

Thrombopoietin mimetic-induced bone marrow fibrosis

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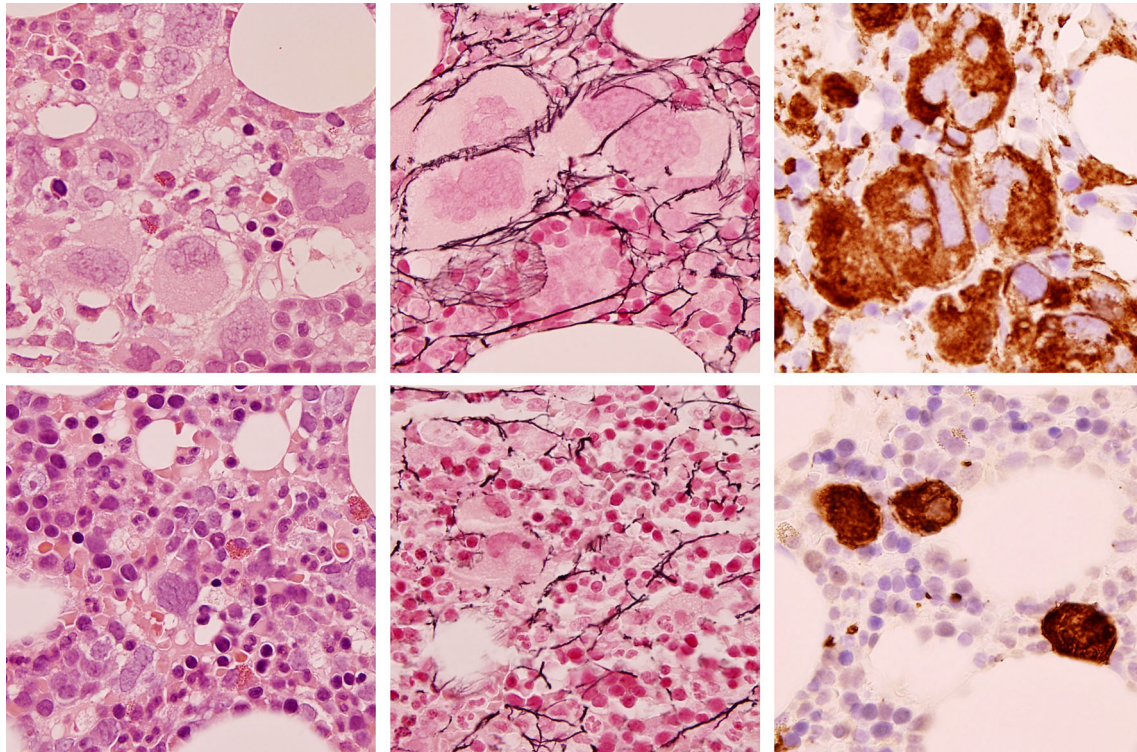
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A 67-year-old man with an 8-year history of autoimmune thrombocytopenic purpura ("ITP"), previously intolerant or unresponsive to multiple treatments (azathioprine, mycophenolate mofetil, rituximab, eltrombopag, and romiplostim), was commenced on avatrombopag. A baseline blood count showed hemoglobin concentration 132 g/L, WBC $8.5 \times 10^9/L$, and platelet count $16 \times 10^9/L$, with the blood film

confirming the platelet count but otherwise being normal. After 4 months of avatrombopag therapy, there was no significant improvement in the platelet count but his blood film now showed prominent tear-drop poikilocytes. Bone marrow trephine biopsy sections were hypercellular (80% overall) (top left) with a dense meshwork of fine and coarse reticulin fibers (MF-2) (top center) with occasional collagen

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fibers. Megakaryocytes were markedly increased in number, size, and ploidy with the formation of large clusters (CD42b, top right). Molecular analysis for *JAK2* V617F, *CALR* exon 9 mutation, and *MPL* W515L showed no abnormality. Avatrombopag was discontinued. He remained thrombocytopenic (platelet count $11 \times 10^9/L$) but without hemorrhage for the next 4 months at which point the marrow biopsy was repeated. The biopsy sections now showed cellularity of 50% overall with a reduction in megakaryocyte size (bottom left) and only a mild increase in reticulin (MF 0–1) (bottom center). There was a mild excess of megakaryocytes but no clustering or abnormal localization (CD42b, bottom right).

Thrombopoietin receptor agonists (TPO-RA) stimulate megakaryopoiesis and can increase platelet production in ITP. An increase in bone marrow reticulin is a well-recognized phenomenon¹ though clinically significant, severe grades with collagen deposition are rare. Discontinuation of TPO-RA may not be necessary in all cases but has been shown to lead to regression of bone marrow fibrosis in cases reported.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

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