Recurrent Intestinal Obstruction with Acquired Angio-oedema, due To C1-Esterase Inhibitor Deficiency

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Abstract

A 52-year male with past history of ulcerative colitis 20 years back (now in remission), developed recurrent small intestinal obstruction at intervals of a few months. CT scan did not detect the cause initially. A repeat CT scan (USA) showed interbowel fluid with transient ascites (serum albumin normal). Angio-oedema was suspected and low C4 with C1-esterase inhibitor (C1-INH) deficiency confirmed the diagnosis. Further investigation showed he was suffering from a chronic low grade small B cell lymphoma. He was treated with Rituximab 375 mg/m² at intervals of one week for 4 weeks. He is asymptomatic with Transexamic acid (500 mg TDS) for last 1½ years.

Case Report

Male (age 52 years, weight 72 kg) had frequency of stool with blood for several weeks in 1990 and was diagnosed ulcerative colitis on colonoscopy. He was treated with steroid for a few weeks and mesacol for years. He improved and was in remission for more than five years.

In 2007, he developed recurrent attacks of abdominal pain, vomiting, distension, gurgling – small bowel obstruction (confirmed on plain X-ray abdomen) at intervals of few months. No cause of obstruction was established on CT abdomen or later on with barium meal follow through. He underwent appendicectomy in 2008, without any relief of attacks of small bowel obstruction. In 2010, during an episode of obstruction, minimal ascites and interbowel fluid between small bowel loops was noted, on repeat CT abdomen; angio-oedema was suspected and confirmed on estimating serum Clq, C3, C4 in USA. No history of peripheral oedema of feet or urticaria, anytime in the past.

Investigations: Hb 12.5 g%, PCV 31.5%, WBC 12,700/cmm, lymphocyte 54%, with atypical cells, platelet 212000/ul, total bilirubin 1.3 mg%, sodium 142 mEq/L, potassium 4.7 mEq/L, chloride 103 mEq/L, bicarbonate 21 mEq/L, BUN 12 mg%, creatinine 1.2 mg%, fasting blood sugar normal and random blood glucose 186 mg%, serum lipase 18 units, transferrin saturation 21% (20-45%), serum ferritin 25.9 ng/mL (38-280), uric acid 3.2 (3.5-8.5) mg/dL, stool for occult blood negative. HIV antibody, anti-HCV antibody, HBsAg negative. Upper G-I endoscopy: normal, Colonoscopy: ulcerative colitis in remission. FDG PET CT (May 2011) : normal. Serum immunoglobulins : IgG 8.2 g/L (5.5-16.5), IgA 1.33 g/L (0.8-4.0), IgM 3.75 g/L (0.4-2.0), Immunofixation confirmed IgM Kappa paraprotein, excess cryoglobulin. Serum protein electrophoresis showed a faint M band. C1 esterase inhibitor level < 45 mg/L (150-350 mg/L), C1 esterase inhibitor function < 25% (> 84%), C3 1.17 g/L (0.75-1.65) : normal. C4 < 0.02 g/L (0.14-0.54) : low. Serum C1q < 3.6 mg/dL (5.0-8.6).

Bone marrow: no infiltration with mature lymphoid cells. Immunophenotyping showed B cell population with CD 19 and CD 20.
Treatment: Any precipitating drugs such as (i) angiotensin converting enzyme (ACE) inhibitors or (ii) angiotensin II receptor blockers (ARBs) or (iii) non-steroidal anti-inflammatory drugs (NSAID) or aspirin, alcohol, vancomycin, opiates are omitted.

Treatment of C1-INH deficiency is either with (i) fresh frozen plasma replacing C1-INH deficiency or (ii) a recombinant C1-INH replacement therapy IV 1500 units (3 vials) in 10 minutes or (iii) a bradykinin-2-receptor antagonist (icatibant), 30 mg sc injection or (iv) a kallikrein inhibitor (ecallantide (DX-88).4,5

The patient was treated with iv Rituximab which is a monoclonal antibody against CD 20 antigen expressed by the lymphoma cells. The dose is 375 mg/m² at intervals of one week for 4 weeks.

Transexamic acid (500 mg) TDS was recommended as long term preventive prophylaxis. He had no attacks of abdominal obstruction during last 1½ years when on transexamic acid therapy.

Discussion

Angio-oedema due to C1-esterase inhibitor (C1-INH) deficiency may be hereditary (HAE) or acquired. HAE is inherited as an autosomal dominant pattern and is rare (1:10,000 – 50,000) prevalence. C1-INH is an important regulator of fibrinolytic coagulation system and the deficiency may be quantitative or functional.

Acquired C1:INH deficiency have reduced C1q, C1-INH, C4 levels; about 15% of the patients have normal C1- INH (dysfunctional deficiency). C 4 level should always be initially estimated and if it is low C1-INH is asked for. Acquired C1 INH deficiency is associated with lymphoproliferator disorder or connective tissue disease.

In angio-oedema, recurrent small bowel obstruction occurs with vomiting in 78%, diarrhoea in 65% and collapse (low blood pressure) in 4%.1,2 Even, acute pancreatitis was reported with angio-oedema.3 Small bowel obstruction due to other causes – hernias (inguinal, umbilical, femoral, incisional), intestinal adhesion (history of abdominal operation in past), healed intestinal strictures (tuberculosis, NSAID, ischaemic), undiagnosed ileal diseases (Crohn’s or tuberculosis), intraluminal malignancy (lymphoma or carcinoma), submucosal or subserosal haematoma (trauma or anticoagulants), should be excluded.

Usually patient with small bowel obstruction is investigated with plain X-ray abdomen, CT enteroclysis, repeat barium meal follow through, small bowel enema, enteroscopy to detect obscure small bowel lesion; even exploration may be occasionally necessary. The observations in our patient suggest that whenever interbowel fluid or transient ascites is detected on CT (serum albumin normal), angio-oedema should be suspected.

Having confirmed the diagnosis of C1 esterase deficiency, the patient was further investigated and associated with a chronic low grade small B cell lymphoma.

Conclusion

In a patient with recurrent intestinal obstruction of unknown aetiology, presence of any interbowel fluid and/or transient ascites should be looked for to suspect angio-oedema as the aetiology. If present, it should be confirmed by demonstrating low C4 serum level and C1-INH deficiency (if possible).

References