Case Report

Newly Diagnosed Crohn’s Disease in Patient with Familial Mediterranean Fever

Tarkan Akar MD1, Gökhan Dindar MD1, Dilek Malkoç MD1, Kemal Karagözoglu MD2, Beyza Kılıvuz MD2, Yücel Üstündağ MD2

Abstract

Chronic abdominal pain sometimes constitute a major challenge, specially when a patient has two diseases with dominant features of abdominal pain in both. At this point, clinicians face a daunting task both in diagnosing and treating an individual’s chronic abdominal pain. Similarly, familial Mediterranean fever disease and Crohn’s disease (CD) have the same clinical features in terms of chronic abdominal pain, and inflammatory properties of these diseases. The association of familial Mediterranean fever disease and Crohn’s disease is very rare and may lead to a remarkable challenge in both diagnosis and treatment. Here, we report a young man with FMF disease presented with extraordinary and intolerable abdominal pain relieved only by excessive narcotic analgesics. The presented case was diagnosed with CD and successfully treated with anti-TNF (tumor necrosis factor) due to steroid refractory.

Keywords: Abdominal pain, comb sign, Crohn’s disease, familial Mediterranean fever, fecal calprotectin, fentanyl, Turkey


Introduction

Chronic abdominal pain sometimes constitute a major challenge, specially when a patient has two diseases with dominant features of abdominal pain in both. At this point, clinicians face a daunting task both in diagnosing and treating an individual’s chronic abdominal pain. Similarly, familial Mediterranean fever (FMF) disease and Crohn’s disease (CD) have the same clinical features in terms of chronic abdominal pain, and inflammatory properties of these diseases. The association of these two diseases leads to a serious clinical challenge even for many good clinicians. In some countries, FMF is frequent, however the addition of the CD to FMF is very rare and may lead to a major challenge for diagnosis and treatment. Herein, we report a young man with FMF disease presented with extraordinary and intolerable abdominal pain relieved only by excessive narcotic analgesics. The presented case was diagnosed with CD that has been successfully treated with anti-TNF (tumor necrosis factor) due to steroid refractory.

Case Report

A 16-year-old young man with previous history of FMF presented with intolerable abdominal pain, vomiting, diarrhea, fever and anemia over a period of three weeks. Following his diagnosis with FMF, the patient had been prescribed treatment with regular colchicine therapy. According to his genetic verification, he was homozygous for M680I mutation. His laboratory tests showed a significant ultra-high C-reactive protein (CRP) level: 265 ng/dL (normal range (NR): 0 – 8 ng/dL). Hypoalbuminemia (albumin: 2.3 gr/dL, NR: 3.5 – 6 mg/dL) and anemia (hemoglobin: 10.5 gr/dL, NR: 12 – 15 gr/dL). Allergic, immune disorders, immunodeficiency, celiac disease and cytomegalovirus infection tests were negative. His severe and intolerable abdominal pain did not respond to painkillers. The patient rated the abdominal pain at 10 on a scale of 0 to 10, with 10 indicating the most severe pain. The abdominal pain was reduced using trans-dermal Fentanyl 100 mg/48 hours. Ten fentanyl strips were used during diagnosis and treatment. Abdomen computed tomography revealed asymmetric wall thickness in almost all of the small bowel, especially in the proximal part of duodenum and jejunum, and showed a special finding as “comb sign” that refers to the hypervascular appearance of dilated vasa recta in the mesenteric border of an acute inflamed bowel (Figure 1). These findings support an intense inflammatory activity in bowel and mesentery related Crohn’s disease. According to the literature, the positive comb sign was the most suggestive finding of CD. Upper endoscopic examination demonstrated the multiple large and deep ulcers (more than 50 ulcers observed) shaped as geographic type and located longitudinally in the mesenteric side of the 2nd and 3rd part of duodenum (Figure 2 a,b). The duodenum biopsy specimen showed no specific findings. Colonoscopy was performed for etiology of prolonged diarrhea, abdominal pain and showed multiple linear and aphthous ulcers in the terminal ileum. The result of the colonoscopy brought to a physician’s attention and associated with the CD. Pathological examination of biopsy specimens had no characteristic features of CD or any diseases. Finally, fecal calprotectin > 1000 mg/kg was measured as significantly high that strongly pointed to the severe bowel inflammation. Consequently, we diagnosed the CD based on clinical, laboratory, endoscopic and supporting radiological findings, as well as high fecal calprotectin level. Before the initial treatment of CD, we had to rule out tuberculosis that commonly detected in young Turkish adults. The tuberculosis screening was performed using tuberculin purified protein derivative-PPD (4 mm) and QuantiFERON-TB Gold-In Tube (interferon-γ release-
se assay (IGRA) test (negative). After that, corticosteroid (Methylprednisolone 60 mg/day) therapy was started by the intravenous route without delay. However, no clinical and laboratory benefit was found within 10 days of observation. CRP levels dropped from 261 to 117 in five days, but increased up to 198 between the 6th and 10th day of steroid treatment. Similar features were observed in fecal calprotectin levels (dropped from >1000 to 437 and again raised up to 665). Therefore, the patient was considered as a steroid-refractory patient. Avoid from risk of bowel perforation UHODWHGGHHSXOFHUVDQWL71)WUHDWPHQW ,QL[LPDEPJNJ, 0, 2, 6 weeks) was started immediately. Then, abdominal pain began to improve within the following days, and elevated high-CRP level dropped to normal range at the 12th day of treatment. After WKHVHFRQGLQIXVLRQRI,QL[LPDEXSSHUHQGRVFRSLFH[DPLQDWLRQ demonstrated the significant improvement in deep ulcers. At the 34th day of hospitalization, he was discharged without complaint.

