

Sickle Cell Disease with Ulcerative Colitis as a Presenting Feature

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Abstract

Sickle cell disease (SCD) is an inherited blood condition which is most common among people of African, Arabian and Indian origin. The sickle gene is widespread among many tribal population groups in India with prevalence of heterozygotes varying from 1-40 percent. It seems to be a North-South divide with more ulcerative colitis (UC) in North and Crohn's disease (CD) in South India.

Keywords: Ulcerative Colitis; Neutrophilia; Sickle cell disease; Vaso-occlusive crisis

Introduction

Sickle cell disease most commonly occurs among people of African, Arabian and Indian origin. There is rising incidence and prevalence of inflammatory bowel disease (IBD) in India topping the Southeast Asian (SEA) countries. There appears to be a North-South divide with more ulcerative colitis (UC) in North and Crohn's disease (CD) in South India.

However, Concurrent presentation of SCD and UC is a very rare incident. Less than 10 cases have been reported worldwide. We report probably the first case described from India.

Case Report

A 37-year gentleman, a known case of Sickle Cell Disease with pain crisis (on hydroxyurea) and recently diagnosed Ulcerative Colitis (on steroids and 5ASA) presented with complaints of high-grade fever and multiple episodes of loose stools and vomiting of 1-day duration. He also gave history of jaundice, weakness and significant weight loss (lost 14 kg over 2 months). On examination, patient had pallor, icterus and was hypotensive. His per abdomen examination revealed a diffusely tender abdomen. His routine blood investigations revealed neutrophilia, low hemoglobin, elevated CRP/ESR, hyponatremia and raised bilirubin. In view of a clinical suspicion of Invasive Salmonellosis, he was admitted to MICU and started empirically on Meropenem and Azithromycin. Blood cultures revealed *Salmonella* species. Patient improved over the next 48 hours [1-4].

During hospital stay, he was noted to have coffee ground vomitus. OGDscopy was done which showed polypoidal lesion of 3-4 cm at D3 area. Biopsy taken from the area showed dilated lymphatics on mucosa. Colonoscopy was done which showed shiny edematous mucosa with granularity and multiple foci of neo-vascularization in rectum, sigmoid colon, descending colon, splenic flexure, hepatic flexure, ascending colon, IC valve and caecum. Biopsies taken from ileum showed no significant pathology. However, biopsies from right colon, left colon and ascending colon showed marked disorganization of crypt architecture with a villiform configuration. Increased cellularity of lamina propria with predominance of lymphocytes and plasma cells. Foci of neutrophilic infiltration with crypt abscess and large lymphoid aggregates – consistent with features of active Ulcerative Colitis with mild activity.

He was treated with IV antibiotics and other supportive measures during hospital stay. For long term management, he was started on

steroids, Mesalazine/Mesalamine 800 mg, Hydroxyurea. He responded well to the treatment on follow up and is currently symptom free (Table 1 and Figure 1).

Discussion

Sickle cell disease (SCD) is one of the most common monogenic disorders globally with an autosomal recessive inheritance [5]. James Herrick, a physician first described the characteristic sickle shaped red cells in a medical student from Grenada in 1910. Linus Pauling and his colleagues showed that sickle haemoglobin (HbS) had an altered electrophoretic mobility and they were the first to define it as a molecular disease in 1949. A few years later in 1957, Vernon Ingram discovered

Test Name	Results	Units	Bio Ref.Interval
Hemoglobin HPLC Electrophoresis (HPLC)			
Hb F	16.7	%	<1.5
Hb Adult	2.8	%	83.24-90.79
Hb A2	2	%	1.50-3.50
Hb D	43.8	%	
Hb Sickle	30.8	%	
Others (Non-Specific)	4.5	%	<10.00
Hemoglobin	10.7		11.50-15.00
RBC Count	2.82	ml/mm	3.80-4.80
Packed Cell Volume	33.5	%	38.00-48.00
MCV	118.8	%	80.00-100.00
MCH	37.9	pg	27.00-32.00
RDW	15.9	%	11.50-14.50

Suggestive Interpretation

Features are suggestive of Compound Heterozygous Condition of Hemoglobin '8' with Hemoglobin 'D'(Punjab). Hemoglobin A2 and E ccelut0065 at the same time and cannot be separated by existing HPLC Technique. Electrophoresis on Capillary shows the band position on Hb E zone. Recommended: Family screening with Hb HPLC to confirm diagnosis.

Table 1: Hemoglobin electrophoresis (HPLC) confirming the diagnosis of Sickle Cell Disease.

