

ACQUIRED FACTOR XIII DEFICIENCY ASSOCIATED WITH CROHN'S DISEASE: A CHALLENGING DIAGNOSTIC AND THERAPEUTIC CASE

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Background. Acquired factor XIII (FXIII) deficiency is a rare bleeding disorder that may be associated with autoimmune diseases, malignancies or inflammatory conditions. Diagnosis is challenging because routine coagulation tests are normal.

Case Report. A 60-year-old man was referred for haematuria, anaemia, and multiple spontaneous muscle hematomas. His bleeding history was negative, despite several haemostatic challenges. Terminal ileitis was found 6 months earlier treated with a 10-week course of budesonide. At presentation, hemoglobin dropped from 14 to 7.5 g/dL. Routine coagulation tests (PT, aPTT) were normal. Acquired von Willebrand syndrome and platelet dysfunction were ruled out. FXIII measurement revealed severe deficiency (2-4%). Neutralizing anti-FXIII antibodies were not detectable, however exogenous FXIII given intravenously was rapidly cleared from the bloodstream. Partial and transient correction was achieved through continuous infusion of pdFXIII concentrate at 2 IU/kg/h. Given the reported association between inflammatory bowel disease (IBD) and FXIII deficiency, intestinal ultrasound and MR enterography were performed suggesting Crohn's disease. Active IBD has been associated with decreased FXIII levels through coagulation activation, accelerated FXIII turnover and consumption during tissue repair and mucosal healing. Initial treatment with in-

travenous corticosteroids and infliximab induction failed to significantly improve FXIII activity (4-7%), and patient experienced multiple recurrent spontaneous hematomas involving the left shoulder and arm, requiring repeated hospitalizations and continuous FXIII infusions. Intravenous immunoglobulin infusion was attempted unsuccessfully. As consequence of the muscle hematomas in the left arm, he developed permanent sensorimotor neuropathy. Two months after initiation of oral corticosteroids and infliximab maintenance therapy, MR enterography showed marked improvement of bowel inflammation, paralleled by stabilization of FXIII levels around 15% and resolution of major bleeding episodes. Infliximab was discontinued because of severe cutaneous rash and replaced with adalimumab, and FXIII levels progressively increased up to 30% despite steroid tapering, with no further haemorrhagic complications (fig.1). Due to radiological evidence of intestinal activity, biologic therapy was recently switched to guselkumab.

Conclusions. This case highlights the diagnostic and therapeutic challenges of acquired FXIII deficiency not due to the presence of anti-FXIII antibodies. Our case supports the evidence of a link between IBD and such acquired coagulopathy. Effective control of the underlying inflammatory condition was crucial for restoring FXIII levels and preventing bleeding complications.

3.02 Rare bleeding disorders

Time since diagnosis (weeks)	FXIII activity	Corticosteroid therapy	IBD therapy	Bleeding complications
0	4%			
3	2%			
6	7%	metilprednisolone 40 mg ev		
11	4%	prednisone 12.5 mg	Infliximab	
17	15%	prednisone 25 mg	Infliximab	Left shoulder and elbow hematomas; left subscapular and antecubital fossa hematomas; left brachial biceps and subscapularis muscle hematomas
24	12%	prednisone 37.5 mg	Infliximab	
41	29%	prednisone 18.75 mg	Adalimumab	Left subcostal and rectus abdominis muscle hematomas
62	40%	prednisone 10 mg	Guselkumab	