Discussion

FMF is an autosomal recessive autoinflammatory disorder characterised by episodic abdominal pain, febrile attacks and serositis. Colchicine is the most effective treatment for prophylaxis of FMF attacks and related complications. Abdominal pain is the major component of FMF disease, but severe and intolerable pain requiring narcotic analgesics and extending up to 3 weeks is usually not related exactly to FMF. In this situation, physicians should be aware the possible coexistence of another disease. Many disorders (organic or functional) cause chronic abdominal pain and show similar clinical manifestation causing a challenge with FMF. Therefore, a careful consideration is necessary, clinical interrogation and appropriate diagnostic tests supported by advanced radiological, endoscopic and fecal inflammatory measurement for accurate diagnosis. In this context, CD and FMF share similar symptoms and signs such as abdominal pain, bowel ulceration. Therefore, CD diagnosis in patient with FMF is not easy, when there is no CD related specific feature. Moreover, non-steroidal anti-inflammatory drugs commonly use excessively for pain relief in patient with FMF, thus multiple ulcers may be observed in all intestinal lumens. Tuberculosis and amyloidosis can also present with the same ulcers and clinic picture mimicking CD. In our case, another organic pathology was considered due to severe abdominal pain requiring narcotic analgesic, anemia, prolonged diarrhea, and ultra-high CRP level. So the diagnosis of CD was made with supporting fecal high calprotectin level, clinic, endoscopic signs, radiologic methods as “multiple deep linear ulces”, “comb sign”, “wall thickening with asymmetric distribution” and exclusion of other diseases such as tuberculosis with QuantiFERON test. CD with duodenal ulcers is a rare entity. Only five cases have been reported and all of them have been treated with anti-TNF due to refractory to all immunosuppressive drugs. To the best of our knowledge, multiple large deep small intestine ulcers have not yet been shown in CD. It is important to consider intestinal tuberculosis in the differential diagnosis of severe abdominal pain and multiple ulcers, because tuberculosis commonly seen in Turkey and

Figure 1. Abdominal CT image demonstrates multiple linear hypervascularity of the distal arterial arcades (vasa recta) that is characteristic for “Comb sign” (green arrow), and asymmetric wall thickening (blue arrow) in duodenum and other part of small bowel.

