Pityriasis rubra pilaris, Vitamin A and Retinol-binding Protein: A Case Study

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A patient with longstanding erythroderma and decreased sweat secretion due to the classical adult form of pityriasis rubra pilaris is described. The patient did not respond to oral megadoses of Vitamin A, even though a large increase of liver content of Vitamin A was demonstrated. Retinol-binding protein levels in serum of this patient and his relatives were normal. Danazol (Danatrol®, Winthrop) therapy caused an increase of retinol-binding protein level, but clinical improvement did not occur. *Key words: Pityriasis rubra pilaris; Vitamin A; Retinol-binding protein; Anabolic steroid; Therapy.* (Received March 16, 1984.)

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High dose Vitamin A therapy has been reported to result in complete remissions in Pityriasis rubra pilaris (PRP) patients (1), although others are less optimistic (2, 3). It has been suggested that defective synthesis of retinol-binding protein (RBP) might be a biochemical marker for PRP (4), which has not been supported by other studies (5). Stanozolol, an anabolic steroid, has been reported to raise the level of RBP, possibly resulting in a remission of PRP (6).

This report deals with the results of treatment of an erythrodermic, hypohidrotic PRP patient with megadoses Vitamin A and an anabolic steroid. The patient was monitored by measurement of Vitamin A content of the liver and serum RBP level. Serum RBP levels were also measured in four close relatives.

CASE REPORT

PRP was diagnosed in a male patient at the age of 22 because of widespread follicular papules with a histology consistent with PRP. In addition erythemato-squamous lesions were seen on the extensor side of the elbows, in the crena ani, in the neck, on the scalp and diffusely on the palms and soles. The skin disease started at the age of 21. From the age of 24 the patient was erythrodermic, apart from some islands of normal skin, with hyperkeratotic thickening of the palms and soles and sunbungual hyperkeratosis. The patient was hypohidrotic in erythematous areas. At the age of 31 high-dose Vitamin A therapy was given, as previous therapy with retinoic acid and etretinate (Ro 10-9359) caused only limited improvement. Treatment with etretinate was arrested 8 months before Vitamin A therapy. Other therapeutic attempts with photo-therapy (UVA + UVB, oral PUVA), methotrexate and topical aminonicotinamide were also unsuccessful. Exposure to mediterranean sunlight repeatedly resulted in almost complete remission, although this became increasingly more difficult to obtain.

Vitamin A was given orally in a total amount of 15 million IU: day 1–10 1 million IU/day in arachis oil, day 14–18 1 million IU/day in aqueous colloid suspension. The liver tests (transaminases, alkaline phosphatase, lactic dehydrogenase and γ-glutamate transferase) remained within normal limits. There was a slight raise of triglyceride levels to just above normal. Serum levels of total Vitamin A were measured 0, 2, 4 and 6 hours after intake. Maximum serum levels were found 4 hours after intake: 30 mmol/L during the first part of the treatment course, 63 mmol/L during the second part. In two liver biopsy specimens total hepatic Vitamin A level was measured, using an extraction method and high performance liquid chromatography. Previous to therapy the level of total Vitamin A (retinol and its esters) was 37.5 μg/g wet liver tissue (normal <300 μg/g), 3 days after discontinuation of treatment the level was 5 180 μg/g wet liver tissue.

The histology of the two liver biopsies obtained immediately before and after the Vitamin A course showed no abnormalities except for an increase in number of Ito cells in both biopsies in 1 μm Epon embedded sections stained with haematoxylin-safranin. In the second biopsy enlargement of the fat vacuoles in the Ito cells and moderate steatosis of liver cells was observed. Fluorescence microscopy on frozen sections of the second biopsy demonstrated abundant yellow autofluorescent perisinusoidal material in the form of droplets of varying size, which is in accordance with liver storage of Vitamin A, presumably in the fat vacuoles of the Ito cells.

The Vitamin A course dit not cause any skin changes except desquamation of the palmoplantar hyperkeratosis. During follow-up no further improvement was noted. Maintenance therapy with oral etretinate was reinstituted 5 months after the high-dose Vitamin A therapy because of a recurrence of incapacitating palmoplantar hyperkeratosis.

7 months after the high-dose Vitamin A therapy the etretinate regimen was interrupted for one month during which treatment with danazol (Danatrol®, Winthrop), an anabolic steroid, 400 mg/day during 4 weeks, was given. RBP levels in serum were measured by radial immuno-diffusion technique, using commercially available plates (Behring Werke, Marburg). RBP levels were measured twice before danazol therapy, the first time 5 months after the Vitamin A megadoses, the second time 2 months later at the start of danazol treatment. The RBP levels were measured again 2 and 4 weeks, 2 and 4 months and 1 year after the start of danazol treatment. This treatment did not give any clinical improvement.

Prior to danazol therapy the retinol-binding protein (RBP) level in serum was normal (4.3 and 4.7 mg/100 ml) compared to 18 male controls (4.3–7.5 mg/100 ml, mean 5.5 mg/100 ml). After 2 weeks of therapy with danazol an increase of RBP level was noted (6.6 mg/100 ml). This level was sustained until 4 months after start of danazol therapy. After 1 year a RBP level of 5.1 mg/100 ml was measured. We also measured the serum RBP levels of the closely related family members. The RBP levels of father (66 years; 5.3 mg/100 ml) and brother (28 years; 5.4 mg/100 ml) were within the normal control range for men. The RBP levels of mother (69 years; 4.7 mg/100 ml) and sister (32 years; 6.2 mg/100 ml) were also normal compared to 13 female controls who did not use oral contraceptives (3.2–6.5 mg/100 ml, mean 4.9 mg/100 ml).

DISCUSSION

High dose Vitamin A therapy did not result in a remission of the longstanding erythrodermic PRP, probably of the classical adult type (7), in the patient described, even though a large increase of total hepatic Vitamin A level was noted. An increase in number of Ito cells, in which Vitamin A is stored in the liver, and prominent fatty vacuolization of these cells has been described in hypervitaminosis A and may be one factor responsible for the non-cirrhotic portal hypertension, which can occur in chronic hypervitaminosis A (8). In

another study (9) we observed the same abnormalities during oral etretinate and retinoic acid therapy, which probably explains the increase in number of Ito cells in the first liver biopsy taken before Vitamin A treatment 8 months after arrest of etretinate treatment.

The serum RBP level, being within normal range in this patient and his close relatives, was increased, but still within normal limits, supposedly by the course of anabolic steroid therapy during 4 weeks. This increase was sustained until at least 3 months after arrest of danazol therapy. Serum RBP levels are influenced by several factors (10), but probably not by etretinate treatment (11). Oral Vitamin A loading causes a large increase of dermal RBP, but only a small rise of serum RBP (12). It cannot be excluded that without the effect of the Vitamin A megadoses the serum RBP levels of the patient before danazol therapy might have been slightly decreased. One wonders whether a decrease of serum RBP level in a PRP patient, when it occurs, could be a secondary instead of a primary phenomenon. In any case the moderate increase of serum RBP level, supposedly caused by anabolic steroid treatment, did not result in clinical improvement of the severe PRP in this patient.

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