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THALASSEMIA MINOR AND PAINFUL ULCERS OF LOWER EXTREMITIES

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Abstract. A case of thalassemia minor with ulcers of the lower extremities is reported. The painful skin lesions, which were the only clinical symptoms, consisted of small haemorrhages, ulcerations and white atrophic lesions on the ankles and dorsal surfaces of the feet. Biopsy of a recent skin lesion showed acute vasculitis with a scanty perivascular, mainly lymphocytic, cellular infiltrate in the upper part of the corium.

In certain types of haemolytic anaemia, leg ulcers are common complications. Thus, leg ulcers occur in 30–50% of patients with sickle cell anaemia (3) and in 6.5% of patients with congenital spherocytosis (9). Coexisting leg ulcers and thalassemia are less common. So far 11 cases have been reported (4, 7, 11, 13, 15, 16, 18, 21). Biopsy specimens have been obtained from ulcers in four cases (7, 13, 15, 21) and have revealed nonspecific changes. It was therefore considered justified to report a distinct clinical and histological picture of a recently observed case of coexisting leg ulcers and thalassemia minor.

CASE REPORT

The patient was a 31-year-old Greek woman who had come to Sweden three years previously. The father had died in Greece, probably from gastric cancer. Otherwise no diseases of interest were known in the family.

The patient had previously felt well, but for two years she had been troubled by increasing pigmentation and recurrent painful small ulcerations on the lower legs and on the dorsal aspects of the feet. She also complained of pain in the lower legs on exertion. No use of drugs was known.

Physical examination revealed nothing remarkable except considerable overweight (height 162 cm, weight 88 kg).

On the anterior aspect of the ankles and on the dorsa of the feet and of the toes the skin was brownish and showed punctate haemorrhages. On the dorsal and lateral aspects of the feet were some ten superficial well defined ulcerations with irregular stamped-out edges varying in size from 2 to 10 mm in diameter and white, atrophic patches of the same size. No varicose veins were seen. The arterial pulsations were good.

Punch biopsy of a recent haemorrhagic skin lesion of the foot was performed.

Histological examination. In the papillae and the upper part of the corium were groups of small vessels with signs of acute inflammation. The lumina of the vessels were filled with fibrin or erythrocyte thrombi and in several vessels the walls had undergone partial or complete fibrinoid necrosis. Also in the deep parts of the corium near the sweat-glands were single vessels with the same type of changes. In the connective tissue were widespread recent bleedings with a scanty admixture of inflammatory cells, mostly lymphocytes. Besides the acutely changed vessels were groups of new-formed capillary vessels. In other parts of the corium and round the sweat-glands was a moderate deposit of iron pigment. The epidermis was flat and covered by a parakeratotic crust, but not ulcerated.

Laboratory values

Hemoglobin 10.3–12.0 g/100 ml blood. Erythrocytes 3.4–5.5 mill/mm^3 blood. White blood count 4700–6000 per mm^3. Reticulocytes 10–20 per thousand. Anisocytosis—poikilocytosis, a large number of basophil red blood cells and target cells. Leucocytes normal. Serum iron 90 micrograms/100 ml. TIBC 340 micrograms/100 ml. Haptoglobin 134–153 mg/100 ml serum. Mean corpuscular volume 66–71. Mean corpuscular hemoglobin concentration 30–34 g%. Sickle-cell test negative. The osmotic resistance of erythrocytes was slightly increased. Alkaline resistant hemoglobin according to Singer 2.3% (normal <2%). Hemoglobin electrophoresis: Hb A_2 5.3% (normal value 1.9–3.1%). Hb F 0.6% (normal value 0–1.0%) (M. Hjelm, Clin. chem. central lab., Uppsala). E.S.R. 8 mm/1 hour. Serum protein electrophoresis normal. No cryoglobulins. No LE-cells. Bone marrow: Reactive hyperplasia of erythropoesis and reticular iron. Roentgen examination of the gallbladder, abdomen, skull, thorax, vertebral column and pelvis showed nothing remarkable.

