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Original Research

Splanchnic Venous Thrombosis, with Spotlight on Occult Malignancies, Anticoagulation, and Bleeding

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ABSTRACT

Objective: Splanchnic venous thrombosis (SVT) conceptually embraces thrombosis in the portal, hepatic, splenic, and mesenteric venous system thrombosis. The SVT risk factors may be classified as abdominal disorders, underlying myeloproliferative neoplasms (MPN), inherited thrombophilic syndromes, and autoimmune disorders. The aim of our study is to evaluate the risk factors for SVT and their relations with the localization of involvement and anticoagulation during the acute period and relation to major bleeding.

Methods: All patients with portal vein thrombosis or splenic venous thrombosis in their radiologic evaluation report were included over a 5-year period.

Results: Of the 96 patients, 87 had an identifiable risk factor for SVT (90.6%). The major risk factor was cirrhosis (60 patients, 62.5%). Other risk factors included thrombophilic conditions (12 patients, 12.6%), 6 patients had the myeloproliferative disorder (6.3%), and most interestingly, 24 had occult malignancy for which SVT was the presenting factor (25%). Within the whole group, 51 patients (53.1%) received anticoagulant treatment. Within the whole group, 30 patients developed major bleeding (31.3%), and 20 of these patients did not receive anticoagulation therapy. Twenty-five of the patients with cirrhosis suffered bleeding, and 18 of them did not receive anticoagulation therapy.

Conclusion: Almost all patients with SVT had an identifiable risk factor. The follow-up and further treatments should be based on this risk factor. SVT may be the presenting finding of occult malignancies and occult malignancy should be investigated in every patient with SVT. Anticoagulation during the initial acute period should not be withheld, even in patients with the chronic liver disease with a concern for major bleeding.

Keywords: Splanchnic venous thrombosis, anticoagulation, bleeding, malignancy

INTRODUCTION

Splanchnic venous thrombosis (SVT) refers to thrombosis in the portal venous system (as portal vein thrombosis [PVT]), the hepatic venous system (as Budd-Chiari syndrome [BCS]), splenic venous system, and mesenteric venous system (as mesenteric venous thrombosis [MVT]). As an unusual site for venous thrombosis (VT), the incidence of SVT in general population is 0.7 per 100,000 person/years for PVT, and 0.8 per 100,000 person/years for BCS, although the incidence of deep VT (DVT) is 100 per 100.000 person/years (1-3).

As all sites for SVT are accepted as different pathologic entities, concomitant involvement as well as acute, subacute, or chronic presentations may telescope. Patients may be asymptomatic, and the presentation in patients depends upon the extent and speed of the thrombosis and coexisting conditions. Acute SVT generally present with a sudden onset of abdominal pain, fever, nausea, vomiting, and diarrhea. Liver functions are generally preserved due to the rapid development of collateral veins and the compensatory capacity of hepatic arterial flow. Acute MVT may also present with intestinal bleeding due to mesenteric ischemia. Pain may radiate to the back, and ileus may be observed if the proximal branches of the mesenteric artery are occluded. Hematochezia may be the sign of intestinal infarction (4).

In patients suffering from cirrhosis, PVT is usually asymptomatic, but in patients presenting with complications of cirrhosis, such as hepatic encephalopathy, gastrointestinal bleeding, or deterioration of ascites, PVT should be suspected. Doppler ultrasonography has a sensitivity of 90% in the diagnosis of PVT and BCS, but in MTV, the overlying bowel gas may complicate the vision obtained by ultrasonography, and computed tomography or magnetic resonance imaging should be performed (5).

Previously defined as primary/secondary or provoked/unprovoked, the distinction of an underlying risk factor is challenging. True unprovoked primary SVT is reported as 15% to 27% of all patients (3).

The SVT risk factors may be classified as abdominal disorders, underlying myeloproliferative neoplasms, inherited thrombophilic

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syndromes and conditions, autoimmune disorders, viruses, and hormones (6).

The aim of our study is to evaluate the SVT risk factors and their relations with localization of involvement and anticoagulation during the acute period and relation with major bleeding.

METHODS

All patients with PVT or splenic VT stated in their radiologic evaluation report were retrospectively included over a 5-year period. Concurrent chronic liver disease (CLD), inherited thrombophilic disorders, and occult malignancies for which splanchnic thrombosis was the presenting symptom were also evaluated and recorded. Major bleeding was defined as fatal, leading to surgery, in a critical organ (intracranial, retroperitoneal, intraocular), overt bleeding with a hemoglobin decrease of 2 g/dL or greater, requiring a red blood cell transfusion of 2 units or more, and requiring hospitalization as defined by International Society of Haemostasis and Thrombosis (ISTH) (7).

