Correspondence

Budd-Chiari syndrome: aetiology and geography

Sir,

Mahmoud et al. have recently reported underlying myeloproliferative disorders (MPD) as the commonest aetiology in Budd-Chiari syndrome (BCS) in their series. There appears to be continuing controversy over the aetiological factors and their geographical variation observed in this disorder. Earlier studies from Western countries have documented polycythemia vera as the commonest aetiology, with a large number of patients in the idiopathic category.

More recently, with the use of in vitro endogenous erythroid colony (EEC) assays, as many as 80% of patients have been identified as having haemopoietic stem-cell defect with or without overt features of MPD. Those cases, without overt features of MPD, were considered to have latent or occult MPD. However, such clonal defects in the absence of overt laboratory features of MPD have not been accepted as the aetiology by many workers, as none has been shown to progress to overt MPD, even after many years of follow-up. However, one cannot overlook the haemopoietic stem-cell defect in these patients.

A recent study in female BCS patients for X-inactivation by restriction-fragment-length polymorphism (RFLP), as well as EEC studies, has further strengthened the evidence for stem-cell defect as the underlying aetiology in BCS patients. Transmission electron microscopy of platelets in our BCS patients has revealed morphological changes akin to activated and exhausted platelets in the circulation, although many have shown EEC growth as well (unpublished data). A few cases of BCS have shown overt features of MPD after liver transplantation or surgery. Valla et al. and Pagliuca et al. in their studies have shown that patients with latent MPD in BCS when investigated showed increased red-cell mass, thereby confirming latent polycythemia vera. However, most studies have not undertaken this approach.

The literature review would suggest a clear-cut geographical difference in the aetiological pattern in BCS. Intraluminal membrane, pregnancy and infection have been frequently reported in patients from Eastern countries. Membranous obstruction of vena cava (MOVC) has been reported more commonly from Japan, China and South Africa. Pregnancy and infections have been reported more commonly from India. There is frequent disagreement in the reports appearing from different centres of India. In an early report from one major centre in India (Chandigarh), hepatic amoebiasis was described as the major cause (26%) followed by pregnancy and MOVC (17.2% and 16%, respectively). However, a recent report from the same centre has identified MOVC and pregnancy as the major causes (28.7% and 20.2%) with infection being reported in only 2.6% of cases. In one recent report from our centre (Delhi), membranes were not identified in any of the patients studied, and the commonest identifiable aetiology was pregnancy. Another Indian centre (Madras) has frequently labelled many cases as coarctation of IVC (showing hourglass constriction) which has not been reported in any other Indian, Western or Japanese studies to the best of our knowledge. These variable observations are probably due to selection bias in these studies. Kage and Okuda were of the opinion that the mural thrombus, if organized without completely occluding the lumen, would produce narrowing like an hourglass.

The aetiology of MOVC is highly disputed and is considered congenital in origin by many authors. MOVC appears to be a very loosely-used term as it has been considered to vary from few mm to a few cm. To our mind, an obstructing element as thick as a few cm cannot be taken as a membrane. The congenital origin of MOVC has been disputed by many authors as the disease rarely presents in early childhood. Moreover, recent autopsy study by Kage et al. in patients with MOVC has clearly shown that such intraluminal membranes were organized thrombus in origin. Underlying MPD and protein C deficiency have already been identified in patients with MOVC in isolated case-reports. Terabayashi et al. have shown transformation of thrombus into a fibromembranous lesion in a patient of IVC obstruction with underlying lupus anticoagulant.

In conclusion, it is advisable to investigate patients of BCS for all the known haematological factors predisposing to a pro-thrombotic state before...
accepting MOVC/coarctation as aetiological factors. Investigations such as red-cell mass may be routinely undertaken in these patients, particularly in patients showing haemopoietic clonal defect, to establish the underlying aetiology.

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References


Sir,

We agree with Professor Pati that the variable appearances of membranous obstruction both in the hepatic veins and inferior vena cava in cases of Budd-Chiari syndrome are most likely the minimal remains of an organized thrombus rather than a congenital lesion as suggested by Kage and Okuda. We also agree that the in vitro finding of clonal red-cell colony formation is not proven in this cohort of patients to be proof of an active myeloproliferative disorder as a cause of the thrombosis. We nevertheless believe that Budd-Chiari syndrome can occur in the early stages of a myeloproliferative state. We further