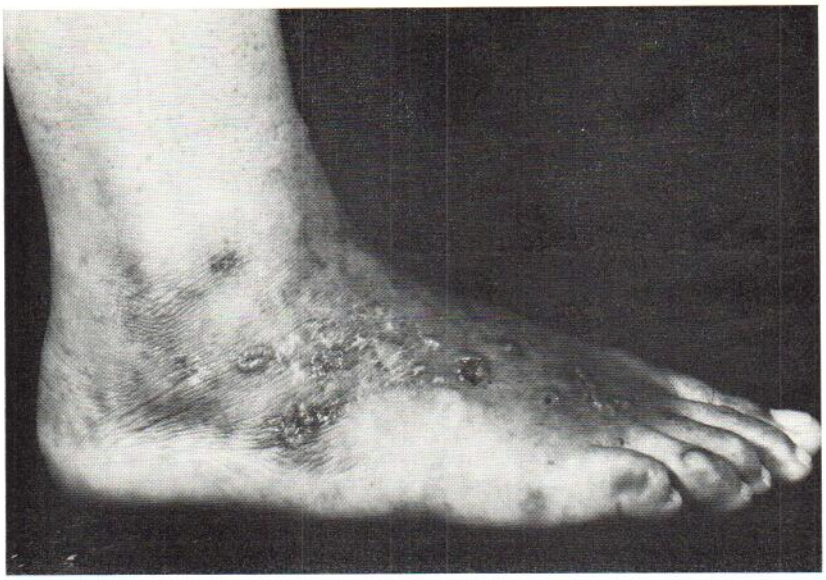

Fig. 1. Purpura, ulcerations and white atrophic scars on dorsal surface of the foot.

Lymphangiography, phlebography and arteriography revealed no abnormalities, and the flow of blood through the leg muscles, as determined with xenon^{133}, was normal. Plethysmography: normal.

Repeated infusions of low molecular dextran (Rheomacrodex®, Pharmacia AB, Sweden) produced no demonstrable improvement of the skin lesions.

DISCUSSION

In view of the immigration from the Mediterranean countries in recent years the frequency of thalassemia minor will probably increase in our country. Thalassemia minor has also recently been described in 2 Swedish aboriginal families (17).

An increased amount of Hb A_2 in hemoglobin electrophoresis has been demonstrated only in patients with thalassemia minor (5, 19). In addition to an increased Hb A_2-concentration our patient had several haematological changes characteristic of thalassemia minor, namely, mild microcytic anaemia associated with normal serum iron and filled iron depots, abundance of basophil punctated red blood cells and target cells as well as slightly increased osmotic resistance. The patient

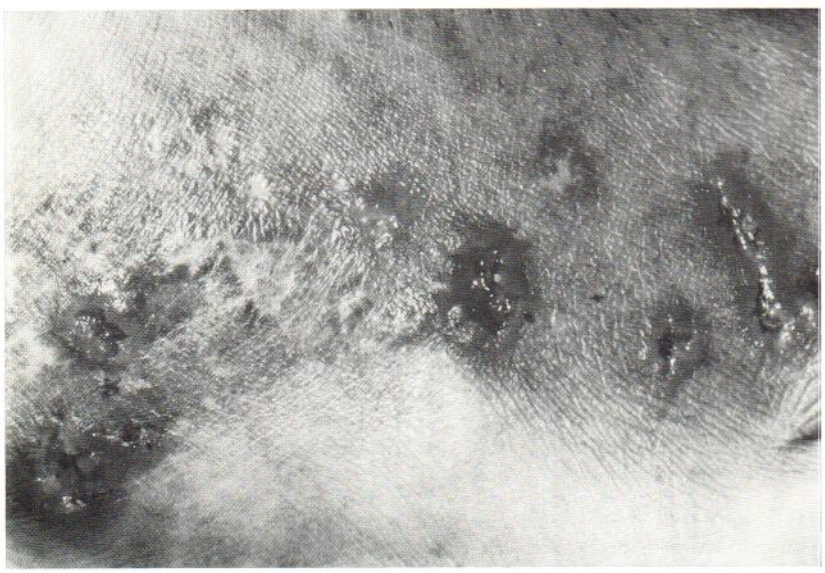

Fig. 2. Close view of Fig. 1.

