Correspondence

Are Alterations of Protein 4.1 Involved in the Echinocytic Transformation of Red Blood Cells?

To the Editor:

It has been recently reported in your journal by Pinder et al1 that glycophorin C possesses two distinct protein 4.1-binding sites.1

It has also been suggested by others that the interaction between glycophorin C and protein 4.1 may play an important role in the regulation of red blood cell (RBC) shape and the mechanical properties of their membrane.

The association between glycophorin C and protein 4.1 may be a component that interacts with membrane lipids. Protein 4.1 is known to interact with other membrane proteins including spectrin actin and band 3.1,3

However, the protein 4.1 is a phosphatidylserine (PS) binding protein. The PS is the major phospholipid in the inner leaflet of RBC’s membrane and in the absence of 4.1, the PS is distributed in the bilayer. The high-affinity association of protein 4.1 with PS is important for the maintenance of structure and function of the RBC membrane.2,5

We have recently reported that uremic patients under hemodialysis (HD) present with echinocytes, which are increased in the first hour of HD (Fig 1) and revert to low levels in the end of HD.6

Echinocytes are RBCs with regular and short spicules on their membrane surface. The echinocytic transformation is caused by the significant alterations in the lipid composition of the RBC membrane with expansion of the outer leaflet and compression of the inner. The RBC transformation may be mild and reversible (discoechinocytes) or serious (spheroechinocytes).6,7 It is unknown whether the component glycophorin C protein 4.1 that interacts with membrane lipids is involved in the echinocytic transformation.

However, there are some factors that cause echinocytic transformation and may affect RBC endogenous proteins, such as an increase in intracellular Ca2+ concentration of RBCs may cause echinocytic transformation and degradation of endogenous RBC proteins; ATP depletion of RBCs may lead to echinocytic transformation and re-

arrangement or aggregation of the membrane proteins6;8 and phorbol esters, which cause phosphorylation of 4.1 protein, may activate protein kinase, resulting in the presence of echinocytes.9,10

According to the above, there is some indirect evidence that supports the involvement of the component glycophorin C protein 4.1 in echinocytic transformation.

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REFERENCES

Fig 1. Echinocytes of uremic patient after 45' HD.
Are alterations of protein 4.1 involved in the echinocytic transformation of red blood cells? [letter; comment]

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