Presentation and natural history of variceal bleeding in patients with portal hypertension due to extrahepatic portal venous obstruction

SUDEEP R SHAH, SUREN德拉 K MATHUR
Gastroenterology Surgical Services, King Edward VII Memorial Hospital, Mumbai 400 012

Background: The natural history of portal hypertension due to extrahepatic portal venous obstruction (EHPVO) in the presence of a non-cirrhotic liver is not well understood. Aim: To evaluate the presenting features and the natural history of EHPVO by assessing the bleed patterns prior to definitive management in these patients. Methods: Two hundred and seven consecutive patients presenting with history of variceal bleeding due to EHPVO were studied prospectively. Clinical, hematological and biochemical features on presentation, and pattern and severity of bleeding prior to institution of endoscopic therapy or surgery were recorded. Results: Ascites was observed in 16% and was invariably transient. Splenomegaly was present in 82%, with hypersplenism in 22%; however, hypersplenism was symptomatic in only 6% of patients. In 127 patients having more than one episode of bleeding, the frequency of bleeding episodes was 0.94/year and transfusion requirement was 1.47 units/year. No fixed pattern of frequency of variceal bleeding was identified. However, number of bleed episodes and transfusion units requirement correlated with each other. The maximum severity of bleeding was between the ages of 12 and 19 years. Conclusion: Hypersplenism causing symptoms is rare in EHPVO presenting with variceal bleed. [Indian J Gastroenterol 2003;22:217-220]

Key words: Esophageal varices, portal vein thrombosis

Thrombosis of the portal vein leading to extrahepatic portal venous obstruction (EHPVO) and portal cavernoma formation in the presence of a normal liver is a common cause of portal hypertension in India. Patients with this condition tend to have a good life expectancy as their liver is structurally and functionally normal. For the same reason, patients tend to tolerate variceal bleeding well. Little is known about the natural history of variceal bleeding in this condition, in contrast to cirrhotic patients. Conflicting reports exist on the change in frequency of gastrointestinal (GI) bleeding with age and whether there is a predictable bleed frequency. Previous studies have also suggested that ascites is a common occurrence in patients with long-standing EHPVO with cavernoma formation.

The natural history of EHPVO is difficult to characterize today. Patients are subjected to definitive treatment immediately on presentation to a tertiary care center, since both endoscopic variceal sclerotherapy and surgery have been found to greatly reduce the risk of re-bleeding in this condition. In India, however, several patients do not have ready access to healthcare and are often not referred to specialist centers until after they have bled repeatedly. Analysis of natural history during this period prior to definitive treatment may allow some insight into the natural history and patterns of variceal bleeding in patients with EHPVO.

This prospectively documented historical cohort study was thus designed to evaluate the associated clinical and hematological features in patients with EHPVO, and natural history of variceal bleeding, as represented by frequency of bleeding and blood requirements prior to definitive treatment, in these patients.

Methods

Between January 1986 and July 1997, 207 consecutive patients with a diagnosis of chronic EHPVO were studied. These patients had presented to our surgical unit, which specializes in the management of portal hypertension, with a history of hematemesis or melena and had presence of varices documented on endoscopy.

On presentation, details regarding the duration since first bleed, number of units of blood transfused, number of bleeding episodes, previous documentation of presence of splenomegaly, and previous treatment received for bleeding were recorded. When a history of definitive treatment in the form of endoscopic variceal sclerotherapy or band ligation or surgery (including splenectomy, devascularization and shunt surgery) was obtained, the data were analyzed only till the point of such intervention, including the last GI bleed before such treatment.

The size of the liver and spleen was recorded, as was the presence or absence of clinically detectable ascites. A complete hemogram was performed and bone marrow aspiration was done in those suspected to have hypersplenism (WBC count <4,000/mm or platelets <100,000/mm). The hypersplenism was considered to be symptomatic when there were symptoms of chronic anemia in the absence of GI bleeding, recurrent upper
respiratory tract infections with a low white cell count, or spontaneous bleeding from mucous membranes or bruising with thrombocytopenia. The diagnosis of chronic EHPVO was made on the basis of ultrasonographic or portovenographic findings of a portal cavernoma with normal liver architecture and normal liver function tests as well as the absence of colloidal shift on technetium-99 mhaubate liver scan. Where the diagnosis was in doubt, liver biopsy was performed to exclude cirrhosis.

The annual bleed rate (ABR) was calculated as the total number of bleeding episodes divided by the period in years since the first episode of GI bleeding. The annual blood transfusion units requirement (ABT) was similarly calculated as the number of units of blood transfused for bleeding per year since the onset of bleeding. The severity of bleeding was analyzed by calculating the total blood requirements divided by the number of bleeding episodes.

Values for any group were calculated by summing the numerator and denominator, while for comparison, individual patient values were compared using the Mann-Whitney test. Linear regression analysis was used to determine association between number of bleed episodes and ABT with time, as well as between ABR and ABT.

Results
The median age of the 207 patients (143 male) was 13 years (range 1-77). The median age at the time of first episode of GI bleed was 10.8 years (6 mo - 75 y). The modal age for first episode of GI bleeding was seven years and that for presentation to us was nine years (Fig 1). History of umbilical sepsis could be obtained in 7 (3%) patients; no identifiable cause was found in the remaining patients. In 5 patients, splenomegaly and portal cavernoma had been documented prior to presentation with variceal bleeding; the interval between such documentation and variceal bleeding in these patients was 9 months, and 3, 4, 6 and 10 years, respectively. The age at first bleed for these patients was 5, 30, 11, 14 and 15 years, respectively.

