Pulmonary hypertension in patients with hematological disorders following splenectomy

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Abstract  Prevalence of pulmonary arterial hypertension (PAH) was studied by echocardiography and Doppler in 43 splenectomized patients with various disorders 1–20 years after splenectomy. Pulmonary arterial hypertension was detected only in thalassemia major, intermedia, hereditary spheroocyte and myelofibrosis groups comprising a total of 21 patients. Six patients out of 21 was found to have PAH with mean pulmonary arterial pressure of 46.28 ± 28.17 mm Hg. Twenty-one controls having similar duration and type of disease also were assessed for PAH in this case control study 3/21 had pulmonary arterial hypertension in this control group. The difference in number of patients showing pulmonary hypertension between case and control was not statistically significant (Chi square test P=0.29) though the difference in pulmonary arterial pressure between case and control were significantly different (t test P<0.0029) with control group showing a mean pulmonary arterial pressure of 25 ± 19 mm Hg.

Platelet count in the splenectomized group was significantly higher (P=0.0029) than the controls. Pulmonary thromboembolism was equally high in the PAH patients with and without splenectomy. Patients undergoing splenectomy due to trauma, immune thrombocytopenia, sideroblastic anemia, extrahepatic portal hypertension, autoimmune hemolytic anemia did not show PAH after splenectomy even years after the procedure PAH following splenectomy is common after certain disorders and control patients in these diseases have tendency to develop PAH even without splenectomy. Pulmonary thromboembolism may be an important pathophysiological mechanism leading to this condition. Patients having hemolytic anemia and myelofibrosis should have regular evaluation of pulmonary arterial pressure whether he/she has been splenectomized or not.

This is particularly important as availability of phosphodiesterase inhibitors such as sildenafil allows one to manage these cases.

Keywords  Pulmonary arterial hypertension (PAH) · Splenectomy · Thalassemia major · Thalassemia intermedia · Myelofibrosis · Pulmonary thromboembolism

Introduction

Splenectomy is widely performed for treating various hematological and non-hematological conditions [1–6]. There are debates as to whether there is increased risk of pulmonary arterial hypertension following splenectomy either as a result of increased thromboembolism [7] or due to loss of some other function of spleen other than its filtration function [8].

There are also debates whether the diseases for which splenectomy is done itself predisposes to PAH. Pulmonary arterial hypertension again can be caused by several pathophysiological mechanisms (i) Increased blood flow through the pulmonary circuit (volume overload) (ii) Occlusion of blood vessels (thromboembolic) or (iii) Plexiform arteriopathy as is classically associated with primary pulmonary hypertension.
Conditions for which splenectomy is done may often be associated with anemia and splenectomy itself produce a hypercoagulable state predisposing to pulmonary thromboembolism. In this case control study we matched these clinical conditions which has produced pulmonary hypertension following splenectomy with disease matched controls. In addition there were several other category of patients who underwent splenectomy but did not develop PAH for these patients no control was used.

Materials and methods

Patients  
Forty-three patients of either sex (25 female and 18 males) underwent splenectomy (1–20 years back) for various indications were included in this study. Of these 43 patients, 21 patients were found to have pulmonary arterial hypertension.

Controls  
Twenty-one control non-splenectomized subjects were matched with similar spectrum and duration of disease as the study subjects with PAH.

Institutional ethics committee permitted this study and detailed informed consent was taken from each of the patients after describing them the objective of the study and the procedure to be followed. They all consented for the study.

All the patients and controls were examined clinically, had routine hemogram, blood chemistry, transfusion history, transfusion transmitted viral infection checked. Chest X-ray, ECG was routinely evaluated in all the patients. Autoimmune profile like ANA, dsDNA, rheumatoid factor was checked in all the patients as also the screening coagulation tests comprising APTT, PT and TT.

Pulmonary arterial pressure was measured using standard published criteria using echocardiography and Doppler Techniques measuring the velocity of the regurgitant jet across the tricuspid valve [4, 6]. Those patients who were found to have PAH as defined by a mean pulmonary artery pressure of >25 mmHg at rest underwent ventilation perfusion scan, spiral CT angiography of chest, arterial blood gas analysis and pulmonary function test in addition to regular investigations described above.

Results

Twenty-five female and 18 male (21–36 years) were in the patient group. Eleven female and 10 male were in the control group (22–38 years). Patients were splenectomized 1–20 years back (M ± 1SD 6.6 years ± 4.2 years). The mean ± 1SD duration from splenectomy to detection of pulmonary hypertension was 11.14 ± 6.49 years which was not very different from the 21 controls with whose disease was detected 3.5–11.5 years earlier.

Pulmonary hypertension was detected in the following group of patients, i.e. β thalassemia major, intermedia, myelofibrosis and hereditary spheroctytosis. Non-splenectomized control of hereditary spheroctytosis did not show any evidence of PAH.

In addition to above diagnostic group a large number of patient with immune thrombocytopenic purpura (ITP) [7] who underwent splenectomy did not develop PAH. Similarly few patients of unstable hemoglobin, AIHA, sideroblastic anemia, trauma, extrahepatic portal hypertension and atypical CML did not develop PAH 1–6 years after splenectomy. Mean pulmonary artery pressure (m ± 1SD) in patients were significantly higher than controls (46 ± 28 vs 25 ± 19 mmHg Student’s t test p<0.0029)

Six out of 21 splenectomized patients and 3 out of 21 cases and duration matched controls developed PAH (λ2 test P>0.05).

The patients with myelofibrosis in both splenectomized and non-splenectomized group had severe PAH (mean PAP >45 mm of Hg) had abnormal chest X-ray and clear cut right ventricular hypertrophy on 12 lead ECG. These patients were clinically symptomatic where as other patients with PAH were clinically asymptomatic. Pulmonary thromboembolism was detected in 3/6 cases (50%) and 2/3 controls (60%). The patients showing thromboembolism were patients of thalassemia syndrome and myelofibrosis. Biochemical autoimmune profiles and screening coagulation tests were normal in all the patients. Platelet count was significantly higher in the cases compared to controls (t test P<0.0029). Details of the patients and controls have been presented in Table 1, Table 2 and similar distribution of cases and matched controls are shown in Fig. 1.

Discussion

Pulmonary hypertension, a hitherto unrecognized complication of splenectomy, has its own pathologic import and hematologists have to include this complication also while taking the decision to go ahead with the procedure.

![Fig. 1a](Distribution of cases)