

Disordini emorragici congeniti: aspetti diagnostici e clinici

VENOUS THROMBOEMBOLISM IN PATIENTS WITH FACTOR VII DEFICIENCY: A CASE SERIES AND REVIEW OF THE LITERATURE

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Background. Factor VII (FVII) deficiency is an autosomal bleeding disorder characterized by a wide spectrum of clinical presentations, ranging from asymptomatic states to life-threatening bleeding, with poor correlation between laboratory and clinical phenotypes. Information about the occurrence and management of venous thromboembolism (VTE) in patients with FVII deficiency is scanty, being heterogeneously described in case reports and small series.

Methods. We report 4 cases (3 recurrent) and review of English language literature (1990-2025) on VTE in patients with FVII deficiency.

Results. Case 1. A 64-yr old man (FVII 20%) had recurrent unprovoked VTE (pulmonary embolism, PE; 8 years later, lower limb superficial/deep vein thrombosis, SVT/DVT); persistent mild thrombocytosis led to detect JAK2 V617F mutation and diagnose an unclassifiable myeloproliferative neoplasm. Direct oral anticoagulants were administered for both events. Case 2. A 64-yr old woman (FVII 12%) developed bilateral PE with lower limb DVT after surgery for endometrial adenocarcinoma on replacement therapy with low-dose recombinant FVIIa. She was treated with low-molecular-weight heparin (LMWH, 75% of therapeutic dose) for 6 months. Cases 3-4. A 38-yr woman (FVII 35%) developed an upper limb SVT after surgery and one year later massive PE with DVT after ankle fracture despite heparin prophylaxis. She was treated with intravenous unfractionated heparin (UFH), followed by LMWH and long-term dabigatran (110 mg twice daily). Her brother had 2 lower limb DVT following air travel and later an unprovoked PE. Thrombophilia screening was negative in the 2 siblings. No bleeding complications occurred during anticoagulation in these 4 patients, who did not show significant bleeding tendency. Missense F7 variants were detected in all patients. The literature review identified 87 potentially relevant papers. After excluding reports on different topics or with insufficient data, 22 articles were retrieved, reporting 33 patients experiencing 45 VTE epiosodes (11 patients >1 event), most DVT and/or PE and including 7 VT at unusual sites. FVII levels were <5% and >20% in 9 (27%) and 8 (24%) subjects, respectively. No relevant bleeding history was reported in 17 patients (51%). Only 5 events were apparently unprovoked. Fourteen VTE episodes (31%) occurred after surgery, on replacement treatment (rFVIIa, plasmaderived FVII, fresh frozen plasma) in 12 cases. Five VTE occurred in cancer patients, 6 were associated with pregnancy or oral contraceptives. Congenital/acquired thrombophilia was found in 5 patients (one with recurrent VTE). In 17 events more than one triggering/risk factors were identifiable. Data about treatment were available for 30 VTE. UFH or LMWH were used in most patients, some received low-dose warfarin or more recently apixaban, often with shorter duration of treatment. In 2 patients vena cava filters were placed. Bleeding complications (2 severe) occurred in 5 cases (16%).

Conclusions. VTE may occurr in patients with FVII deficiency, particularly in subjects with milder factor reductions/clinical phenotype. In most cases established predisposing/risk factors are found. The role for possible specific genetic variants or co-inherited factors, suggested by cases of recurrent VTE and/or family history, deserves further investigations. In most cases anticoagulation is safely and effectively used, type and duration of treatment aiming at minimizing bleeding risk.