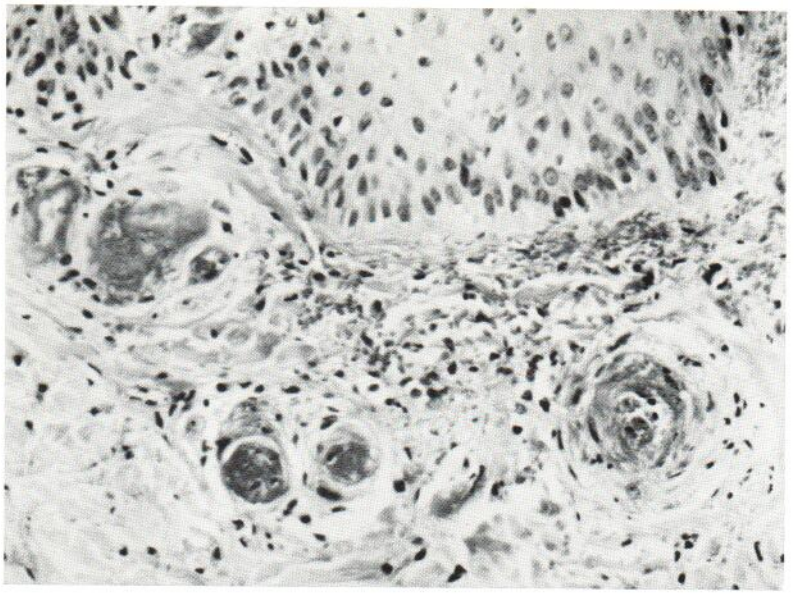

Fig. 3. Acute vasculitis of small vessels in upper corium. The vessel lumina are filled with fibrin thrombi. In the connective tissue are numerous extravascular red blood cells and a few lymphocytes. Haematoxylin-eosin, × 250.

had skin changes with purpura, small ulcerations, pigmentations and white atrophic scars on the ankles and dorsa of the feet. Angiography excluded arterial, venous and lymphatic vascular insufficiency. The histologic examination of a recent skin lesion showed acute vasculitis of capillary vessels with fibrin and erythrocyte thrombi, fibrinoid necrosis in the vessel walls and widespread recent haemorrhages in the surrounding connective tissue. This type of vasculitis has been described in thrombotic thrombocytopenic purpura (2), cryoglobulinaemia (6, 14), livedo reticularis (1, 8) and in atrophie blanche (10) and differs from so-called necrotizing vasculitis (allergic angiitis) by the nature and intensity of the inflammatory cellular infiltration (20). In the 4 diseases first mentioned the cellular infiltration is scanty and consists almost exclusively of lymphocytes, while in necrotizing vasculitis there is an abundance of mainly polymorphonuclear leucocytes with an admixture of numerous nuclear fragments. Thrombotic thrombocytopenic purpura and cryoglobulinaemia can be excluded by the examinations performed. Livedo reticularis did not occur in our patient and the vasculitis in livedo reticularis appears to occur mainly in vessels in the deeper parts of the corium (1, 8).

The clinical and histological picture of our patient appears to agree well with a disease entity recently dealt with in detail by Gray et al. (10). They used the term "atrophie blanche" to characterize a spectrum of changes beginning with telangiectatic purpuric areas which undergo superficial necrosis and later heal leaving residual white atrophic scars. But according to Milian (12) who coined the term "atrophie blanche" this diagnosis should be reserved for white atrophic lesions not preceded by ulcerations. The lesions described by Gray et al. occur periodically, they are frequently painful and only involve the legs, ankles and dorsal surfaces of the feet. In biopsy specimens of recent changes they found haemorrhages and acute vasculitis with fibrin thrombi and fibrinoid necrosis in the small vessels in the upper corium. The cellular infiltrate varied from slight to moderate and the predominant cells were lymphocytes. Thalassemia minor has never before been seen in association with the described vasculitis. It is probable that vasculitis was diagnosed because a recently appeared skin lesion was selected for biopsy which does not seem to have been the case in previous histological investigations of leg ulcers in thalassemia minor.

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