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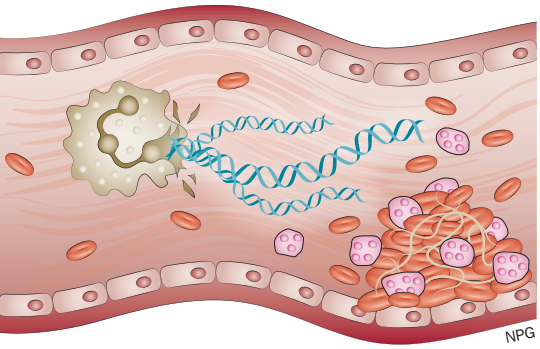
CONNECTIVE TISSUE DISEASES

Neutrophil extracellular traps—a mechanism of thrombosis in patients with antiphospholipid syndrome?

Antiphospholipid antibodies (aPL), a hallmark of antiphospholipid syndrome (APS), have been implicated in arterial and venous thrombosis frequently observed in patients with APS. A new report now shows that aPL from patients with APS can stimulate neutrophils to produce neutrophil extracellular traps (NETs, chromatin-based structures that are extruded from neutrophils), a possible mechanism for thrombi formation.



Yalavarthi and colleagues compared serum, plasma and isolated neutrophils from 52 patients with primary APS (without systemic lupus erythematosus) and healthy volunteers. Sera and plasma from patients had higher levels of cell-free DNA and myeloperoxidase–DNA complexes (an indicator of the presence of NETs), and neutrophils from patients with APS showed higher spontaneous release of NETs *in vitro*.

aPL specific for β-2-glycoprotein 1 (β_2GP1, a lipid-binding protein present in the circulation and plasma membrane of endothelial cells and monocytes) have been reported to activate cells and promote thrombosis. Researchers now show that β_2GP1 is also bound to the cell surface of neutrophils, and that β_2GP1-specific antibodies stimulate NET formation; this effect was shown to be dependent on production of reactive oxygen species and on activation of Toll-like receptor 4. Furthermore, *in vitro* stimulation of neutrophils with purified aPL or with serum from patients with APS potentiated NET formation and thrombin production.

Although NETs were first identified as a defence mechanism against microbes, it is now widely accepted that they can activate platelets and the clotting cascade, serving as scaffolding for the assembly of thrombi. These data suggest that NETs present in the circulation can contribute to thrombotic events but, as Yalavarthi and colleagues highlight, "to fully understand these pathways, NET release will need to be studied *in vivo* using experimental models of APS."

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Original article Yalavarthi, S. *et al.* Antiphospholipid antibodies promote the release of neutrophil extracellular traps: a new mechanism of thrombosis in the antiphospholipid syndrome. *Arthritis Rheumatol.* doi:10.1002/art.39247