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Letters to the Editor

Link between pulmonary megakaryocytes and cardiovascular and respiratory disease

We are delighted that the recent study of Sharma and Talbot¹ provides support for our original hypothesis² that pulmonary platelet production could be the "missing link" between cardiovascular and respiratory disease.

Although the presence of pulmonary megakaryocytes does not prove that the lungs are the only site of thrombopoiesis, the wealth of additional evidence cited in our earlier study³ and reiterated by Sharma and Talbot¹ makes pulmonary platelet production seem highly likely. In particular, the number of megakaryocytes/ml of blood in the pulmonary artery needed to maintain a normal steady state platelet count³ and the number observed in central venous blood of man⁴ is of the same order of magnitude. Hence bone marrow production is not necessary for platelet or megakaryocyte homeostasis. Furthermore, pulmonary thrombopoiesis allows a simple mechanism of platelet production to be invoked. The process of sequential random binary division of megakaryocyte cytoplasm provides a physical analogue of mitosis,³ which can be simulated on a computer.⁵ No quantitative evidence to support the theory of bone marrow thrombopoiesis has been proposed.

It is worth noting that the statistical comparisons based on the stereological procedure advocated by Sharma and Talbot¹ should be treated with caution. Larger three dimensional structures—for example, megakaryocytes with cytoplasm—are more likely to be sectioned than smaller structures (naked nuclei). Unless the appropriate correction factors are applied,⁶ the counting procedure will be biased toward the larger structure. In addition, the total number of pulmonary megakaryocytes is also influenced by their size. A characteristic of the polyploid megakaryocyte is its ability to increase in size in response to stimulation,⁷ resulting in an increased probability of pulmonary trapping.⁸ Megakaryocytes are larger than normal in cardiovascular disease⁹ and in experimental models of atherosclerosis.¹⁰ Hence under these and similar pathological conditions, more pulmonary megakaryocytes are likely to be seen even though megakaryocyte counts in central venous blood may be normal. This may explain the pulmonary megakaryocyte count differences reported in hospital and forensic necropsies.¹¹

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Drs Talbot and Sharma reply:

We agree with Drs Trowbridge, Slater, and Martin that our estimates of the numbers of megakaryocytes trapped in the pulmonary capillary bed would be even higher if we had applied a correction for variations in megakaryocyte size.

Although our own data cannot prove the hypothesis that the lungs are the principal site of thrombopoiesis, there are persuasive arguments for this. Evidence which has not to our knowledge been considered, is provided by the blood of lungless vertebrates such as fish,¹ which lack platelets, their role being performed by large nucleated cells known as thrombocytes, which resemble the other blood cells in cytological appearance.

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Peripheral thrombocytopenia in human parvovirus infection

Human parvovirus (HPV) causes aplastic crises in patients with hereditary¹ or acquired² haemolytic anaemias. HPV induced red cell aplasia in patients without a shortened red cell survival is difficult to establish because of the transient nature of the erythroblastopenia. On the other hand, a moderate thrombocytopenia of central origin seems common during these aplastic crises.^{3,4}

We describe here the first documented case of peripheral thrombocytopenia with HPV associated aplastic crisis in a patient without shortened red cell survival.

Case history

A five year old girl was admitted to hospital because she had had petechial purpura on her face and legs for 24 hours after an episode of upper respiratory tract infection. Oral examination showed the presence of a superficial haemorrhagic bulla. Neither lymphadenopathy or splenomegaly was detected. The patient was febrile. The blood test showed normal haemoglobin concentration and white cell count but a platelet count of $8 \cdot 10^9/l$, although it had been $304 \times 10^9/l$ 15 months previously. Bone marrow examination performed on the day of admission showed an increased number of megakaryocytes, suggesting a peripheral origin of thrombocytopenia and an absence of erythroid precursors. The reticulocyte count was then found to be less than $5 \times 10^9/l$. This erythroblastopenia suggested a recent HPV infection, which was confirmed by the presence of anti-HPV IgM in the serum.⁵ Other recent infections were excluded by tests for infectious mononucleosis, cytomegalovirus, rubella, mumps, hepatitis A and B. Treatment with high dose intravenous gammaglobulin (daily dose of 30g) was started immediately. Two days later the platelet count remained low (figure) and gammaglobulin was discontinued. Consequently, corticosteroids (prednisone 2mg/kg/day) were given, and the platelet count returned to normal within three days. Haemoglobin concentration and white cell count remained normal during the evolution. The daily dose of steroids was progressively reduced after one month and the treatment finally discontinued after two months. Further controls showed normal platelet counts.

Discussion

This observation suggests that HPV may be

associated with intense peripheral platelet destruction. Haemoglobin concentration was not modified as a consequence of an aplastic crisis, as anaemia does not occur as long as red cell survival is normal; the transient nature of the erythroblastopenia is responsible for the difficulty in detecting red cell aplasia in normal people infected with HPV. To our knowledge, these findings of an HPV associated aplastic crisis in a patient free of chronic haemolytic anaemia have not been reported previously. None the less, the HPV associated aplastic crisis seems to be totally different from the "transient erythroblastopenia of childhood," whose mechanism remains to be explained.

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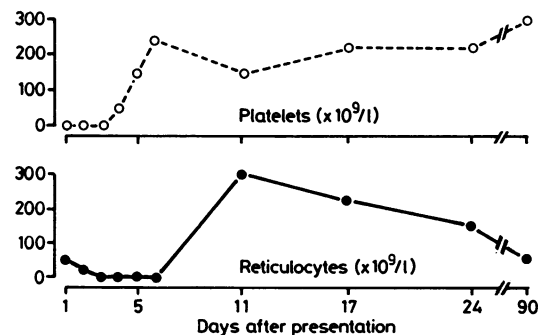


Figure Haematological data in patient studied.