Editorial

Of Acanthocytes, Spurs, Burrs and Membranes

By ROBERT SILBER

IN 1950 BASSEN AND KORNZWEIG described an unusual morphologic distortion of the human erythrocyte in two siblings with retinitis pigmentosa, neurologic abnormalities, and a history of steatorrhea. The red cells showed thorny excrescences when examined in suspension or on stained smears. Twenty other cases were reported over the next 18 years. In 1958 Jampel and Falls documented the low plasma cholesterol and suggested that this disorder, by now designated with the euphonious but inaccurate term “acanthrocytosis,” was a disease of lipid metabolism. The name was corrected to acanthocytosis (from the Greek word acanthos—spine) one year later. The important observation that the light density, beta lipoprotein was not detectable in the plasma of these patients led to the concept of a plasma abnormality, affecting proteins, lipids or the interaction between these compounds. The names beta lipoprotein deficiency or abetalipoproteinemia may be closer to the genetic abnormality leading to the disease than the term acanthocytosis.

The ratio of sphingomyelin to lecithin is decreased in the patients’ plasma. This abnormality probably results in the erythrocyte lipid defect; in contrast to normal erythrocytes where lecithin is the predominant membrane phospholipid, acanthocytes contain more sphingomyelin and less lecithin. The finding of a low lecithin content in acanthocytes was the first example of a lipid alteration in the human erythrocyte. The importance of the plasma environment was documented by Ways and Simon, who demonstrated that the striking increase in autohemolysis observed in this disorder could be corrected by a factor associated with lipid fractions of normal serum. Later studies indicated that the deficiency of α-tocopherol in the plasma may account for the increased autohemolysis. In the absence of tocopherol, the red cell membrane becomes susceptible to oxidative damage by peroxides.

Within the last ten years, spinous erythrocytes have been described in a variety of clinical disorders including uremia, microangiopathic hemolytic anemia, thrombotic thrombocytopenia purpura, pyruvate kinase deficiency, and carcinoma. Of particular interest is the report of Smith and co-workers who described a cirrhotic patient with “spur” cells and hemolytic anemia in which the plasma could induce the morphologic abnormality in normal erythrocytes. Conversely, when the patient’s erythrocytes were in-
cubated with normal plasma they lost their spurs and were restored to normal shape. This report offered the first example in disease of how the plasma environment can affect the red cell's shape, extending earlier studies by Ponder\textsuperscript{18} on the disc-sphere transformation of normal erythrocytes, and by Switzer and Eder\textsuperscript{19} who converted acanthocytes from beta lipoprotein deficient patients to biconcave cells with detergents. The plasma factor capable of distorting the membrane of normal erythrocytes has been described in two later studies of patients with cirrhosis\textsuperscript{20,21} but was not detected in three other reports\textsuperscript{22-24}. It appears possible, therefore, that spur cell formation in this disorder may develop by several mechanisms. The complexity of this problem is illustrated in Nathan's report\textsuperscript{25} which summarizes the wide variety of conditions associated with erythrocyte “spicules” and points out that incubation with sera from apparently normal individuals can occasionally result in spicule formation.

The close interrelationship between serum lipid, red cell membrane, and the shape of the erythrocyte was suggested by the recent work of Cooper and Jandi, who showed that an accumulation of cholesterol in the red cells of patients with obstructive jaundice results in formation of target cells\textsuperscript{26}. The increase in red cell cholesterol is a consequence of the elevated levels of bile salts. Studies from one laboratory have suggested that the elevated cholesterol is found not only in the target cells but also in acanthocytes of experimentally produced beta lipoprotein deficiency\textsuperscript{27}. In contrast, other workers\textsuperscript{28-30} have suggested that the increased erythrocyte surface area in liver disease is associated with an increase of both phospholipid (particularly lecithin) and cholesterol. More kinetic studies of lipid transfer rates between plasma and red cells or further knowledge about the interaction of membrane lipids with structural proteins might help our understanding of the morphologic problem.

It is safe to say that much remains to be learned about the pathogenesis of this group of disorders. Lees\textsuperscript{31} has recently suggested that in hereditary abetalipoproteinemia, the protein component of light density lipoprotein is present and that the underlying defect involves the mechanism by which the lipid is attached to the protein. This concept also raises the possibility that structural abnormalities may be present in the lipoproteins of some cirrhotics. Evidence for the suggestion that the mechanisms underlying these disorders are still unresolved is offered in a recent report of a kindred with acanthocytes, a neurologic deficit different from that described in patients with abetalipoproteinemia, and normal levels of beta lipoprotein\textsuperscript{32}. A family with markedly decreased (but not absent) beta lipoprotein without red cell abnormalities has also been reported\textsuperscript{33}.

The terms acanthocyte, burr cell, and spur cell have been used interchangeably by many authors. It should be pointed out that the red cell in abetalipoproteinemia may differ from that found in patients with liver disease. It is perhaps advisable to limit the term acanthocyte to those cells with a low MCV found in patients with hereditary beta lipoprotein deficiency and use spur cell for the remainder. It is noteworthy that the conditions summarized above have been associated with a severe hemolytic anemia in some instances, while an almost normal red cell survival was found in other
cases. Future studies on erythrocyte stiffness or on the interaction of these deformed cells with histiocytes may help explain these apparent discrepancies.

At present, it is difficult to classify this group of disorders in a lucid fashion relating etiology and morphology. This is reminiscent of the time when the nonspherocytic hemolytic anemias were first classified into Dacie types I and II. Most of these hemolytic anemias are now known to stem from specific enzyme deficiencies. A major problem in the study of a membrane lesion has been the insolubility of membrane components under gentle conditions. Recently, approaches to the study of intact membranes have been made, not only in the study of their ultrastructure, but also in the analysis of their physical structural properties by means of optical rotatory dispersion, circular dichroism, and paramagnetic resonance studies. In addition, the biosynthesis and composition of bacterial membranes has been elegantly elucidated by the identification of precursor molecules and reconstitution of membranes from carbohydrate and protein components.

Several methods have recently been described which solubilize the lipids and proteins of the erythrocyte membrane. Once in solution, it may become easier to characterize some aspects of the interaction between the proteins, lipid, and carbohydrate components of the red cell membrane and their derangement in disease. Hopefully, progress in the understanding of the red cell membrane disorders which cause acanthocytes, spurs, and spicules will then parallel that of the enzymopathies.

REFERENCES

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