Figure 2. Endoscopic view of a) second; and b) third part of duodenum. Prominent, multiple (more than 50 ulcers observed), large and deep ulcers is shown in mesenteric side of duodenum lumen and beyond.
immunosuppressive drugs could deteriorate the clinic condition if the patient had tuberculosis. A physician should not use immunosuppressive drugs for CD until tuberculosis rules out exactly in regions where tuberculosis is endemic or semi-endemic like Turkey. When there is no specific histopathological or clinical findings for CD and tuberculosis, the differential diagnosis have to be created with sophisticated radiological methods and fecal calprotectin. Although many signs have been shown for differential diagnosis in magnetic resonance imaging and computed tomography, we use “comb sign” due to highly suggestive and related early and active CD. While this sign is not specific for CD, the presence of comb sign help in differentiating CD from tuberculosis and neoplasms such as lymphoma or metastases in case of no powerful evidence supporting these diseases. Comb sign is also a useful marker in predicting CD activity. Intolerable abdominal pain requiring narcotic analgesics in the course of CD could not be expected unless obstruction or perforation. We think that the cause of severe abdominal pain in our patient is related to multiple large and deep ulcer located in proximal part of duodenum having intense nerve roots provided by celiac plexus and excessive inflammation presenting with serious ultra-high CRP level. Therefore, we had to use fentanyl, because the abdominal pain did not respond to available painkillers in Turkey. Fentanyl is a narcotic analgesic that commonly use for cancer-related and postoperative pain. However, there is limited data on the use of fentanyl as painkiller for CD related abdominal pain. To the best of our knowledge, this case was the first report that used fentanyl for relief in Crohn’s disease related abdominal pain. Fentanyl can be a useful drug for intolerable abdominal pain, if the diagnostic process extends unwillingly for a long time. It is claimed that the association of inflammatory bowel disease and FMF is more common than it has been assumed. However, there are only few published case reports consistent with this claim. The age of onset of CD was reported to be significantly higher in FMF patients than in patients with Crohn’s disease-only. In reported cases, many patients were over three decades age, except an 8-month and 11 years old patients. Our case had different properties in terms of disease onset as a young age unlike the previous reports. In a few published cases, it was reported that the CD clinical course and treatment in patients with FMF was more aggressive and did not respond to intensive medical therapy, including: intravenous corticosteroid, azathioprine, and cyclosporine. Similarly, the clinical features of FMF in patients with CD is shown more severe like frequent disease attacks, secondary amyloidosis and subsequent renal failure. Postulated mechanism was speculated that FMF and CD share common genetic and inflammatory pathway. Therefore, the one disease triggers the other and the more severe clinic is observed. The reasons for failure of that medical treatment were not fully understood. For solving the treatment problem, anti-TNF drugs commonly used and became frequently successful in many cases. The use of anti-TNF agent is commonly needed due to the failure of all immunosuppressive drugs including, corticosteroids in all published cases. Similarly, in our patient the corticosteroid failed, so the success of treatment was achieved with the anti-TNF treatment and a quick decision using literature knowledge.

In conclusion, a physician should be aware of the coexistence disease with FMF in case of abnormal findings suspecting another organic disease like CD, tuberculosis and amyloidosis. Differential diagnosis should be made with helping endoscopic, sophisticated radiological methods and fecal calprotectin. This should be kept in mind that the treatment of two diseases (CD and FMF) is difficult, as is the diagnosis. The association of FMF and CD is very rare, the clinician should study published literature like our case.

Authors’ contributions

T. Akar diagnosed, researched and wrote the manuscript of the case, G. Dindar created the figure, K. Karagözolu and B. Kilaç took the pathology images, D. Malkoç made clinical follow, used fentanyl and Y. Üstündag made critical review. All authors participated in editing and approving the manuscript.

Conflict of Interest

The authors declare that they have no conflict of interest.

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Informed Consent

The patient informed consent for this case report was obtained from him.

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References


