circumflex coronary arteries. With the color Doppler on, the course of the circumflex artery was easily tracked. After its origin, the circumflex artery angled sharply posteriorly to lie between the aorta and the left atrium, and then appeared to resume its normal course bordering the posterolateral aspect of the left atrium (Fig. 1). The patient underwent replacement of the bicuspid aortic valve, which was found to be moderately stenotic. The anomalous origin of the circumflex artery from the right sinus of Valsalva was further confirmed during surgery. The patient had an uneventful postoperative course and was discharged home in a satisfactory condition.

The incidence of an aberrant coronary artery origin ranges from 0.6% to 1.2% of patients undergoing coronary arteriography and is more common in men than in women.[1] The anomalous origin of the left circumflex artery from the right coronary sinus is a well-recognized entity and accounts for almost half of all cases of aberrant origin of coronary arteries.[2] It is important to document this congenital anomaly, since it may contribute to myocardial infarction and sudden death. Symptoms attributed to the anomalous origin of a coronary artery are angina pectoris (42%), atypical chest pain (28.9%), syncope (17.7%), and palpitation (46.7%). There is a high incidence of associated systemic hypertension (40%) and valvular heart diseases (31%).[1]

The diagnosis of an anomalous origin of a coronary artery becomes all the more important if the patient has to undergo an open-heart procedure because failure to diagnose and perfuse the aberrant coronary ostium during bypass may lead to myocardial necrosis of the area supplied by that vessel.[3] Though conventional two-dimensional and color Doppler echocardiography have been used in the past to evaluate the proximal coronary arteries, the images are not optimal in most cases due to the difficulty in obtaining high resolution images of small caliber vessels.[4] Since TEE utilizes a high-frequency transducer (5 MHz) that can be positioned adjacent to cardiac structures without interposition of the chest wall, it provides superior quality resolution of small caliber vessels such as the coronary arteries.[5] A recent report from our laboratory[6] has demonstrated the usefulness of TEE in the diagnosis of separate but adjacent origins of the left anterior and circumflex coronary arteries from the left sinus of Valsalva. The present case further illustrates the potential of TEE in the assessment of aberrant origin of the coronary arteries.

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Thrombocythemia and coronary artery disease

Michael G. Scheffer, Jan J. Michiels,
Maarten L. Simoons, MD, and
Jos R. T. C. Roelandt, MD.
Rotterdam, The Netherlands

The existence of acquired platelet-mediated thrombophilia in thrombocythemia has received little attention. This specific platelet-mediated microvascular thrombotic disease, which is first seen with erythromelalgia, acrocyanotic ischemia, or peripheral gangrene is now well recognized as a manifestation of thrombocythemia.[1-4] There is also good evidence that patients with thrombocythemia and a significantly increased platelet count in excess of 500 to 650 $\times 10^9$/L tend to have thrombosis of the cerebral or coronary circulation.[2, 4-6] Cardiovascular complication rates in large series of patients with primary thrombocythemia vary from 4% to 21%.[5, 6] Acute ischemic coronary artery disease may be the presenting symptom of thrombocythemia.[7-11] We report seven cases of coronary heart disease associated with thrombocythemia. Evidence is presented that control of platelet function by aspirin or reduction of the platelet count to normal with busulfan is associated with elimination of thrombotic events.

Methods. Clinical, cardiologic, and hematologic data and results of treatment were obtained prospectively. Polycythemia vera and primary thrombocythemia were diagnosed according to the criteria of the Polycythemia Vera Study Group.[12] Platelet counts in excess of 500 $\times 10^9$/L and an increase of clustered megakaryocytes in a bone marrow biopsy without any cause for reactive thrombocytosis are mandatory for the diagnosis of primary thrombocythemia. Confirmative criteria for primary thrombocythemia are an elevated score for the leukocyte alkaline phosphatase stain, the presence of reticulin fibers in bone marrow biopsy material, and slight splenomegaly.

Results. Primary thrombocythemia was diagnosed sub-

From the Thoraxcenter, Department of Cardiology, and The Department of Hematology, University Hospital, Erasmus University Rotterdam.

Reprint requests: J. J. Michiels, Department of Hematology, University Hospital, Erasmus University Rotterdam, Molewaterplein 40, 3015 GD Rotterdam, The Netherlands.

