

CASE REPORT**Coronary Vasculopathy in Polycythemia Vera**Benita HERMANN,¹ Stefan HANDT,¹ Joachim KINDLER,² László FÜZESI¹¹Department of Pathology, Medical Faculty of the Technical University of Aachen, ²Department of Internal Medicine of the Hospital Marienhöhe, Würselen, Germany

Thrombosis is a common complication in polycythemia often causing death. In coronary artery occlusion, thrombosis due to hyperviscosity and thrombocytosis is mostly discussed as the origin of the infarction. We discuss the case of a 30-year-old male patient, with polycythemia, who died of myocardial infarction. On autopsy the vessels showed neither atherosclerotic changes nor thrombotic occlusions. Instead, a marked intima proliferation was

found leading to multiple occlusions whereas media and adventitia were unchanged. This pattern of a coronary vasculopathy has not been described before, and can be interpreted as an alternative mechanism for vascular occlusion in polycythemia. Similar histopathological changes have already been found in skin lesions in erythromelalgia, a common symptom in polycythemia. (Pathology Oncology Research Vol 4, No 1, 37-39, 1998)

Key words: polycythaemia vera, myocardial infarction, coronary vascular disease, intima proliferation

Introduction

Polycythaemia vera (PV) is a myeloproliferative disease with increasing number of blood cells which causes hyperviscosity, and in 20-40% lethal thrombosis or hemorrhage.^{3,4} The thrombotic complications are connected with thrombocytosis, but they can also occur when the hematocrit and platelet numbers return to normal values.^{7,9} The most common cause of death is myocardial infarction and heart failure.^{2,12} Nevertheless, pathological changes of the coronary vessels are only seen in 5% of the patients.^{1,4,10,13} A case of a 30-year-old male patient is presented who died of myocardial infarction as first manifestation of PV. Peculiarly, coronary vascular changes were observed without atherosclerotic changes or clots, but with an uncommon vascular morphology.

Material and Methods

A 30-year-old male patient with a history of polycythemia vera died of posterolateral myocardial infarction. Following autopsy the nature of the occlusion of

coronary arteries was examined histologically and immunohistochemically. The histomorphological evaluation was carried out by hematoxylin-eosin and elastica van Gieson.

Immunohistochemical investigations used indirect peroxidase technique with antibodies against smooth muscle actin, fibronectin, desmin and laminin, CD 45, CD 68, PGM 1, cytokeratin and Ki 67 (all antibodies were from DAKO, Hamburg, Germany), each with positive and negative controls.

Case Report

A 30-year-old caucasian male patient with no history of serious disease collapsed accompanied by the first onset of retrosternal chest pain. He was not under any regular medication. He smoked 20-40 cigarettes/day over 13 years. Latent arterial hypertension was observed. Family history had no cardiac disease.

On admission the patient was hemodynamically unstable (systolic blood pressure 70 mmHg). The electrocardiogram revealed a posterolateral myocardial infarction, ultrasound studies ruled out pericardial tamponade. Peripheral blood cell counts were: erythrocytes $7.28 \times 10^9/L$, granulocytes $27.2 \times 10^9/L$, thrombocytes $859 \times 10^9/L$. The hematocrit was 61%. Despite immediately performed thrombolytic therapy with tissue-plasminogen-

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Correspondence: László FÜZESI, M.D., Institute of Pathology, RWTH Aachen, Pauwelsstr. 30, D-52057 Aachen, Germany; Tel: +49-241-8089281, fax: +49-241-8888439

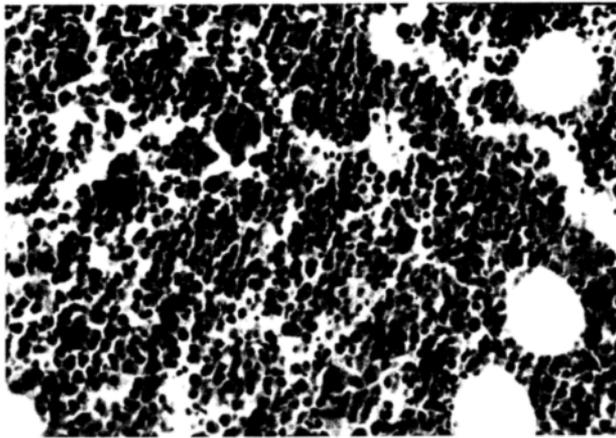


Figure 1. Light microscopy of bone marrow showing markedly increased hematopoiesis and megakaryocytes (HE, x200).

activator (100 mg/2h, Actilyse, Thomae, Germany) a severe cardiogenic shock developed. Unsuccessful resuscitation was stopped after 60 minutes.

