

the case of photoallergy, one would rather have expected a narrower action spectrum. And the photopatch test does not confirm the supposition of photoallergy. It should be mentioned that the Xenon testing, in addition to UV-B, also included UV-A radiation, but this was assumed to be negligible.

The conclusion is that the patient has a photosensitivity with unknown mechanism but with clinical signs identical with a fixed drug eruption.

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Propylthio-uracil-induced Cutaneous Vasculitis

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Abstract. Three cases of cutaneous vasculitis, leukocytopenia and arthralgia, presumably caused by the antithyroid drug Propylthio-uracil, are presented. Acute vasculitis of the superficial and deep dermal blood vessels accompanied by vascular thrombus formation were found in biopsy specimens. Direct immunofluorescence studies demonstrated deposits of C₃ or IgM and C₃ in the walls of vessels in affected and unaffected skin, suggesting immune complex deposition. The skin lesions and leukocytopenia rapidly disappeared on discontinuation of

the drug, while the arthralgia continued for weeks or months.

Key words: Propylthio-uracil; Cutaneous vasculitis; Immune complex disease

Propylthio-uracil (PTU) is regularly used in the treatment of hyperthyroidism. Adverse reactions may arise at any time during therapy but are most commonly noted during the first 3 weeks (7). The most serious complication, agranulocytosis, occurs in 0.2-0.3% of patients, while skin rashes occur in 3-5% of adults and up to 18% of children (7). PTU is recognized as a frequent cause of allergic vasculitis and even lupus-like (1) and polyarteritis nodosa-like syndromes (6) have been reported. Purpura and vasculitis due to PTU have been described in several case reports showing clinical features varying from one patient to another. They may arise at any time during treatment, and may vary from a mild purpuric rash to severe vasculitis with multisystemic involvement (8).

We report here 3 cases of vasculitis due to PTU seen within one year.

CASE 1

A 13-year-old girl was admitted suffering from malaise and a rash on the face and the arms. She had been treated with PTU 250 mg a day and levothyroxin (Eltroxin*) 0.1 mg per day for 2 years for thyrotoxicosis. Two weeks before admission to the clinic, she initially noted reddening of the right cheek and one week later, she subsequently developed localized tender erythema of the cheeks, the right ear lobe and left arm. On admission the lesions were bluish red, thickened and painful, especially on the ears. Other lesions developed during the following days, while the original lesions subsided. Systemic symptoms including fatigue and migratory polyarthralgia accompanied the skin symptoms.

PTU and Eltroxin was discontinued. The skin lesions disappeared without ulceration or scarring and the arthralgia subsided within 2 weeks.

The thyrotoxicosis recurred, and treatment was resumed with karbimazol, without side effects.

Laboratory findings

Initially a white blood cell count of 2.0 (normal 3.0-9.0) billions/l, rising after withdrawal of PTU to 6.0 billions/l. ESR and platelet counts were normal, and there were no coagulation defects.

Histopathology

The main changes were found in the reticular dermis where the vessel walls and their surroundings were infiltrated with red blood cells. In addition, perivascular



Fig. 1. Patient No. 2.

infiltrates of eosinophils and neutrophils were found with some nuclear dust. Many vessels were thrombosed. Immunofluorescence staining was not performed.

CASE 2

A 41-year-old female was admitted suffering from a rash on the buttocks.

For 1½ years before admission to the Department of Dermatology she had been treated with PTU 100 mg daily and levotyroxin (Eltroxin®) 0.1 mg daily for thyrotoxicosis. After more than one year on this regimen, she developed intermittent exanthema on the abdomen and the buttocks. After 3 months, the rash worsened and it was accompanied by burning, itching and painful swelling of ankles and knees. On admission, a rash was found with initially purple-red thickened skin lesions which later turned to bluish red (Fig. 1). Lesions continued to develop during the first days after admission, and joint pain worsened and spread to elbows and shoulders. Propylthiouracil and eltroxin were discontinued. The vasculitis disappeared after one week, whereas the joint pains continued for one month, and then slowly disappeared.

Laboratory findings

These included a white blood cell count of initially 2.3 billions/l, later rising to 4.6 billions/l. Platelet counts were normal. ESR was initially 54 mm. IgM was 2.08 g/l (normal 0.18-1.29). All other laboratory findings were normal, including IgA, IgG, creatine kinase, ANA, T₃, T₄, serum creatinine, urinary sediment, ECG, Wasserman reaction, and thorax X-ray. No blood was found in the stools.

Histopathology

Oedema of papillary and reticular dermis, perivascular granulocytes, nuclear dust and red blood cells, together with mononuclear cells but no eosinophils. The vascular walls were necrotic in some areas and several lumens were obliterated by amorphous eosinophilic material (Fig. 2).