At presentation, 33 (16%) patients had ascites that was detectable clinically and was confirmed on ultrasonography. However, it was transient, and by the time of discharge from hospital, no patient required diuretic treatment. Splenomegaly was present in 169 (82%) patients; an additional 11 patients had undergone splenectomy as part of treatment of variceal bleeding prior to presentation at our center, and 27 had no palpable splenomegaly. The spleen size varied up to 21 cm below the costal margin (mean [SD] 5.8 [3.9] cm). Evidence of hypersplenism based on hematological markers was present in 44 of 196 (22%) patients with the spleen in situ; however, only 11 (6%) of them had symptomatic hypersplenism.

A complete history pertaining to variceal bleeding was obtained from 201 patients. Of these, 74 presented after one episode of GI bleeding, 48 of these in the emergency setting with active bleeding. Another 54 patients had had two bleeding episodes before definitive
The overall annual bleed rates and blood transfusion requirements for patients in various age groups having more than one variceal bleed are shown in Table. The ABR and ABT for the patients having more than one bleeding episode was 0.94 bleeding episodes per year and 1.47 blood transfusion units per year.

Thirty-four patients (17%) had fundal gastric varices detected on presentation. Of these, 18 had presented with more than one bleed episode. These patients had an overall ABR and ABT of 1.30 and 1.93, in contrast to those presenting with esophageal varices alone (n=109; ABR 0.91, p=0.36; ABT 1.30, p=0.12; Mann Whitney test; Fig 3).

The ABR had a good linear correlation with the ABT requirement, when all patients with more than one bleed were taken into account (r=0.48, p<0.0001; Fig 4). When various age groups were compared (Table), the ABR was relatively constant, whereas the ABT was higher in the 12-19 year age group than in all other age groups taken together (p=0.04, Mann-Whitney test).

**Discussion**

We tried to answer some questions on the natural history of patients with EHPVO by analyzing the data of a large cohort of patients in whom definitive treatment had been delayed. Among patients with liver cirrhosis, the maximum risk of re-bleeding is within the first six weeks, after which the risk returns to baseline. Our data suggest that this is not true for patients with EHPVO who stop bleeding spontaneously; these patients often have long bleeding-free periods, as is also reflected in the low ABR of 0.94 per year. No regular periodicity of bleeding was observed, in contrast to what has been previously reported. A regular periodicity would lead to a strong correlation of time interval since the first episode of bleeding with the number of bleed episodes or blood transfusion units required, which we did not find.
Gastric varices are known to be more difficult to treat than esophageal varices and to have a higher frequency of recurrent bleeding and mortality. In our study, the ABR and ABT among patients with gastric varices were similar to those in patients without gastric varices. This lack of difference may be related to (a) the small number of patients with gastric varices in our study, (b) the possibility that gastric varices were not present throughout the period of observation, and (c) a selection bias, since patients with recurrent gastric variceal bleeding may not have tolerated recurrent bleeding well, leading to early institution of definitive treatment or death.

The direct correlation between ABR and ABT among patients is of interest. This implies that among patients who tolerate multiple bleeding episodes without definitive treatment, a relatively constant amount of blood is lost per episode. The amount of blood lost per bleeding episode may be self-limiting, as a fall in blood volume below a critical level may decompress the portal system and cause cessation of bleeding.

The maximum ABR was observed during the teenage years. This is in keeping with the report of Webb and Sherlock, in which the bleed frequency fell after the age of 15 years. The reason for this finding is not clear.

Our study underlines that patients with EHPVO have preserved liver function. Though transient asciites and derangement of liver function were present in a proportion of these patients during the bleeding episode, no patient had prolonged asciites requiring diuretic therapy. Similarly, though splenomegaly was present in a majority of our patients, symptomatic hypersplenism was infrequent; thus, splenectomy is not necessary in the majority of patients.

Studies based on historical data have several shortcomings. First, the data are collected from patients and their family members, and recall errors cannot be discounted. Second, there is a natural bias towards selection of patients in whom disease is not severe enough to cause death. The best way of studying the natural history of variceal bleeding in patients with EHPVO would probably be to follow up those patients who present with splenomegaly in the absence of bleeding. However, this would give information only about time interval from diagnosis to first bleed, since it would be unethical to withhold treatment once the first bleeding episode has occurred. We had five patients who had been diagnosed to have EHPVO in the absence of GI bleeding; the interval to first bleed varied widely from 0.75 to 10 years in these patients.

In summary, patients with recurrent variceal bleeding from EHPVO have a low frequency of recurrent bleeding episodes and do not show any fixed bleeding pattern. The severity of GI bleeding in these patients does not increase with increase in the number of bleeding episodes. The transfusion requirements in these patients are higher during teenage years than in other age groups. Ascites in these patients is uncommon and transient, and symptomatic hypersplenism is infrequent.

References

Correspondence to: Dr Mathur, Bombay Hospital and Medical Research Center, Mumbai 400 021. E-mail: skmathur@vanl.com

Received June 9, 2003. Received in final revised form October 5, 2003. Accepted October 29, 2003