Iron alters red blood cell morphology

Under physiologic conditions a small percentage (< 3%) of red blood cells (RBCs) are irreversibly trapped within the fibrin clot mesh. By contrast, in prothrombotic states such as diabetes mellitus, significantly more RBCs are tightly bound to fibrin fibers. Such interactions affect clot properties, making it more resistant to fibrinolytic degradation. This phenomenon may explain thrombotic resistance frequently seen in diabetic patients. In most cases these patients also have higher-than-usual levels of iron.

Using scanning electron microscopy (SEM) to study whole blood smears, RBCs from healthy individuals have the typical sphere-like appearance (panel A). The ferritin and transferrin of these individuals were within the normal ranges at 10 to 120 ng/mL and 2.5 to 3.8 g/L, respectively. However, we found unusual configurations of fibrin fibers interacting with RBCs in diabetes (panel B, where the ferritin and transferrin levels were slightly elevated). In addition, mixing whole blood samples obtained from healthy subjects with ferric chloride (15mM FeCl₃ (panel C), as well as a very low concentration of 0.03mM FeCl₃—similar to physiologic levels of iron overload) resulted in the formation of similar fibrin-like deposits. Such deposits are closely associated with RBCs, altering the morphology of their cell membranes to trap fibrin fibers (panel C). More than 70% of RBCs have a changed ultrastructure in smears of both diabetic patients and controls with added FeCl₃. We conclude that there is a striking similarity between the SEM patterns of whole blood smears from diabetes patients and that of a normal blood samples, mixed with ferric ions. This may explain the pathogenic role of iron overload associated with prothrombotic conditions.

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