Immunofluorescence studies

In involved skin, massive deposits of C₃ were demonstrated in the vessels. In clinically normal skin, deposits of IgM and C₃ were seen in the vessel walls, and granular deposits of IgM and C₃ were noted at the dermo-epidermal junction.

CASE 3

A 62-year-old female was treated with PTU 100 mg daily together with Eltroxin® 0.1 mg every 3 days due to thyrotoxicosis. After 3 years on this regimen she developed a slight erythema of the cheeks and nose. This erythema gradually worsened and spread to the legs. She was admitted to the hospital suspected of collagen disease. Livedo reticularis was found on the thighs as well as a slight erythema of the face. A few days after admittance the patient developed small petechiae on the legs and a large painful swelling of the right foot. Propylthiouracil and eltroxin were discontinued, and the petechiae and the swelling disappeared in 2 weeks. The patient continued to complain of painful ankle-joint movements for about 3 months. The livedoid pattern on the legs remained unchanged during the observation period. She developed a slight thyrotoxicosis which was treated with radio-iodine.

Laboratory examinations

These were normal except for the white blood cell count which initially amounted to 2.4 billions/l but later normalized, and IgM which was 5.70 g/l (normal 1.18-1.29). ANA and anti-DNA were negative. Immunofluorescence staining of a biopsy from involved skin revealed deposits of IgM and C₃ in the small blood vessels, while faint deposits of IgM and C₃ were found at the dermo-epidermal junction in both involved and uninvolved skin.

DISCUSSION

The patients described show similarities as the vasculitis developed after more than one year on the drug. The eruption was accompanied by slight malaise and arthralgia, and leukocytopenia was found in all. Histologic examination revealed the usual features of an allergic vasculitis (2, 5). Immunofluorescence-staining demonstrated deposits of IgM associated with C₃ in the blood vessel walls, which is highly suggestive evidence of tissue-fixed immune complexes (2). The clinical features and laboratory results closely resembled previously described cases (3, 4, 8). Most frequently, the vasculitis presents as symmetrical tender purpuric lesions, often in a livedoid pattern. In three of six published cases facial involvement was noted and ear-lobe involvement was described in two of six (8). The immunoglobulin deposits detected are also in agreement with other investigations (1, 3, 4, 8).

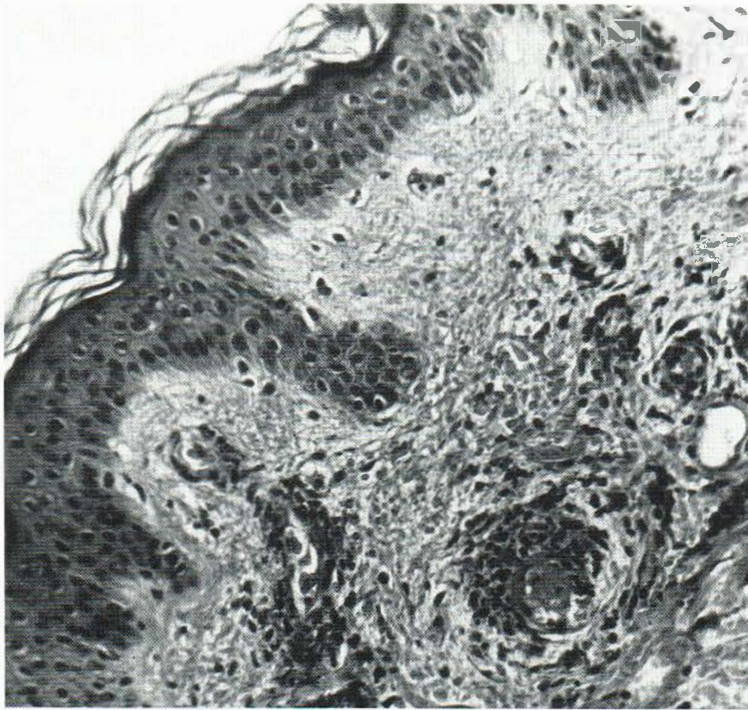


Fig. 2. Skin histopathology in case No. 2. For description, see text.

Rechallenge with the drug was not done as this procedure caused a fatal periarteritis in one case previously described (6). In all other cases, PTU was only indirectly proved to be the cause of the vasculitis, as the skin symptoms subsided when the medication was discontinued. The polyarthralgias seem to be a more persistent problem, as it may continue for several months after discontinuation of therapy (8). Karbimazol can replace PTU without further occurrence of cutaneous vasculitis (8) despite the basic structural similarity of the two drugs. However, it may be safer to discontinue thionamide drug therapy entirely (7).

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Malignant Clear Cell Hidradenoma: A Case Report

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Abstract. A 73-year-old man developed a malignant clear cell hidradenoma on the nose. Although it was treated