ties, gives the trioxsalen bath treatment a high rank in the choice of type of PUVA treatment.

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Disturbances in the Metabolism of Calcium and Vitamin D in a Case of Sarcoidosis

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Abstract. A case of subcutaneous nodular sarcoidosis presented low 25-hydroxy-vitamin D levels during the active phase of the disease, while the serum calcium levels were increased. During spontaneous remission both 25-OHD levels and serum calcium levels returned to normal.

Key words: Vitamin D; Serum calcium; Sarcoidosis

Vitamin D is now known to undergo hydroxylation in the liver to 25-hydroxy-vitamin D (25-OHD), which is the main circulating metabolite of the vitamin. A further hydroxylation occurs in the kidneys, where 1,25-dihydroxy-vitamin D (1,25-$(OH)_2$-D) is synthesized. This metabolite is regarded the most potent vitamin D metabolite (2).

The hypercalcaemia of sarcoidosis is well known. A recent study (1) has provided evidence that the cause of the hypercalcaemia in sarcoidosis is the increased quantity of circulating 1,25-dihydroxy-vitamin D.

We have recently seen a patient suffering from sarcoidosis and hypercalcaemia. Remission occurred without any treatment, concomitant with changes in the serum 25-OHD and calcium concentrations.

METHODS

Serum calcium and serum and urinary phosphate and creatinine were analysed on a Greiner GSA II by routine colorimetric methods. Urinary calcium was analysed by atomic absorption spectrophotometry (Perkin Elmer 300). 25-OHD was assayed in duplicate by a competitive protein-binding assay after extraction and purification on Sephadex LH 20 columns (5).

CASE REPORT

A 40-year-old woman was admitted 20th April 1978 with 6–7 subcutaneous noduli of hazel-nut size which were indolent and bluish-red, and localized on the arms, thighs and back. They had developed during the preceding 2 years, following the appearance of an erythema nodosum.

Dilated telangiectatic vessels were seen in the overlying skin, and subsequent skin biopsy revealed massive fused granulomatous structures ranging from the upper layers of the dermis and down to the subcutis. These granulomas consisted mainly of epithelioid cells with relatively few multinucleated giant cells and there was a well defined border between them and the surrounding tissues. A few areas showed central necrosis but no fibrinoid necrosis was observed. There was no other organ involvement and she was otherwise in good health.

Laboratory findings

The serum calcium concentration was, in April, 3.60 mmol/l, in June, 2.50 and in August, 2.36 mmol/l, whereas serum 25-OHD concentrations increased from less than 20 nmol/l in April to 32 nmol/l in June and to 65 nmol/l in August. The level of immunoglobulin A was high, at 7.92 mg/ml, other immunoglobulins were normal, and electrophoresis did not show any acute phase reaction. Kveim and tuberculin reactions were negative. Urine contained *E. coli* (>100000 bacteria/ml urine), but there were no signs of nephritis or nephrocalcinosis. Urography, bone- and chest X-rays were all negative.

The patient received no treatment and the final tests showed both normal tubular phosphate and calcium reabsorption.

DISCUSSION

The diagnosis is based on the clinical features (cutaneous and subcutaneous manifestations) together with the histology. The negativity of the Kveim reaction does not exclude sarcoidosis, as about 30% are Kveim-negative with any antigen. In sarcoidosis, hypercalcaemia occurs in about 10% of cases, hypercalciuria in 36% (7). In our case the serum calcium concentration was elevated during the active phase of the disease. At the same time the serum 25-OHD concentration was low.

It is generally accepted that the concentration of 25-OHD reflects the sum of endogenous synthesis in the skin and dietary intake of vitamin D (3). Since our method is equally sensitive to 25-OHD_2 as to 25-OHD_3, the low 25-OHD concentration demonstrates that in our patient the hypercalcaemia was caused neither by a high intake of vitamin D nor by an enhanced endogenous synthesis in the skin.

25-OHD is strongly bound to a transport protein (4). Since the concentration of other proteins was normal (exept for IgA) and since electrophoresis did not show any acute phase reaction, it is unlikely that the low concentration of 25-OHD was caused by disturbances in the vitamin D binding protein.

The 25-OHD concentration shows a significant seasonal variation, due to variations in exposure to sunshine (3, 5). Thus, seasonal variation could be the main explanation for the low concentration of this metabolite in April. However, values below 20 nmol/l are rare, even in our area at 70° north. In 70 healthy persons (5, 6) only 2 had lower serum concentrations (17 and 19 nmol/l, respectively) in winter. An additional explanation for the low 25-OHD concentration during the active phase of the disease may therefore have been a higher turnover of this metabolite to more polar metabolites, especially 1,25-$(OH)_2D$. The hypercalcaemia and the low 25-OHD concentration could then have been caused by a high concentration of this metabolite.