All analyses were performed by the IBM SPSS version 20. Descriptive analysis, chi-squared, and Fisher's exact test were performed and all significant parameters were assessed by the logistical regression method. The study was approved by local ethical committee (2014/62) as a retrospective data collection study. Informed consent was obtained from every patient who have been reached and living.

The study has been conducted according to the Helsinki Declaration. As it was conducted as a retrospective study, all data were collected from the files, and patients' personal information was protected.

RESULTS

Out of 96 of patients with SVT, 48 were female (50%), while 48 were male (50%). The mean age was 53.8 years (19–94). Sixty had PVT (62.5%), 10 had splenic VT (10.4%), 3 had BCS (3.1%), and 22 had multiple thromboses in the splanchnic area (22.9%).

Fifty were incidental, while 46 had concurrent known CLD. The main presenting symptom was an abdominal pain (64 patients 66.6%), whereas 32 patients were asymptomatic (33.3%). Seventy-five patients had acute SVT (78.1%), whereas 21 had chronic SVT (21.9%). Most of the patients with asymptomatic SVT had occult solid tumors and myeloproliferative neoplasms (MPN) (33 patients, 66%). The mean age of patients with MPN was 44.6 and 56.2 in patients with CLD.

Regarding the SVT etiology, 87 had an identifiable risk factor for SVT (90.6%). The major risk factor was cirrhosis (60 patients, 62.5%). Other risk factors included thrombophilic conditions (12 patients, 12.6%), 6 patients had MPN (6.3%), and most interestingly, 24 had occult malignancy for which SVT was the presenting factor (25%). In 36 patients, SVT was the main reason for the deterioration of the clinical condition (60%). Fifty-seven of the patients with CLD had PVT (95%), while almost all patients with MPN (70%) had multiple thromboses in the splanchnic area, and the majority of patients with tumors had PVT (18 patients, 75%).

DISCUSSION

The major issue and finding of our study are about treatment and bleeding. Within the whole group, 51 patients (53.1%) received anticoagulant treatment (including the initial acute post-thrombotic period), and a significant percent of patients did not receive anticoagulant treatment. Within the whole group, 30 patients developed major bleeding (31.3%), and 20 of these patients did not receive anticoagulation (p=0.008). Again, regarding anticoagulation and bleeding, 2 of the patients with MPN suffered bleeding and were not on anticoagulation, 7 patients with a solid tumor had to bleed, and 3 of them did not receive anticoagulation (not statistically significant). None of the patients with thrombophilia had to bleed, and all were on anticoagulation (p=0.003), and 25 of the patients with cirrhosis had to bleed, and 18 of them did not receive anticoagulation (p=0.000).

The first noteworthy observation of this study is the high incidence of occult malignancies. Patients presenting with acute abdominal pain without a clinical history should be evaluated for these unexpected diagnoses (8). In these patients, the most common pre-diagnosis for the radiology request was surgical acute abdomen such as acute appendicitis. Likewise, patients with CLD are most likely to be disregarded as any chronic disease, and awareness of both the caregivers and patients should be encouraged. Likewise, any difference in the clinical condition should raise the concern for the SVT development (5).

Majority of the patients with SVT, with CLD or not, had been undertreated. This reluctance to include anticoagulation therapy in acute or chronic, or asymptomatic SVT, may be due to the lack of suggestive guidelines or reviews. Prospective studies and expert opinions are needed, especially in patients with asymptomatic SVT and chronic SVT without an identifiable etiologic factor.

Only 53.1% of patients with acute SVT received anticoagulation, and within this group, 10 patients had major bleeding. Indeed, major bleeding was observed more frequently in patients who did not receive anticoagulation therapy. The decision not to include such therapy may be due to the concerns about bleeding, and in patients with CLD, due to the condition called "already anticoagulated due to liver failure" This persuasion has been cleared away with a definition of "rebalanced hemostasis" in patients with CLD, since all levels of the hemostatic process may be impaired, including primary hemostasis with thrombocytopenia and platelet dysfunction, coagulation with an impaired coagulation factor production, and increased fibrinolysis due to increased levels of tissue plasminogen activator, decreased levels of alpha 2 antiplasmin, factor XIII, and thrombin-activatable fibrinolysis inhibitor, and increased levels of fibrin degradation products that may influence normal hemostatic process (9-11). However, in our study, patients with CLD who were not on anticoagulation had more episodes of major bleeding than patients who were on anticoagulation.

CONCLUSION

Almost all patients with SVT had an identifiable risk factor, and the follow-up and further treatments should be based on this risk factor. SVT may be the presenting finding of occult malig-

nancies and should be sought in every patient with SVT. Anticoagulation during the initial acute period should not be withheld even in patients with CLD with a concern for major bleeding.

Ethics Committee Approval: Ethics committee approval was received for this study from the local ethics committee ofTUTF GOKAEK2014/62

Informed Consent: Informed consent was obtained from parents of the patients who participated in this study.

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