EXTRAINTESTINAL MANIFESTATIONS OF CROHN'S DISEASE

Ferizat Dika – Haxhirexha¹, Agron Dogjani, Lutfi Zylbeari¹, Ledia Kaçi, Vjosa Elezi, Kastriot Haxhirexha¹

Medical Faculty – University of Tetove

Abstract

Extraintestinal manifestations of Crohn's disease are common and are the consequence of the autoimmune inflammatory pathology into organs outside of the gastrointestinal system such as hepatobiliary tree, pancreas, skin, eyes and oral cavity.

Case report: a 58 -years-old male patient was referred to our Department due to severe abdominal pain. The patient medical history show that he has suffered from Crohn's disease for fifteen years. He has resection of terminal ileum in 2009. After that he has treated because of constriction at the major duodenal papilla and bile duct prosthesis was inserted. For five years the remission of disease was maintained with azathioprine. Three months after stopping the therapy with azathioprine, he began to complain for upper abdominal pain and in the back. After admission in our Department abdominal CT with contrast show the change in pancreas, whereas the leukocyte count was $30 \times 109/L$, CRP level - 98 mg/L, and severe hypoalbuminemia - 22 g/liter was present. Patient was sent to the reanimatory unit for intensive care and treatment.

Conclusion: Crohn disease is a systemic disease which may be associated with many extraintestinal manifestations. For these reason it is very important to understand the complexity of this disease which require systemic treatment of autoimmune disturbances.

Key words: Crohn's Disease, extra intestinal, complications

Introduction

The inflammatory bowel diseases (IBD) are chronic inflammation of the gastrointestinal tract comprised of the two heterogeneous disorders Crohn's disease (CD) and ulcerative colitis (UC). Crohn's disease (CD) is a chronic inflammatory granulomatous disease with primary intestinal involvement. Crohn disease is characterized by phases of exacerbation and remission, while the main symptoms of this disease are stomach pain, weight loss, diarrhea etc. Although during Crohn's disease the terminal ileum and the right colon are the most commonly involved sites, pathological and clinical disorder can affect any part of the gastrointestinal tract, from the mouth to the perianal area. Inflammation during Crohn's disease extends through all the intestinal wall from mucosa to serosa. Crohn's disease is a relapsing and remitting disease with the potential to progress extensively. The etiology of Crohn's disease is unknown, but recently some genetic causes are suggested with a higher incidence in Jews than in other population. This disease usually appears early in life and often surgical resection of inflamed segments must be realized. Surgery may temporarily arrest symptoms but relapse of disease is likely to recur. It is astimated that about 40 % patients can exhibit extra intestinal manifestations of the disease (6). The most frequent extraintestinal manifestations affect the hepatobiliary system, joints, eyes, blood vessels, skin, oral cavity, heart, lungs and genitourinary and endocrine system.

Case report

A 52 -years-old male patient was referred to our clinic due to abdominal fever, diarrhea, nausea, and vomiting abdominal pain and jaundice for ten days. The patient past medical history revealed that he has been suffering from Crohn disease for twelve years. He has underwent the resection of terminal ileum and sigmoid colon in 2012. Post-surgical remission was maintained with azathioprine therapy for four years, sometimes accompanied by corticosteroid therapy. The last two weeks the disease became active and the abdominal pain and jaundice were evident. Other complaints are fatigue, pruritus, jaundice, and abdominal discomfort. A liver biochemical tests, showed a marked elevation of transaminases (SGOT and SGPT), alkaline phosphatase, hyper gamma globulinemy and moderate elevation of bilirubine. Serum albumin levels was also decreased and and the presence of hypoalbuminemia was registered.

The ultrasonography and abdominal CT showed multifocal strictures and dilations of the intra- and extrahepatic bile ducts. These changes suggested the presence of primary sclerosing cholangitis as a late complication of the Crohn's disease. After that, liver biopsy was undertaken and infiltrates of lymphocytes and histiocytes as well as giant cell granuloma limited to the portal areas was showed and the diagnosis of PSC was confirmed. Endoscopic retrograde cholangiopancreatography (ERCP) is realized and a common biliary duct prosthesis was placed. The patient was managed with administration of ursodeoxycholic acid (UDCA) and symptomatic care. His biochemical liver tests returned to normal 2 months later.

