ROLE OF CHANGES IN MINERAL METABOLISM IN STRUCTURAL BONE DISTURBANCES IN EXPERIMENTAL POLYCYTHEMIA

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In rabbits with experimental cobalt polycythemia foci of osteolysis, transverse striation, and widening of the medullary canal are found roentgenologically in the bones. Histologically partial replacement of dense bone tissue by proliferating hematopoietic tissue of the bone marrow is observed. The Ca and K content and, to a lesser degree, the P content in the bone tissue is lowered, and this is accompanied by an increase in concentration of these elements in the blood of the experimental animals. Biochemical changes correspond to the degree of structural changes in the bone tissue and are found in the early stages of development of polycythemia.

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Lesions of the osseous system occupy a considerable place in the clinical picture of polycythemia vera [4]. If it is remembered that the development of polycythemia is based on prolonged hyperplasia of the bone marrow with the appearance of foci of extramedullary hematopoiesis [1, 5], the high incidence of pathological changes in the bone apparatus will be understandable. However, very little information is to be found in the literature concerning the mechanism of the bone disturbances.

In the present investigation some aspects of disturbances of mineral metabolism were studied and their possible role in the pathogenesis of structural changes in the bones in experimental polycythemia was examined.

EXPERIMENTAL METHOD

Experiments were carried out on 2 groups of rabbits (chinchilla) weighing 3.5-4.5 kg; group 1 consisted of 19 animals with cobalt polycythemia and group 2 of 11 intact animals (control). This experimental model was chosen because, from available data [3], cobalt polycythemia in rabbits bears a certain resemblance to polycythemia vera in man in many of its hematologic, roentgenologic, and pathohistological indices. Polycythemia was produced by subcutaneous injection of cobalt chloride solution in a dose of 25 mg/kg body weight daily for 10 days. To compare the biochemical changes with structural disturbances, the latter were determined roentgenologically and histologically at the height of the hematologic changes (considerable increase in hemoglobin concentration, erythrocyte, reticulocyte, and platelet counts, etc.) and when they had subsided (1-1.5 and 3-3.5 months respectively after the beginning of cobalt injection). Roentgenographs were taken of the whole length of the bones of the leg, thigh, and pelvis, the ribs, spine, and skull. The total phosphorus and calcium concentrations in the blood of the rabbits were determined at the same times. The bones were mineralized in a muscle furnace at 450° after first being dried to constant weight at 105°. The content of Ca, P, K, and Na in the ash was determined. Ca was determined by de Waard's method, P by the Fiske–Subbarow method, and K and Na by flame photometry [2]. The percentage of calcination of the bone was calculated from the ratio between the weight of ash and the total weight of the bone.

EXPERIMENTAL RESULTS

Roentgenologic changes appeared in the bones at the height of the hematologic disturbances and were also detected at the end of the period of observation, when the hematologic indices had returned to normal.

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TABLE 1. Changes in Mineral Composition of Bones in Experimental Polycythemia

Statistical index	Ash, in percent		Ca (in %)		P (in %)		Na (in ‰)		K (in ‰)	
	1	2	1	2	1	2	1	2	1	2
M	61	50	60	47	33,8	29,9	817	887	238	130
$m\pm$	2,9	3,7	4,3	2,8	1,8	2,1	49	64	21	32
P	—	<0,01	—	<0,05	—	>0,1	—	>0,4	—	<0,01

Note: 1) Control animals; 2) animals with experimental polycythemia.

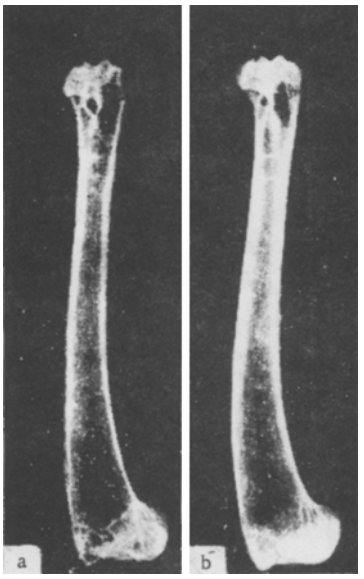

Fig. 1. Roentgenograms of femora of rabbit. a) Before experiment; b) at height of hematologic changes: foci of osteolysis, transverse striation.

Fig. 2. Photomicrograph. Femoral diaphysis of rabbit. Splitting of cortical layer. Hematoxylin-eosin, ocular 7, objective 8.

The main changes observed were foci of osteolysis in both the long and the flat bones. In addition, transverse striation characteristic of a disturbance of the elasticity of the bone tissue was observed in the long bones (Fig. 1). Similar changes in the bone marrow were previously observed in patients with polycythemia vera. Corresponding disturbances were found on histological examination of the bones.

These disturbances in the structure of the bone tissue were accompanied by gross changes in the mineral composition of the bones (Table 1).

As Table 1 shows, experimental polycythemia was accompanied by a marked decrease in the Ca and K content in the bones, whereas the changes in P and Na were much smaller. All these changes took place against a background of a marked decrease in the content of inorganic residue of the bone.

The foci of osteolysis discovered roentgenologically can be assumed to be caused by demineralization of the bone accompanied by disturbances of the solidity of the bone tissue. This may also be associated with some degree of dynamic compression, reflected on the roentgenograms as transverse striation. In all the experiments a decrease in the level of mineral residue of the bone corresponded to the degree of the roentgenologic changes.

Considering the similarity betwenn the roentgenologic changes in bone structure in experimental polycythemia in animals and in polycythemia vera in man, it may be postulated that the bone changes in these patients are based on analogous disturbances of mineral composition. Probably this also influences the intensity of repair processes, the sluggish course of which we have observed in polycythemic patients with bone injuries.

TABLE 2. Concentration of Ca and P in Blood of Rabbits with Experimental Polycythemia

Statistical index	Ca concentration (in mg %)			P concentration (in mg %)		
	control animals	animals with experimental polycythemia		control animals	animals with experimental polycythemia	
		at height of hematologic changes	after normalization of hematologic indices		at height of hematologic changes	after normalization of hematologic indices
M	9.6	17.8	12.7	35.7	48.8	40.2
m ±	1.9	2.7	2.4	2.1	4.7	3.5
P	–	0.01	0.1	–	0.01	0.1

The disturbances of mineral composition may be associated with the extreme proliferation of marrow tissue. This leads to the appearance of new foci of hematopoiesis actually in the cortical layer, as histological investigations revealed (Fig. 2). These new foci replace the dense bone tissue and are visible roentgenologically as osteolytic areas (Fig. 1).

The disturbances in the mineral composition of the bones discovered in experimental polycythemia obviously must have been reflected in changes in the content of these elements in the blood. This was confirmed by discovery of hyperphosphatemia and hyperkaliemia (Table 2).

A raised blood level of P and Ca was observed at the time of the most marked hematologic changes, while toward the end of the period of observation a tendency was noted for these blood levels to return to normal, although the Ca and P concentrations were not completely restored.

Depletion of the content of mineral substances in the bone tissue was thus accompanied by a marked simultaneous increase in their blood concentration. It can be assumed that the disturbances of mineral metabolism, severe in character in the early stages of polycythemia, are an important factor in the pathogenesis of this disease.

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