During clinical remission from April to August the 25-OHD concentration increased threefold. The reason for the increase may have been, at least partly, a slower turnover to more polar metabolites. Seasonal variation alone, however, may have caused the increase. Despite the increase in serum 25-OHD concentration, serum calcium concentration returned to normal. Thus, our results suggest that the course of the hypercalcaemia in sarcoidosis is mainly correlated with the activity of the disease, and seems to be independent of dietary intake or endogenous synthesis of vitamin D. Our observations are consistent with the view that high circulating levels of 1,25-$(OH)_2D$ may be the cause of the hypercalcaemia in sarcoidosis (1).

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Eosinophilic Fasciitis (Shulman Syndrome) in Association with Morphoea and Systemic Sclerosis

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Abstract. A case of Shulman syndrome or diffuse fasciitis with eosinophilia is reported. Both superficial scleroderma (morphoea) and systemic sclerosis accompanied the subcutaneous changes.

Key words: Shulman syndrome; Diffuse fasciitis with eosinophilia; Morphoea; Systemic sclerosis

Shulman (3, 4) described a syndrome which he termed diffuse fasciitis with eosinophilia. Over 20 cases have now been reported (1) in which the usual features are a rapidly progressing sclerosis of the skin over limbs, contractures, eosinophilia and immunoglobulin G elevation, but an absence of Raynaud's phenomenon and a good response to anti-inflammatory treatment. The fascia between fat and muscle is greatly thickened, with collagen hypertrophy and infiltration by lymphocytes and plasma cells.

We report such a case which in addition showed both superficial and systemic involvement, so linking the Shulman syndrome with the more commonly encountered forms of scleroderma.

CASE REPORT

A 59-year-old man reported an 8-week history of progressive tightening of skin over arms and legs following ankle swelling attributed to unaccustomed exertion. Skin on forearms and shins was pigmented and firmly bound down to muscle and bone. Proximal limbs and trunk were less affected. Wrist, elbow, knee and ankle joint movement was limited. Digits were unaffected. The margins of the sclerosis on feet and wrists showed erythema.

Investigations showed: erythrocyte sedimentation rate, 36–40 mm in first hour; eosinophil count in peripheral blood, 152–1 008/mm^3; serum immunoglobulins normal; negative RA Latex test; antinuclear antibodies present to dilution of 1 in 16; partial right bundle branch block on ECG; normal peristalsis on barium swallow; no calcification of subcutaneous tissue in limbs; chest X-ray showed heart size at upper limit of normal; fibrosis was present in both lower lobes; respiratory function studies indicated restrictive and obstructive defects; carbon monoxide transfer factor was significantly reduced at 18 ml/min/mm^3/hg. Electromyography of limb muscle showed normal activity. Biopsy of abdominal skin showed thick collagen in the dermis, consistent with morphoea or localized superficial scleroderma, while a deep forearm biopsy not only showed excess collagen in dermis but also the presence of thick collagen bundles in subcutaneous fat and a marked thickening and oedema of the muscle fascia in which there was a heavy perivascular infiltrate composed mainly of lymphocytes with moderate numbers of plasma cells. Occasional histiocytes and polymorph leukocytes were also seen, but eosinophils were scanty. Blood vessel walls were slightly oedematous but there was no evidence of vasculitis. Direct and indirect immunofluorescence examination for C3, fibrinogen and immunoglobulins G, M and A in epidermis, dermis, fascia and muscle was negative.

During initial treatment with D-penicillamine in a dose of 125 mg daily for 4 weeks, increasing to 250 mg daily for a further fortnight, there was resolution of sclerosis in the trunk skin. Weight loss of 10 kg during this time led to the substitution of 40 mg prednisolone daily for the D-penicillamine. Over the following 8 weeks, there was complete clearing of sclerosis from upper arms and thighs except for some puckering of skin on the inner aspects, a feature often reported in diffuse fasciitis. However, there has been no obvious improvement on forearms and lower legs where the skin remains firmly bound down.

DISCUSSION

Except for the absence of demonstrable immunoglobulin abnormalities in the tissues, our patient shows the constellation of clinical and histological features described in the Shulman syndrome or diffuse fasciitis with eosinophilia. In addition, however, he has both dermal sclerosis and lung involvement consistent with systemic sclerosis. A recent review of 16 cases of the Shulman syndrome reported from the Mayo Clinic (2) showed that 5 had superficial dermal changes, while another 4 had pulmonary and 3, oesophageal involvement.

We would support this view of the Shulman syndrome as being a form of subcutaneous scleroderma that has a greater inflammatory element than other forms of scleroderma and hence a greater likelihood of responding to prompt anti-inflammatory therapy.