4/4/29735

Table I. Clinical manifestations and results of treatment in six patients with primary thrombocythemia and one patient with polycythemia vera and thrombocythemia

A. Hematologic findings								*Normal values*
Clinical case	1	2	3	4	5	6	7	
M/F	M	M	M	M	F	M	M	
Age at presentation (yr)	33	55	47	47	59	62	75	
Date	1974	1983	1973	1984	1987	1988	1989	
Sedimentation of erythrocytes	2	1	1	0	1	2	1	mm/1 hr
Hemoglobin	9.8	9.9	8.4	11.4	8.6	7.2	7.4	8.7-10.5 mmol/L
Hematocrit	0.47	0.46	0.42	0.60	0.41	0.35	0.36	0.42-0.51
Leukocytes ($\times 10^9$)	8.1	6.8	7.2	15	9.8	6.0	8.1	$4.1\text{-}10 \times 10^9$/L
Leukocyte alkaline phosphate score	—	67	101	217	80	134	123	30-90
Platelets ($\times 10^9$)	740	675	694	1008	750	812	854	$150\text{-}350 \times 10^9$/L
Bone marrow								
Cellularity	N	N	N	↑	N	N	↑	Normal (N)
Megakaryocytes	↑	↑	↑	↑	↑	↑	↑↑	Increased (↑)
Reticulin fibers	N	N	↑	↑	↑	↑	↑	
Diagnosis	PT	PT	PT	PVT	PT	PT	PT	
B. Cardiologic data and thrombotic events								
Risk factors								
Smoking	−	−	−	+	+	−	+	Present (+)
Hypertension	−	−	−	−	−	−	+	Absent (−)
Cholesterol	N	N	N	N	↑	N	↑	
Diabetes	−	−	−	−	−	−	−	
Family history of CAD	−	−	−	−	+	−	+	
Extent of coronary vessel disease	None	One	One	One	Three	Three	Three	
Thrombotic event sequence	MI	MI	E*	UAP	UAP	TIA	TIA	
	TIA	TIA	UAP	E*	E*	UAP	UAP	
Time lapse of thrombotic events	2 yr	5 yr	1 yr	5 yr	1 yr	½ yr	Several years	
C. Outcome of treatment								
Treatment	B	A	B	A	B	A	B	
Outcome	R		R		R		R	
Platelet count ($\times 10^9$)	N	650	N	1,000	N	800	N	$150\text{-}350 \times 10^9$/L
Event-free period	>5 yr	>4 yr	>6 yr	>5 yr	>1 yr	>1 yr	>1 yr	

PT, primary thrombocythemia; PVT, polycythemia vera with thrombocythemia; MI, myocardial infarction; UAP, ustable angina pectoris; TIA, transient ischemic attack; E, erythromelalgia; CAD, coronary artery disease; A, Low-dose aspirin; B, busulfan; R, remission of thrombocythemia; N, normal platelet count.

*Complete relief of erythromelalgic symptoms by low doses of aspirin.

sequent to the first cardiac event in six patients and polycythemia vera with thrombocythemia in one patient (Table I, *A*). The presenting acute coronary events were myocardial infarction in two patients and unstable angina pectoris in five. Cardiac catheterization was performed in all seven patients. The first patient with myocardial infarction had normal coronary arteries (Table I, *B*). The second patient with myocardial infarction had a totally occluded left anterior descending coronary artery, but no other signs of coronary atherosclerosis were found in the remaining coronary arteries 7 years after myocardial infarction, suggesting a thrombotic embolism. The five patients with unstable angina pectoris who had coronary artery disease (one-vessel disease in two and two-vessel disease in three; Table I, *B*) underwent coronary bypass graft surgery. All four patients less than 50 years of age had one-vessel disease (Nos. 2, 3, and 4) or no vessel disease (No. 1, Table I, *B*). All three patients more than 50 years of age had three-vessel disease (Nos. 5, 6, and 7; Table I, *B*). A thrombotic tendency appeared to be present because transient cerebral ischemic attacks or erythromelalgia caused by platelet-mediated thrombosis[2] preceded or followed the cardiac events in all patients (Table I, *B*). Time lapses of thrombotic events ranged from 1 to 5 years. Risk factors for

coronary disease were absent in four patients. All patients with thrombocythemia had very low erythrocyte sedimentation rates (Table I, *A*). There were no obvious predisposing factors for reactive thrombocytosis, and in particular there was no evidence of malignancy, chronic infection, diabetes, or other systemic disease. During continuous treatment with low doses of aspirin (500 mg/day) for 1 to 5 years, there was no recurrence of vascular events in three patients with primary thrombocythemia at platelet counts of 650, 800, and 1000 × 10^9/L, respectively. Four patients maintained complete remission of primary thrombocythemia (platelet counts less than 300 × 10^9/L) for more than 1 to 6 years after treatment with busulfan and remained asymptomatic (Table I, *C*).

