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HIDDEN "CROHN'S" IN T.B. ENDEMIC REGIONS – DIAGNOSTIC DILEMMA & DELAY : A CASE REPORT

Pediatrics

Dr. Tanushree Joshi Consultant, MD (Pediatrics) ,Northern Railway Central Hospital ,New Delhi.

Dr. Himanshu S Dave DCH, DNB(Pediatrics) Resident , Northern Railway Central Hospital , New Delhi.

Dr. Renu Jaggi Consultant & HOD, MD (Pediatrics), Northern Railway Central Hospital , New Delhi.

Dr. Kathakali Das Consultant , MD (Pediatrics), Northern Railway Central Hospital , New Delhi.

ABSTRACT

Crohn's disease is a chronic inflammatory condition affecting the gastrointestinal tract at any point from the mouth to the rectum. Patients may experience diarrhea, abdominal pain, fever, weight loss, abdominal masses, and anemia. In India, Crohn's disease is considered as a rare disease in pediatric population (2.8/100,000 in <18 years age group) and is usually confused with abdominal tuberculosis. Here we describe a case of 9 year old female patient who presented with pain abdomen, long standing fever, poor appetite and weight loss. The patient was initially misdiagnosed as abdominal tuberculosis. She was later diagnosed as Crohn's disease and was successfully treated.

KEYWORDS

Crohn's , Delayed diagnosis, Tuberculosis.

INTRODUCTION

Tuberculosis (TB) is a chronic granulomatous disease produced by *Mycobacterium Tuberculosis*. The estimated prevalence of tuberculosis is 10.4 million of cases worldwide, with 1.8 million of annual deaths . India is the country with the highest number of reported cases, representing approximately 26% of the patients with tuberculosis in the world . With such high incidence, it becomes very difficult to differentiate cases of pediatric Inflammatory Bowel Disease (IBD) from Abdominal TB in Indian subcontinent. We present a case in which there was delay in diagnosis of IBD due to overlapping presentations of abdominal TB. This case highlights the need to consider the differential diagnosis of IBD in all suspected cases of abdominal TB in endemic regions.

Case report:

A 9 year old female presented with complaints of pain abdomen since 2 years and fever (on & off) since 3 months with associated loss of weight and appetite. Patient also had few episodes of blood in stool in the past 3months.She had no history of contact with TB. She was being managed as clinically suspected abdominal tuberculosis and was on Anti Tubercular Treatment (ATT) for last one month along with oral steroids. In the absence of isolation of tubercle bacillus in the patient in previous investigations and no clinical improvement on ATT, the diagnosis of clinically suspected abdominal tuberculosis was questioned and she was re-evaluated.

On general physical examination; patient was having sick look. She was conscious and well oriented. Her weight and height were below the third percentile.She had low grade fever with moderate pallor, no icterus, no cyanosis, no clubbing, no pedal edema and no generalized lymphadenopathy. Vital signs showed a pulse rate of 92 / min, no tachypnoea and systemic examination had no other significant finding except abdominal tenderness in right iliac fossa. There was no mass or hepatosplenomegaly. Proctoscopy done under GA was suggestive of anal fissure at 6"O clock position and was treated conservatively.

Preliminary work up:

Initial blood work up was done. CBC showed moderate anemia with normal TLC and platelet counts. CRP was positive. Liver and kidney functions were normal. Urine routine microscopy showed no significant finding. Stool routine and microscopy suggested presence of RBCs. Chest X ray was normal. USG abdomen revealed mesenteric lymphadenopathy with largest node measuring 1.5 cm. Mantoux test was negative. Gastric aspirate for Gene Xpert shows no tubercular bacilli.

CECT abdomen was done which revealed multiple discrete retro peritoneal, para aortic and mesenteric lymphadenopathy of 5-15 mm size probably suggestive of abdominal tuberculosis. Consultation of pediatric gastroenterologist was taken. MRI Enterography was done which showed segmental areas of wall thickening, stratification and abnormal enhancement in terminal ileum and ileocaecal junction along with multiple enlarged mesenteric and ileocaecal lymphnodes which are found both in inflammatory bowel disease and tuberculosis.

Course of illness:

With high clinical suspicion of abdominal tuberculosis, CECT and MR Enterography supporting the diagnosis and since the patient was already on ATT for one month; the Anti Tubercular Treatment was restarted and further workup was done. The patient continued to have mild grade fever. Within one week of restarting ATT, the patient developed pain abdomen and recurrent vomiting ; was diagnosed as ATT induced hepatitis and the regimen was altered as per the protocol. The liver function showed improvement in few days and patient was shifted back to normal ATT regimen as per protocol.

Patient improved symptomatically. She was afebrile and the appetite was improving so was discharged with advice to continue ATT for 6 months with regular follow up on OPD basis.

After 10 days of discharge, patient was readmitted with complaints of high grade fever and abdominal pain. CBC was suggestive of neutrophilic leukocytosis (TLC~22,000).LFT and KFT were within normal limits.Urine routine microscopy showed 15-20 pus cells, urine culture was sent. Empirical antibiotics (Intravenous) were given along with ATT considering the provisional diagnosis of UTI. Patient showed improvement in symptoms and total counts after 5 days of antibiotics and was discharged.

After 3 months of ATT (1 month before reporting to us and 2 months after that) patient continued to have weight loss, decreased appetite and abdominal symptoms though she was afebrile.

