HYPOHIPOFIBRINOGENEMIA AS THE FIRST SIGN OF AUTOIMMUNE DISEASE

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BACKGROUND

Fibrinogen disorders are rare conditions that could be congenital or acquired, which can be associated both with bleeding or thrombosis. The management of these disorders usually is based on experience of some services and case reports.

OBJECTIVE

To report an uncommon case of hypofibrinogenemia related to autoimmune disease.

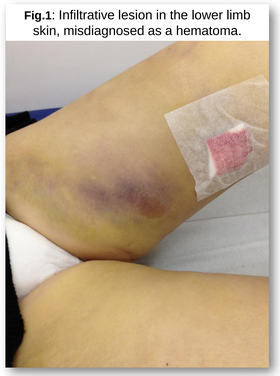


Fig.1: Infiltrative lesion in the lower limb skin, misdiagnosed as a hematoma.

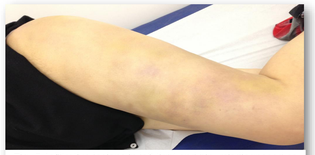


Fig. 3: Infiltrative lesions in left tight and hip, misdiagnosed as hematomas

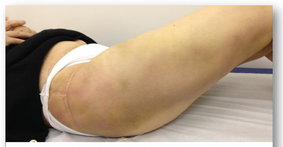


Fig. 2: Infiltrative lesions in right tight and hip, misdiagnosed as hematomas

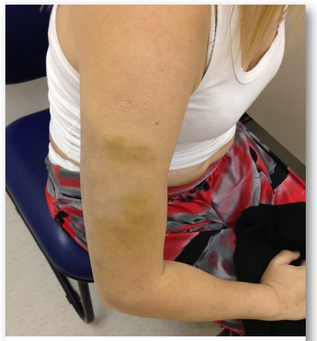


Fig. 4: Infiltrative lesions in upper limbs, misdiagnosed as hematoma

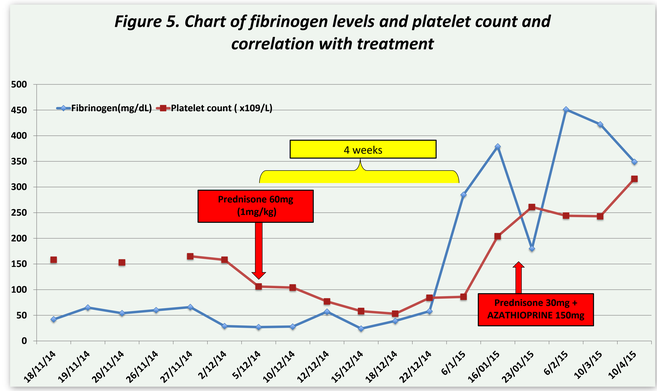
CASE REPORT

A 40-year-old caucasian woman, with a history of heart disease secondary to rheumatic fever, was admitted at our service in 2014. She presented with paresthesia in left leg and skin infiltrative lesions in lower limbs and hip that disseminated to gluteal region, upper limbs and abdomen, and initially misdiagnosed as superficial hematomas (***Figures 1, 2, 3 and 4***). The patient had fever without other complains or changes on physical examination. Hemostasis tests: PT activity=44%, aPTT R=1.4 TT=66.1 sec, fibrinogen=42mg/dL, correction of PT and aPTT in 1:1 mixing test. It was evidenced hemoglobin=7,5 g/dL, normal WBC count and platelet count, antinuclear antibody: positive, nuclear fine speckled 1:640. Dysfibrinogenemia test was negative. CT of thorax, abdomen and pelvis: no lymphadenomegalies. Skin biopsy was compatible with thrombotic vasculitis (see ***Table***). Lymphoproliferative disease was considered to be unlikely and the final diagnosis was undefined systemic autoimmune disease. She developed progressive worsening PT, TT, fibrinogen =27mg/dL and thrombocytopenia (58.000/mm3). Immunosuppressive was introduced with regression of the skin lesions and normalization of coagulation tests (***Figure 5***). Nine weeks after immunosuppressive treatment she had an extensive thrombosis in cervical veins, without B symptoms or worsening of skin lesions. Hemostasis tests were normal and she received anticoagulants. After 9 months of follow-up, fibrinogen levels were 400 mg/dL and the patient received immunosuppressive and anticoagulant. Sjöegren syndrome has been investigated.

Table: Relevant initial tests

PT: activity= 44%	PT 1:1 mixing = 75%
aPTT: R= 1.4	aPTT 1:1 mixing R= 1,17
TT= 66,1 seg	TT 1:1 mixing= 27,9 s
Fibrinogen= 42 mg/dL	D-Dimer=>10.000ng/mL Euglobuline lysis time test= 245 min (normal)
Owren test=85% (70-120%)	Fator V=80% (50-150%) FVIII=56% (50-150%)
Hb=7,5g/dL Ht=22,8% MCV=92fL MCH=29pg RDW=15,4% reticulocytes=178.000 WBC=8.800/mm3 platelet count= 158x10^9/L Ferritin=598ng/mL Transferrin saturation= 20% Direct antiglobulin test: negative	
ANA positive, nuclear fine speckled 1:640 Anti-Ro +, Anti-La + C3= normal C4= slighted reduced	ESR=77mm Reactive protein C=191,6 mg/L
Skin biposy: compatible with thrombotic vasculitis	
Throrax/abdomen/pelvis CT: increased number of lymphonodes but no lymphadenomegalias	

Figure 5. Chart of fibrinogen levels and platelet count and correlation with treatment



CONCLUSIONS

It is reported that autoimmune diseases may be responsible for hemostatic changes due to mechanisms mediated by autoantibodies that interact with platelets, and coagulation factors. They are classically reported as cases of immune thrombocytopenia, and despite rare, acquired hemophilia and von Willebrand's disease, but the association with changes in fibrinogen is not common. This report is a rare case of acquired hypofibrinogenemia, secondary to an autoimmune disease wherein the treatment of the underlying cause was crutial to normalization of the hematological abnormality.

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