Discussion

Crohn's disease can be complicated with more extraintestinal manifestations some of which are hepatobiliary manifestations such as elevation of liver enzymes, pericholangitis , primary sclerosing chollangitis (PSC), autoimmune hepatitis, gallstones etc. Primary sclerosing cholangitis (PSC) is a chronic inflammatory disease of the hepatic bile ducts that likely develops in a patients with inflammatory bowel disease some of them in a form of Crohn disease.

It seems that the association between PSC and IBD is depending on geographical location, with stronger association in Europe and America, and weaker association in Japan [5]. Kaplan et al. [10] reported the PSC prevalence rate among adults as 1.11 cases per 100,000 person-years. PSC is one of the most serious complication of CD and occurs with a 2:1 male predominance [6]. Almost all studies emphasize some association between gender and age distribution of PSC in patients with CD. This distribution had two peaks the first peak in their 20s and the second peak between 50s and 60s [3].

Treatment goals of PSC associated with Crohn's disease are the control of symptoms and the management of complications. Ursodeoxycholic acid (UDCA) has been shown very effective in treatment of patients with PSC. Studies show the improvement of liver function improvement based on biochemical tests but it had no any effect on requirements for liver transplantation or development of cholangiocarcinoma.

Conclusion

Among extraintestinal manifestations of CD hepatobiliary disorders are common whereas PSC represents the most prevalent disease in the group of this disorders. Early diagnosis of this complications is complex and often requires close interaction between gastroenterologist and hepatologist.

References

- 1. Broomé U, Bergquist A. Primary sclerosing cholangitis, inflammatory bowel disease, and colon cancer. Semin Liver Dis 2006; 26: 31-41
- 2. Chapman R, Fevery J, Kalloo A, Nagorney DM, Boberg KM, Shneider B, Gores GJ. Diagnosis and management of primary sclerosing cholangitis. Hepatology 2010; 51: 660-678
- 3. Ngu JH, Gearry RB, Wright AJ, Stedman CA. Inflammatory bowel disease is associated with poor outcomes of patients with primary sclerosing cholangitis. Clin Gastroenterol Hepatol 2011; 9: 1092-107
- 4. Navaneethan U, Shen B. Hepatopancreatobiliary manifestations and complications associated with inflammatory bowel disease. Inflamm Bowel Dis 2010; 16: 1598-1619
- 5. Navaneethan U, G K Venkatesh P, Lashner BA, Lopez R, Kiran RP, et al. Severity of primary sclerosing cholangitis and its impact on the clinical outcome of Crohn's disease. See comment in PubMed Commons below J Crohns Colitis. 2012; 6: 674-680.
- 6. Stiehl A, Rudolph G, Kloters-Plachky P, Sauer P, Walker S. Development of dominant bile duct stenosesin patients with primary sclerosing cholangitis treated with ursodeoxycholic acid: outcome after endoscopic treatment. J Hepatol 2002;36:151–6.
- Lindor KD, Kowdley KV, Luketic VA, Harrison ME, McCashland T, Befeler AS, Harnois D, Jorgensen R, Petz J, Keach J, Mooney J, Sargeant C, Braaten J, Bernard T, King D, Miceli E, Schmoll J, Hoskin T, Thapa P, Enders F. High-dose ursodeoxycholic acid for the treatment of primary sclerosing cholangitis. Hepatology 2009; 50: 808-814
- 8. Olsson R, Boberg KM, de Muckadell OS, et al. High-dose ursodeoxycholic acid in primary sclerosing cholangitis: a 5-year multicenter, randomized, controlled study. Gastroenterology 2005;129:1464–72.
- 9. 45 Shi J, Li Z, Zeng X, Lin Y, Xie WF. Ursodeoxycholic acid in primary sclerosing cholangitis: meta-analysis of randomized controlled trials. Hepatol Res 2009; 39: 865-873
- 10. Kaplan MM: Primary biliary cirrhosis. The New England journal of medicine 1996, 335(21):1570-1580.
- Ashraf I, Choudhary A, Arif M, Matteson ML, Hammad HT, Puli SR, Bechtold ML. Ursodeoxycholic acid in patients with ulcerative colitis and primary sclerosing cholangitis for prevention of colon cancer: a metaanalysis. Indian J Gastroenterol 2012; 31: 69-74