Therefore, colonoscopy with intestinal biopsy was done which showed pancolitis and biopsy revealed evidence of chronic inflammation with crypt hyperplasia, crypt abscess and lymphoplasmocytic infiltration suggestive of Inflammatory Bowel Disease ;specially Crohn's disease (CD). MTB was not detected in the mucosal smear and culture. Upper GI endoscopy also showed mucosal disease with multiple punctuate and healing ulcers in fundus and body of stomach. The mucosal biopsy of stomach showed growth of H. pylori. Serum amylase, lipase and LDH were within normal range. CRP was elevated. Fecal calprotectin levels were > 700. ATT was stopped and management for Crohn's disease was started.

Thyropurine Methyl Transferase (TPMT) Type 1- Wild type was detected. Patient was kept on exclusive "Peptamen Junior" diet (1.2 L/Day) for 2 weeks, Mesalazine, VSL#3 capsules and other nutritional

supplements. Patient showed improvement in abdominal symptoms and appetite was improved. After 15 days other food grains were introduced which were well tolerated by the patient.

After one month of CD management gastroenterologist review was done. Fecal calprotectin levels dropped from 700 to 125. There was no complain of blood in stool and stool occult blood test was also negative. Patient was then started on steroids (Prednisolone) which is currently on tapering regime. Patient has gained 3.5 kg weight in last 2 months and is active and feeling healthy now.

DISCUSSION

Crohn's disease is still an enigma despite 90 years of observation and research since Crohn, Ginzburg and Oppenheimer summarized the classic description of the disease in 1932[1]. CD and ulcerative colitis are the two important forms of inflammatory bowel disease (IBD) and a cause of chronic morbidity in children and adolescents. [1]

In India, CD was thought to be uncommon and is commonly misdiagnosed as tuberculosis.[2] IBD burden is on the rise in TB endemic regions and as per a recent report, the overall disease burden of IBD in India is the second highest in the World after USA.[3]

Unlike the western and European countries, IBD is still not considered the first differential in patients with chronic gastrointestinal symptoms in India. Moreover, not initiating ATT is also difficult owing to the high burden of TB. The diagnosis of CD becomes more difficult due to lack of gold standard serological and histological tests and overlapping clinical features of IBD and intestinal TB. This often leads to delay in the treatment of Crohn's disease. Studies have shown median delay in diagnosis of 15 months. [4]

Clinical feature of both intestinal TB and CD are overlapping and include fever, blood in stools, abdominal pain, intestinal obstruction, perforation and fistulization. CD can involve any region of the GI tract but the initial presentation commonly involves Ileocaecal region, also the commonest site of involvement in intestinal TB. [5] The ascending colon may be involved with the ileocaecal region but isolated colorectal involvement is rare in intestinal TB.

Colonoscopy with ileoscopy and biopsy is valuable in the diagnosis of Crohn's disease at the junction of the ileum and colon . Characteristic endoscopic findings include skip lesions, cobblestoning , apthoid ulcerations, and strictures. Histology may show neutrophilic inflammation, noncaseating granulomas, Paneth cell metaplasia, and intestinal villi blunting. The endoscopy findings in intestinal TB are suggestive of transversely placed shallow ulcers, hypertrophied lesions and caseating granulomas involving the jejunum, and ileocaecal region with a patulous ileocaecal valve. [5]

Demonstration of MTB in biopsy smear/culture is the gold standard for diagnosis of intestinal TB. However, smear and culture to demonstrate MTB have low sensitivity. [6]

Fecal calprotectin test is a functional quantitative measure of intestinal inflammation. It is a test that usually supplements endoscopy clinically and, at times, can even replace the procedure. There are numerous intestinal diseases and drugs (eg, NSAIDs, alcohol) associated with low-grade intestinal inflammation with average calprotectin levels between 50 and 300 µg/mg. However, only untreated IBD and certain food infections are associated with very high levels. Levels over 500-600 µg/mg are extremely predictive of IBD. Fecal calprotectin certainly has the potential to serve as a diagnostic screening test. [7]

There have been multiple reports on the clinical, endoscopic, pathologic, microbiologic, serologic and radiologic features in differentiating CD and ITB, and several predictive models have been developed [9, 10, 11] . Except for positive AFB smear, culture, gene-Xpert, and caseating granulomas on biopsy and necrotic lymph nodes on imaging, none of the other features are diagnostic in a patient with CD/Intestinal TB dilemma. Moreover, most of these exclusive features are also present in less than 50% of patients, thereby limiting the diagnostic accuracy of a single feature/modality in differentiating CD and Intestinal TB. [8]

Recent Asia-Pacific consensus statements for CD have also mentioned, that in a patient with CD/Intestinal TB dilemma, the diagnosis of CD should only be considered in a patient who doesn't respond to ATT, and subsequently responds to CD-specific therapy.[12] But this therapeutic trial of ATT poses a risk of toxicity, as seen in our patient. The treatment of the primary disease, i.e. CD is delayed. In contrast, treatment with steroids alone (for CD) can be disastrous, if diagnosis of Intestinal TB is missed. Emergence of multi-drug resistant TB can further complicate the issue. Therefore, there is a constant need for a model or a parameter for better differentiation and reduction in the need for an ATT trial.

In our case, the treatment for CD was initiated considering the chronicity of symptoms, growth failure, features of pan colitis and multiple ulcerations in video colonoscopy, AFB stain negative mucosal lesion, very high levels of fecal calprotectin, which reduced drastically with treatment and poor therapeutic response to ATT.

CONCLUSION

This case report emphasize the importance of considering IBD as an important differential in patients presenting with chronic gastrointestinal symptoms at the outset so the treatment is not delayed. Fecal calprotectin levels can be used as screening method. Therapeutic ATT trial is associated with a delay in diagnosis of CD. Better biomarkers and predictive models are required for differentiation and reduction in the need for anti-tubercular therapy trial.

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