Comments. The main presenting symptom in primary thrombocythemia is erythromelalgia, a characteristic syndrome of painful burning distress and red congested extremities.[2,3] The histopathologic features of skin biopsies from areas of erythromelalgia are overshadowed by nonspecific inflammation and specific fibromuscular intimal proliferation and thrombotic occlusions of the arterioles in the absence of preexistent vascular disease.[1] The vascular changes in erythromelalgia are restricted to the arterioles and small arteries, but the peripheral pulses remain normal. Complete relief of pain and elimination of circulatory disturbances are generally accomplished with low doses of aspirin that are specific for erythromelalgia.[1-3] The prompt and lasting clinical relief with aspirin, because of its irreversible inhibition of platelet cyclooxygenase activity, indicates that erythromelalgia is provoked by intravascular platelet activation and aggregation. Treatment with warfarin appears to be ineffective, but reducing the platelet count to a normal level eliminates the erythromelalgia.[2,3] In cases of reactive thrombocytosis, erythromelalgia did not occur, which indicates not only a quantitative but also a qualitative disorder of platelet function in thrombocythemia. This unknown platelet defect in thrombocythemia in its primary form or associated with polycytemia vera is postulated to lead to an increased risk of microvascular thrombotic complications also involving the coronary and cerebral circulation.

In patients with primary thrombocythemia, thromboembolism in normal coronary arteries has been noted as the cause of myocardial infarction.[7-11] The cases presented illustrate that coronary artery disease can be related to thrombocythemia and can be the presenting symptom. Myocardial infarction seen in two patients with thrombocythemia did occur in coronary arteries without atherosclerosis, and coronary artery disease was present in the five patients with thrombocythemia with unstable angina pectoris. This suggests that thrombocythemia may have contributed to the coronary artery disease. An increasing chance of acute coronary events is to be expected, because atherosclerotic arteries exhibit an increased platelet–vessel wall interaction. The presence of a thrombotic tendency in all of our patients and the absence of coronary risk factors in the two patients with myocardial infarction and normal coronary arteries and in two of the five patients with unstable angina pectoris indicate that thrombocythemia alone is a main risk factor for coronary artery disease. Control of platelet function with low doses of aspirin for 1 to 5 years in three patients and remission of thrombocythemia after cytostatic treatment with normal platelet counts for 1 to 6 years in four patients was associated with no recurrence of thrombotic events. Thus intravascular platelet activation and aggregation in thrombocythemia play a significant initiating role in both erythromelalgia and acute coronary syndromes. As an extension of previous data on platelet-mediated thrombosis in thrombocythemia,[1-3] it is assumed that aspirin or cytostatic treatment to control platelet function are effective in the prevention and elimination of thrombotic events in thrombocythemia.

In summary, primary thrombocythemia in six patients and polycythemia vera with thrombocythemia in one were diagnosed subsequent to an acute cardiac event, myocardial infarction in two patients with primary thrombocythemia and unstable angina pectoris in one patient with polycythemia vera with thrombocythemia and four with primary thrombocythemia. The latter five patients underwent coronary artery bypass graft surgery. A thrombotic tendency appeared to be present in all patients, because transient cerebral ischemic attacks or erythromelalgia caused by platelet-mediated thrombosis preceded or followed the cardiac events within 1 to 5 years. Prospectively no recurrence of thrombotic events was observed during treatment with aspirin for 1 to 5 years in three patients, and the platelet count was reduced to normal levels in four patients treated with busulfan for 1 to 6 years. There are strong indications that control of platelet function by aspirin or cytostatic reduction of the platelet count to normal is effective in the prevention of thrombotic heart disease in thrombocythemia.

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Flash pulmonary edema secondary to upper airway obstruction

Keith D. Meyer, MD, and M. Rashid Chaudhry, MD.
Brooklyn, N.Y.