Pathological examination

Gross Findings – The autopsy revealed a plethora of all parenchymatous organs, moderate cardiomegaly (408 g) and left ventricular hypertrophy (16 mm wall thickness). The central parts of the coronary arteries showed smooth plaques. The circumflex coronary artery had a severe, concentric stenosis at 0.5 cm after its beginning. The anterior, posterior and septal wall of the left ventricle showed multiple, 1 x 1 cm large, old and fresh myocardial necrosis. Additionally, splenomegaly (817 g) with subcapsular wedge-shaped infarctions of up to 1.5x1.5 cm of diameter was found. Chronic central blood congestion of

the liver with concomitant hepatomegaly (2219 g) was diagnosed.

Microscopy – The bone marrow of the spinal column displayed markedly increased hematopoiesis and megakaryocytes (*Figure 1*). The spleen revealed a significant hyperplasia of red pulp. The coronary arteries showed partly or completely occluding stenoses due to circular intima proliferation (*Figure 2*). A considerable proliferation of fibroblasts was found with increased number of collagen fibres as well as crosswebbing which radiated into the lumen of the blood vessel. Proliferation of capillaries took place in the intima proliferation (*Figure 2a*). Furthermore, an earlier intima fibrosis was found without fibroblastic activity, which occluded the lumen and left some symmetrically localized capillaries (*Figure 2b*). Despite the pathological findings in the intima, both the media and adventitia appeared to be unchanged.

Immunohistochemistry – Immunohistochemical studies were performed by using indirect peroxidase technique to differentiate between myogenic and endothelial proliferations in the coronary arteries. The intraluminal occluding cells were markedly positive for smooth muscle actin, less positive for fibronectin, desmin and laminin, and negative for CD45, CD68, PGM I, cytokeratin and Ki 67.

Discussion

In the present case thrombocythaemia was diagnosed as a manifestation of PV. Moreover, a considerable intima proliferation was found to lead to coronary occlusions. According to our knowledge, this pattern of coronary vascular changes has not been described before. Similar histomorphological changes have merely been reported in erythromelalgia, which is a common symptom in PV.^{5,6} In the afflicted skin areas, the arteries show swollen endothe-

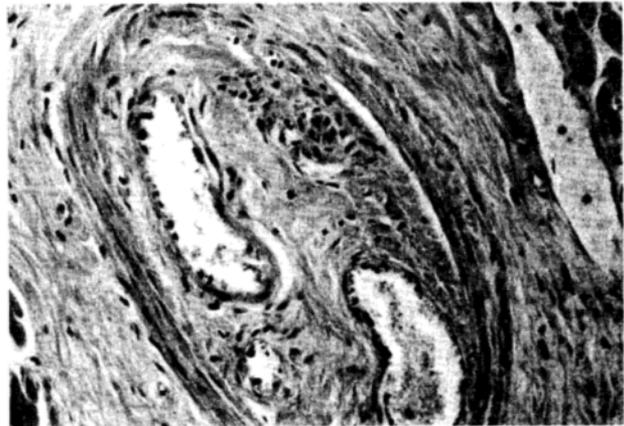
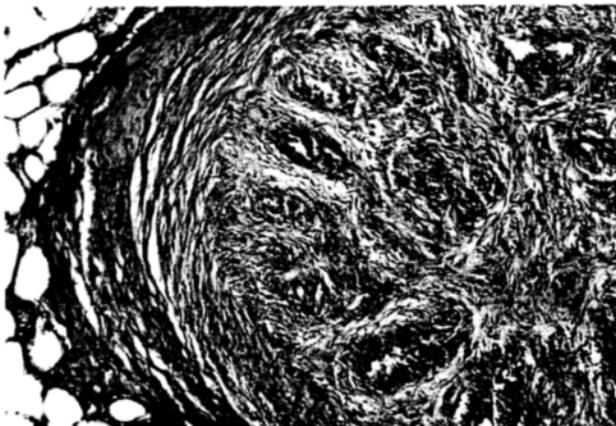


Figure 2. Histomorphology of coronary arteries. (a) Coronary artery with almost completely occluded stenosis based on circular intima proliferation with increased number of collagen fibres, crosswebbed and radiating into the lumen. Media and adventitia appeared unchanged. (b) Coronary artery showing older intima fibrosis without fibroelastic activity occluding the lumen and leaving some symmetrically localized capillaries.

lium with signs of inflammation. The arteriolar lumen is occluded due to fibromuscular intima proliferation and raveling out of the internal elastic lamina. It is interesting that, in erythromelalgia only arteries are involved in vascular changes, as seen in our case. Nevertheless, the origin of coronary changes in PV is histomorphologically not well analyzed and disputable. Peoples et al⁸ demonstrated that T-lymphocytes can induce hyperplasia of smooth muscle cells in arteriosclerotic plaques by secreting heparin-binding epidermal growth factor-like growth factor and basic fibroblast growth factor. Other studies have likewise shown an important binding of T-lymphocytes in coculture with endothelial cells which produce growth factor as platelet-derived growth factor-like protein.¹¹ However, the speculative role of T-lymphocytes in fibromuscular intima proliferation in PV needs further studies.

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