With the increasing use of AICDs, an increasing number of complications will be seen. In these patients, the etiology of hemoptysis should be aggressively pursued. In this case, the standard angiographic approach did not identify the bleeding artery. If a bleeding vessel cannot be identified or embolized, alternative measures must be considered. Life-threatening hemoptysis can be temporarily managed by unilateral, or, as in this case, segmental bronchial occlusion via endotracheal intubation using a balloon catheter to occlude the bronchus of the hemorrhaging lobe.

The technique of segmental bronchial occlusion limits the lung parenchyma lost to a lobe. This should be valuable in all patients, particularly those with a compromised pulmonary reserve. Furthermore, the remaining lung can be efficiently ventilated. As in this case, fluoroscopic guidance and familiarity with guidewire catheter technique would be essential. This technique should reduce the complications and mortality associated with massive hemoptysis when the hemorrhaging lobe can be isolated.

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Pulmonary Hypertension Associated with Long-standing Thrombocytosis*

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A case of thomboembolic pulmonary hypertension associated with long-standing thrombocytosis is presented. In this patient we found a significant local pulmonary platelet activation and thrombin generation as indicated by the existence of a transpulmonary gradient for thromboxane A₂, beta thromboglobulin and fibrinopeptide A. Prolonged heparin and acetylsalicylic acid treatment resulted in improvement of clinical and hemodynamic conditions. These findings support the usefulness of anticoagulating and antiaggregating therapy in selected cases of pulmonary hypertension. (Chest 1991; 99:1303-05)

PPH = primary pulmonary hypertension; PVR = pulmonary vascular resistance; beta-TG = beta-thromboglobulin; FpA = fibrinopeptide A; ELISA = enzyme-linked immunoabsorbant assay; CO = cardiac output; PAP = pulmonary artery pressure; PWP = pulmonary wedge pressure; CI = cardiac index

About half of all the cases of primary (unexplained) pulmonary hypertension are of the thromboembolic type. Pulmonary endothelial damage and local platelet activation have been hypothesized to play a significant role in the pathogenesis of this type of PPH. Moreover, abnormalities in platelet function and an increased thrombin generation have been demonstrated in patients suffering from primary pulmonary hypertension.

We report a case of unexplained pulmonary hypertension in a young man with moderate thrombocytosis, secondary to splenectomy performed in infancy for minor thalassemia. This case underlines the possible role of chronic pulmonary endothelial damage and local platelet activation in the pathogenesis of the thromboembolic type of PPH and supports the usefulness of antithrombotic treatment in selected cases of pulmonary hypertension.

CASE REPORT

A 29-year-old man suffering from minor thalassemia underwent splenectomy at the age of nine years. Afterwards, repeated hematologic controls showed a mild thrombocytosis (platelet count between 400,000 and 700,000/cu mm) and leucocytosis (white blood cell count between 17,000 and 25,000/cu mm). However, after splenectomy the patient did not receive any treatment and was asymptomatic until the age of 25 years when he began to experience mild dyspnea on exertion. Cessation of smoking did not result in any improvement. In the following months, fatigue and dyspnea progressively worsened and the patient was compelled to limit his physical activity. Moreover, the patient noticed an increase in weight (about 5 to 6 kg) and the occurrence of dependent edema.

For these reasons, in May 1984 he came to our clinic for observation. On admission to the hospital, the patient had dyspnea with minimal effort. Physical examination showed cyanosis of the lips, distended jugular veins, hepatomegaly and dependent edema.

