation can involve any part of the digestive tract from the oral cavity to the anus, without continuity, and can affect all mucosal layers (1).

Although extraintestinal manifestations and complications, involving almost any organ, are common in patients with IBD, secondary amyloidosis is a rare condition which could be seen in adults; meanwhile, there are a few reports on only sporadic cases of amyloidosis in children with IBD (2). Herein, a teenage boy with Crohn’s disease is presented who developed nephrotic syndrome due to renal involvement secondary to amyloidosis.

Case Report

An 8 years and 7 months old boy, weighing 17 kg, was referred to the Rheumatology Ward of the Children’s Medical Center, the Pediatrics Center of Excellence, because of high fever, pain, and swelling of his right knee and ankle since 10 days before admission. The patient was not able to walk at the time of admission. In the first day of his admission, pain and swelling without erythema appeared on his left knee and ankle. He suffered from the anorexia, abdominal pain and weight loss during last year. He was the second child of an unrelated Iranian couple. There was no familial or hereditary disease in the family. In physical examination, arthritis of both knees and ankle joints were detected. The other sites such as lung, heart, and eyes were normal. Laboratory analysis demonstrated moderate leukocytosis and considerable rising in the levels of Erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) (120 mm/hr and 55 mg/L, respectively). During hospitalization, he suffered from frequent bloody diarrhea. In stool examination, white blood cells and red blood cells were detected, while the culture of stool did not reveal any pathogenic organism. It was imperative for doing more comprehensive studies because of over two weeks elongation of problems. Gastroenterology consultation was requested for the patient. Total abdominal and pelvic sonography were performed which showed mild thickening of descending colon wall associated with non-significant enlargement of a few mesenteric lymph nodes. No organomegaly was detected with this modality. The patient was a candidate for colonoscopy in future days. Small bowel follow-through (SBFT) was performed, demonstrating

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segmental wall thickening in the terminal ileum and intact proximal portion of bowel (Figure 1A). Anti-
saccharomyces cerevisiae antibody (ASCA) and perinuclear anti-neutrophil cytoplasmic antibody (PANCA) were checked, which were normal. Stool calprotectin was 850 µg/g. Blood urea nitrogen, creatinine, and liver function tests were all normal. He underwent upper endoscopy and colonoscopy up to presplenic flexure. Upper endoscopy was within normal. Colonoscopy revealed several aphthous ulcers throughout the colon. Histopathologic examination showed mild focal crypt destruction, neutrophil infiltration in lamina propria, focal crypt abscess and cryptitis formation. The diagnosis of Crohn’s disease (CD) was made for the patient; partial parenteral nutrition with prednisolone and sulfasalazine therapy was started. The patient showed significant clinical improvement. Eight months later, the patient was hospitalized for a recurrence of problems, which was managed with intravenous antibiotics and corticosteroid followed by 6-mercaptopurine (6-MP).

The patient was followed-up for 6 years until he was admitted again because of abdominal pain and loose stool when physical examination identified peripheral edema and erythema nodosum in lower limbs (15th birthday). His investigation revealed urinary protein excretion exceeds 40 mg/m2/hr (124 mg/hr). The serum albumin level was 2.3g/dL. Serum complement levels, blood urea nitrogen, creatinine and liver function tests were normal. Total abdominopelvic sonography did not show any pathologic changes in kidneys of the patient. Kidney biopsy was performed, as of suspicious to secondary systemic amyloidosis, which showed mesangial hypercellularity and expansion with deposition of amorphous PAS-positive material (Figure 1B). Congo red stained slides were examined by light microscopy and by polarized light, which showed amyloid deposits (Figure 1C). Subsequently, he underwent a colonoscopy, and multiple endoscopic biopsy samples were seen by polarized light after congo red staining of slides. Intestinal amyloid deposits were detected in the patient (Figure 1D). Oral colchicine at a dose of 1.5 mg/day was added, while he was maintained on prednisolone and 6-MP. During his hospitalization, further complementary tests were done, including human leukocyte Antigen (HLA-B27) and caspase recruitment domain protein (CARD15) genes studies, which were both intact. During his hospitalization, further complementary tests were done, including human leukocyte Antigen (HLA-B27) and caspase recruitment domain protein (CARD15) genes studies, which were both intact. Also, no mutation was detected in the MEFV gene. On more than the 26-month follow-up, renal function tests were normal, and he showed a clinical improvement of his amyloidosis without any surgical treatment or anti-TNF agent.

**Figure 1.** A) Ileum involvement in the patient with Crohn's disease. B) Glomerular involvement in the case before treatment. C) Congo red stained slide B shows amyloid deposit in glomeruli. D) Intestinal amyloid deposits.

**Discussion**

Systemic amyloidosis is a rare but life-threatening complication of inflammatory bowel disease (IBD), the most cases being reported among adults with Crohn's disease (CD) (1), but only sporadic cases of amyloidosis have been recognized in children with IBD (2). The reported cases of ulcerative colitis (UC) and secondary
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amyloidosis are much fewer than those reported on CD (3). The reported prevalence of secondary amyloidosis in CD varies from 0.5% to 29% with a lower prevalence clinically and a higher prevalence at autopsy. Amyloidosis is the more common in ileocolitis (1.3-1.6%) than in ileitis (0.3-0.5%) or colitis (0.6-1.3%) (3). There is a male preponderance of an approximately 3-fold. In Amyloid A (AA) amyloidosis, kidney, liver, and spleen are the major sites of involvement. It becomes clinically overt mainly when renal damage occurs, manifesting either as proteinuria, nephrotic syndrome, or derangement in renal function (4). A possible relationship to supportive complication and extraintestinal manifestation is noted in patients with IBD and AA amyloidosis (5). In the presented patient, the medical history and physical examination was significant for a diagnosis of IBD and based on serologic markers, imaging techniques and histopathologic changes were diagnosed as having CD that involved ileum and colon (ileocolitis) at 8 years old. Upon initiation of treatment with steroid and sulfasalazine the patient's symptoms disappeared, and considerable clinical improvement was observed. The patient was under follow-up in the pediatric outpatient clinic. On one episode of CD flare-up edema associated with proteinuria led us to consider the involvement of kidneys in the course of AA amyloidosis. We faced a CD case with secondary amyloidosis (15th birthday). In the following years, US LU et al., (6) and Yildirim et al., (7) showed that MEFV mutations are more frequent in patients with inflammatory bowel disease compared with general population; thus before starting of colchicine treatment, MEFV gene mutation for FMF disease was performed, and the result was negative. Although very limited cases of amyloidosis have been reported in children with IBD in the world, the exact incidence of secondary amyloidosis in inflammatory bowel disease is unknown in Iran (8). In our extensive review of the literature, we did not come across any other case of amyloidosis in children with IBD in Iran, which indicated that this is the first Iranian IBD case with secondary amyloidosis in teenage.

References