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FINAL REPORT

CLINICAL DATA:

Known case of Sickle cell anaemia.
Being treated for Ulcerative colitis since September 2017.

SPECIMEN:

Biopsy I) Ileum II) Right colon III) Transverse colon IV) Left colon

GROSS DESCRIPTION:

I-IV) 4, 4, 3, 4 pieces of grey-brown soft tissue each measuring 0.2-0.4 cm A.E.

MICROSCOPIC DESCRIPTION:

I) Sections show pieces of ileal mucosa with intact villi and crypts. Lamina propria shows normal cellularity.

II) Sections show pieces of colonic mucosa with marked disorganisation of crypt architecture with a villiform configuration. Lamina propria shows increased cellularity with a predominance of lymphocytes and plasma cells. Foci of neutrophilic infiltration with crypt abscess seen. Foci of lamina propria fibrosis noted. Large lymphoid aggregates seen.

III) Sections show pieces of colonic mucosa with marked disorganisation of crypt architecture with a villiform configuration. Lamina propria shows increased cellularity with mixed inflammatory infiltrate with prominence of lymphocytes and plasma cells. Basal plasmacytosis and basal lymphoid aggregates seen.

IV) Sections show pieces of colonic mucosa with marked disorganisation of crypt architecture with a villiform configuration. Lamina propria shows increased cellularity with a predominance of lymphocytes and plasma cells with scattered eosinophils and neutrophils. Focal Paneth cell metaplasia seen. Foci of lamina propria fibrosis noted. Basal lymphoid aggregates seen.

IMPRESSION:

I) Biopsy from ileum showing no significant pathology.

II,III,IV) Biopsy from the right colon, transverse colon and left colon showing features of chronic active colitis - Consistent with Ulcerative colitis with mild activity.

Figure 1: Biopsy report from Colon confirming Active Ulcerative colitis.

that sickle haemoglobin resulted from a single amino acid substitution in the haemoglobin molecule [6,7]. The disease results from a single base A>T mutation in the triplet encoding the sixth residue of the β -globin chain, leading to a substitution of valine for glutamic acid and the abnormal haemoglobin S (HbS).

Sickle cell disease (SCD) usually manifests early in childhood. For the first 6 months of life, infants are protected largely by elevated levels of Hb F; soon thereafter, the condition becomes evident. The most common clinical manifestation of SCD is vaso-occlusive crisis. A vaso-occlusive crisis occurs when the microcirculation is obstructed by sickled RBCs, causing ischemic injury to the organ supplied and resultant pain. Pain crises constitute the most distinguishing clinical feature of sickle cell disease and are the leading cause of emergency department visits and hospitalizations for affected patients. Other most common manifestations include bone pains, anaemia, aplastic crisis, splenic sequestration, infection (encapsulated respiratory bacteria – *S. pneumoniae*; in adults – gram negative organisms – *Salmonella*). The most common Gastrointestinal manifestation is Cholelithiasis in children and Liver involvement in adults.

Ulcerative Colitis (UC) is an idiopathic chronic inflammatory disease affecting the mucosa of the rectum and extending proximally to affect a variable length of colon. The incidence reaches 24.3 per 100000 population per year [8]. Unlike its counterpart Crohn's Disease (CD), UC characteristically involves only the large bowel. Most common manifestations include Rectal bleeding, frequent stools, mucous discharge from rectum, severe diarrhoea and cramps, fever, leucocytosis. UC has been classically described to have extracolonic manifestations which include uveitis, pyoderma gangrenosum, erythema nodosum, ankylosing spondylitis. Conditions that have been described to be associated with UC include Primary sclerosing cholangitis, Multiple Sclerosis, Immunobullous disease of skin [9-12].

Conclusion

Several dozen genes appear to be differentially expressed in both CD and UC compared with profiles for healthy patients. The most highly expressed gene commonly elevated in both IBDs was the protease

inhibitor *SERPINB2* (also called PAI, plasminogen activator inhibitor, type II). Increased plasminogen activator levels have been reported in mucosal lesions of IBD patients and increased PAI-1 was found in IBD patient plasma. The UC-specific gene set was dominated by overexpression of immunoglobulin-encoding sequences, reminiscent of the active IgG plasma cell component observed in UC patients. This finding is consistent with studies on B-cell receptor gene usage that have demonstrated that infiltrating lymphocytes in UC mucosa are of peripheral rather than mucosal origin. IgG1 and IgG4 antibodies predominate in UC, whereas IgG2 antibodies are increased in CD.

In our scenario we see a case of Sickle cell disease presenting with abdominal pain due to UC as the presenting feature.

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