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On cardiac auscultation, a presystolic gallop rhythm (heart rate, 120 beats per minute), a widely split second sound with accentuated pulmonary component and a grade 2/6 pulmonary systolic murmur were disclosed. Systemic arterial pressure was 125/80 mm Hg. Arterial blood gas values at room air showed a pH value of 7.46; Po2, 63 mm Hg; and Pco2, 36 mm Hg. A chest x-ray film revealed right atrial and ventricular enlargement, a prominent main pulmonary artery and diminished pulmonary vascularity. The ECG showed sinus tachycardia and signs of right ventricular hypertrophy. The right atrium and right ventricle were significantly enlarged at echocardiographic examination. Doppler examination revealed a significant tricuspid regurgitation. Technetium 99m radionucleide angiography showed an increased right ventricular volume while right ventricular ejection fraction (27 percent) and ejection rate were significantly decreased. No abnormalities of left ventricular volume and function were detected. Multiple small peripheral defects were identified on a pulmonary perfusion scan while a ventilation pulmonary scan did not show any abnormalities. Venous Doppler examination showed normal patent of iliac, femoral and popliteal veins with preserved flow respiratory changes. Antinuclear antibodies and antibodies against cardiolsphin or anticardiolipid lupus-like antibodies were absent. A clinical diagnosis of PPH was made.

Right heart catheterization was performed using a triple-lumen balloon-tipped thermodilution catheter inserted into an antecubital vein of the right arm. Systemic arterial pressure was monitored through a 20-G Angiocath catheter inserted into the femoral artery. Cardiac output was measured as thermodilution as the average value of three determinations. Systemic and pulmonary vascular resistance were calculated according to standard formulae. During each study, blood samples from a peripheral vein, right ventricle and femoral artery were collected for determination of blood gas values, TxB2, 6-keto-PGF1α, PGE2, beta-TG, FpA, platelet count, epinephrine and norepinephrine.

A platelet count was taken using automated equipment (Baker Instruments 810 Platelet analyzer). The stable derivative of TxA2, TxB2, was assayed by radioimmunoassay according to Granstrom et al.20 using a commercial kit (ABT, West Berlin, FRG). The stable derivative of PGI2 (6-keto-PGF1α) and PGE2 were assayed by radioimmunoassay according to Patrono et al.15 Fibrinopeptide A was assayed by ELISA as previously described15 using a commercial kit (Mallinkrodt Inc., St. Louis, MO). The beta-TG was assayed according to Ludlam et al.23 using a commercial kit (Beta TG RIA, Amershorn, United Kingdom). Epinephrine and norepinephrine were assayed by high-performance liquid chromatography according to Mefford et al.4 Intra- and inter-assay variation coefficients for the different tests were respectively comprised within 5.3 and 8.7 percent and between 8.1 and 10 percent.

RESULTS

First Study

Hemodynamic data are summarized in Table 1. Platelet count in peripheral venous blood was 820,000/cu mm. Peripheral plasma levels of beta-TG, TxB2 and FpA were significantly higher than values found in healthy subjects (Table 2), but no significant difference was found between the levels in peripheral vein and in right ventricle. On the contrary, a significant step-up gradient of beta-TG, TxB2 and FpA existed between the right ventricle and femoral artery (Table 3) while platelet number was significantly lower in samples from the femoral artery.

The 6-keto-PGF1α and PGE2 levels were under the detection limit of the assay method both in samples from the right ventricle and femoral artery. No significant difference was found in plasma levels of norepinephrine and epinephrine among the different sites of blood collection (Table 3) at variance with healthy subjects in which a significant decrease of norepinephrine and epinephrine levels was found throughout the pulmonary vascular bed.

The patient was discharged from the hospital on antiaggregating therapy (acetylsalicylic acid, 100 mg/day) and low-dose heparin (12,500 U subcutaneous/day). Moreover, vaso-dilating treatment was prescribed (nifedipine, 10 mg three times a day, and hydralazine, 25 mg three times a day). Clinical conditions improved and the patient could fully resume his employment even if he had to avoid heavy physical activities. During the follow-up period, indices of platelet activation and of thrombin generation in samples from peripheral venous blood showed an almost complete normalization, while the platelet count (620,000/cu mm) was persistently elevated.

