Factor VIIa: Mounting evidence or anecdotal reports

Approximately 1-10% of patients receiving anticoagulation therapies will experience a hemorrhagic complication.[1] In cases of severe or life-threatening bleeding events such as intracranial hemorrhage, rapid reversal of anticoagulation is associated with clinical improvements.[1] Unfortunately, conventional therapies used for hemorrhage have unpredictable reversal of anticoagulation, rarely act rapidly and may only be effective for specific hemorrhagic etiologies.

Recombinant factor VIIa (rFVIIa) is approved in most countries for the treatment and/or prevention of bleeding in hemophiliac patients. Nonproprietary indications, however, represent at least 90% of its use.[2] Compared to conventional therapies used for hemorrhage, rFVIIa offers several potential benefits including a unique mechanism of action targeted at sites of exposed tissue factor and rapid and predictable reversal of anticoagulation. However, several limitations exist including the high acquisition cost, short duration of action and the potential risk of thrombosis that has been reported to be as high as 9.8%.[3]

In this issue, a retrospective analysis[4] of 18 patients with refractory hemorrhage to various anticoagulants showed that all patients had at least considerable slowing of their bleed after the administration of rFVIIa at a median dose of 87.4 µg/kg. Twelve patients displayed a noticeable response within two hours of rFVIIa. Anticoagulation was rapidly reversed and the use of blood products was significantly reduced. Clearly, this analysis has several limitations including the retrospective design; lack of control group; heterogeneous patient population, anticoagulation regimens and treatment therapies; and the absence of consistent definitions for severity of hemorrhage. These results, however, must be taken in context with the paucity of data. Several studies of healthy volunteers demonstrate that rFVIIa reverses anticoagulation from low molecular weight heparin.[4] Several small case reports support the use of rFVIIa for controlling hemorrhage due to anticoagulation. A study of seven patients with presumed warfarin-induced intracranial hemorrhage reported rapid reversal of anticoagulation after rFVIIa was administered at a mean dose of 62.1 µg/kg.[5] Another study showed that of 16 patients with severe hemorrhage from warfarin, 14 displayed rapid hemostasis after receiving a mean dose of 16.3 µg/kg.[6]

While all these case reports are hindered by the same limitations as the analysis in this issue, these data provide evidence that rFVIIa may rapidly reverse anticoagulation and effectively control hemorrhage. In addition, these results warrant additional research in the form of randomized, double-blind studies to determine the role of rFVIIa in managing hemorrhage from anticoagulation. Several questions need to be addressed including when in therapy should rFVIIa be used (early or only after conventional therapies have failed), the appropriate dose, its effectiveness for different anticoagulants, cost-effectiveness and the risk of thrombosis in patients presumably anticoagulated because they are at risk for a thromboembolic event. Until these data are known, case series remain anecdotal reports that provide mounting evidence for further research, and clinicians are guided by expert opinions that recommend using low-dose rFVIIa (20-40 µg/kg) for anticoagulation-induced hemorrhage only after conventional therapies have failed.[4]

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Thyroid intrafollicular neoplasia: A spectrum of morphological appearances from benign cytologic precursors to microscopic papillary thyroid carcinoma (PTMC) appears as a secondary phenomenon in which it's possible to see a tubular pattern of the atrophic follicles, cellular polistratification and budding of papillae with a fine fibrovascular stroma and microcalcifications. The follicle pattern, chromatin clearing, grooves of nuclear membrane, nuclear overlapping, pseudoinclusions, nuclear overlapping, nuclear chromatin clearing, and characteristic dysmetric nuclei with fine chromatin atypia consists of a small single follicle with irregular shape.