Pulmonary edema is a condition commonly encountered in clinical cardiology. The term "flash" pulmonary edema has been used to describe sudden episodes of life-threatening pulmonary edema.[1] The causes of pulmonary edema are myriad; nonetheless, a popular cardiology textbook does not include upper airway obstruction among the possible causes.[2] We report a patient who developed flash pulmonary edema in the absence of identifiable heart disease, associated with upper airway obstruction secondary to a goiter compressing the trachea.

From the Divisions of Cardiology and Otolaryngology, The Brookdale Hospital Medical Center.

Reprint requests: Keith D. Meyer, MD, Division of Cardiology, The Brookdale Hospital Medical Center, Brooklyn, NY 11212.

4/4/29737

The patient was a previously healthy 59-year-old Oriental woman with no risk factors for coronary artery disease and no history of heart disease. She was well until the morning of admission, when she awakened with severe dyspnea. She was brought to the Emergency Room, where she was noted to have tachypnea and tachycardia. The initial arterial blood gas, drawn while the patient was wearing a partial rebreathing mask, revealed that the Pa_{O_2} was 70 mm Hg, the Pa_{CO_2} was 45 mm Hg, and the pH was 7.13. The patient was intubated and transferred to the Coronary Care Unit. On admission to the Coronary Care Unit, with the patient receiving assisted ventilation and an inspired oxygen concentration of 60%, another specimen of arterial blood revealed that the Pa_{O_2} was 146 mm Hg, the Pa_{CO_2} was 35 mm Hg, and the pH was 7.43. Physical examination was remarkable only for bilateral rales. An initial chest x-ray film revealed pulmonary edema with a normal heart size (Fig. 1). The electrocardiogram revealed poor R wave progression in leads V_1 to V_3, with no ST segment abnormality. Serial electrocardiograms and cardiac enzymes failed to reveal evidence of myocardial necrosis. There was rapid clinical improvement with furosemide and nitrates. However, the patient developed inspiratory stridor, which complicated repeated attempts at extubation. A tracheostomy was performed on day 8, at which time tracheal deviation to the left and tracheomalacia were noted. Noninvasive cardiac evaluation included a gated blood pool scan, which revealed an ejection fraction of 70% with normal wall motion. An echocardiogram was normal; left ventricular hypertrophy was not present. The thyroid function tests were normal. A computed tomography (CT) scan of the neck revealed a large right lobe of the thyroid compressing the trachea (Fig. 2). Because of the possibility of severe coronary artery disease, the patient underwent cardiac catheterization prior to thyroidectomy. All intracardiac pressures, the coronary arteries, and left ventriculography were normal. The patient underwent uneventful right thyroid lobectomy and isthmectomy. Subsequently,

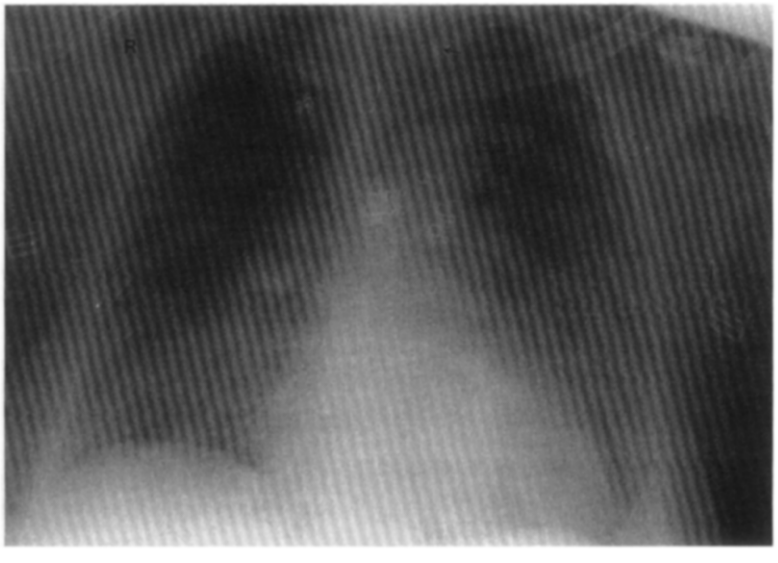

Fig. 1. Chest x-ray film made with portable technique. There is evidence of pulmonary edema as well as a suggestion of tracheal deviation to the left (*arrow*).