Second Study

A second study was performed three and a half years later. The patient had been on the prescribed treatment all during that period. Acetylsalicylic acid, heparin and vasodilators were discontinued five days before the study. Pulmonary artery pressure showed unimportant changes; however, CO was nearly doubled in comparison with that in the first examination so that calculated PVR significantly decreased (Table 1). Peripheral venous plasma levels of beta-TG, TxB2 and FpA decreased by two or three times in comparison with those values in the first study. Moreover, the transpulmonary gradient of these metabolites was appreciably blunted (Table 3).

At variance with the first study, detectable plasma levels of vasodilating prostaglandins, PGE2 and 6-keto-PGF1α, were found in samples both from the right ventricle and peripheral artery. Norepinephrine and epinephrine plasma levels, however, did not show significant changes between the two studies.

DISCUSSION

In this 29-year-old man, the diagnosis of PPH was formulated on the basis of a careful clinical and instrumental evaluation. A potential bias to our study is the absence of a histologic confirmation of the morphologic abnormality of
pulmonary vessels. However, the scintigraphic pattern observed in our patient was similar to that indicated by Rich et al.\textsuperscript{3} as typical for the thromboembolic type of PPH.

Thrombotic complications frequently occur in primary and secondary thrombocytosis and elevated plasma levels of beta-TG have been previously described in these patients;\textsuperscript{4} however, no case of pulmonary hypertension has been reported yet. The short clinical course of most clinical conditions associated with relevant thrombocytosis probably hastens the development of a clinically detectable pulmonary hypertension.

Clear evidence of hemostatic activation existed in our patient in peripheral venous blood (high levels of FpA, beta-TG and TxB\textsubscript{2}). Moreover, we found a transpulmonary concentration gradient for TxB\textsubscript{2}, beta-TG and FpA, suggesting local pulmonary platelet activation and thrombin generation. Widespread endothelial damage is suggested by the marked impairment of the pulmonary clearance of catecholamines and the decreased production of vasodilating prostaglandins.

Evidence from experimental and clinical studies\textsuperscript{5,10,19} suggests that pulmonary endothelial damage and platelet and clotting activation may play a relevant role in the pathogenesis of thromboembolic pulmonary hypertension. Thus, increased platelet aggregation and clotting activation associated with the unusual long-lasting thrombocytosis could have played a role in the development of pulmonary hypertension in our patient.

Natural history of PPH is characterized by a rapidly progressive course with a 79 percent mortality within five years from clinical diagnosis.\textsuperscript{13,17,21} Outcome is scarcely influenced by vasodilator treatment, particularly in patients with fixed obstructive vascular lesions. Beneficial effects of anticoagulant treatment on histologically documented thromboembolic pulmonary hypertension were previously reported by Cohen et al.\textsuperscript{22} Moreover, in a large series, anticoagulant treatment was the only item strongly correlated to a longer survival in patients with PPH.\textsuperscript{1} In our patient, long-term treatment with low-dose subcutaneous heparin and acetylsalicylic acid resulted in a subtle, but significant improvement of pulmonary hemodynamics. Even if we cannot exclude a benefit from the associated vasodilator treatment, the close association between clinical (and hemodynamic) improvement and impressive decrease of the indexes of platelet and thrombin activation with suppression of transpulmonary gradient for TxA\textsubscript{2}, beta-TG and FpA observed in our patient supports the usefulness of antithrombotic treatment in selected cases of PPH.

### REFERENCES


### Table 3—Transpulmonary Gradient of Beta-TG, TxB\textsubscript{2} and FpA before and after Treatment*  

<table>
<thead>
<tr>
<th></th>
<th>First Study</th>
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<tr>
<td></td>
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<td>FA</td>
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<tr>
<td>Platelets, cu mm</td>
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<td>Beta-TG, ng/ml</td>
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<td>TxB\textsubscript{2}, pg/ml</td>
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<td>Norepinephrine, pg/ml</td>
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*DL = detection limit; RV = right ventricle; FA = femoral artery.