

Papular Eruption in Helminth Infestation – A Hypersensitivity Phenomenon?

Report of Four Cases

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This communication reports on generalized papular eruption in Man, coinciding with infestation due to dwarf tapeworm (*Hymenolepis nana*), pinworm (*Enterobius vermicularis*) and whipworm (*Trichuris trichiura*). The assumed allergic-hyperergic reaction was evident from itching, blood and tissue eosinophilia, increased serum IgE and clearing up after focus of infestation therapy. Pinworm and whipworm therapy was initially accompanied by Jarisch-Herxheimer phenomenon. Key words: *Hymenolepis nana*; *Enterobius vermicularis*; *Trichuris trichiura*.

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The symptoms well known to dermatologists, which may arise from helminth infestation and warrant parasitological investigation are urticaria, facial edema and flush, as well as generalized pruritus (1,2). This communication reports on occurrences of papular eruption coinciding with dwarf tapeworm, pinworm and whipworm infestation in Man. Though the relationship to papular – sometimes very chronic – skin on is not very common in Western Europe, the problem might be on the increase because of world-wide tourism and the influx of refugees.

CASE REPORTS

Case 1

A 40-year-old Turkish man living in Anatolia had been suffering from intensely itching papular eruption for more than 15 years. Past medical, family and environmental history were negative. Papular eruption and intense pruritus even led the patient having to avoid social contacts. The pruritus could only be temporarily alleviated by internal administration of glucocorticosteroids, whereas antihistamines were not effective.

There was a generalized, highly pruritic eruption of red and flesh-coloured papules densely aggregated on the arms (Fig. 1). Throughout the corium there was a dense peri-

vascular infiltration by lymphocytes, eosinophils and histiocytes. The face, scalp, palms, soles and oral mucosa were not affected. There was no swelling of lymph nodes.

The haemogram revealed leukocytes, $13.8 \times 10^9/l$. The differential blood count showed monocytes, 7% and eosinophils, 9%. The concentration of IgE was 515 kU/l; there were no other abnormal laboratory findings. Dwarf tapeworm eggs (*Hymenolepis nana*) were found repeatedly in the faeces.

Following antihelminthic therapy with oral niclosamide (Yomesan®) at 2×1 g (on day 1) and 2×0.5 g (on days 2 to 7) the intense itching disappeared and the papular eruption subsided completely within 3 weeks. Check-up examination of the faeces revealed no eggs of *Hymenolepis nana*. The patient declined a check-up examination of the blood (eosinophils, IgE) and returned to Anatolia. Four weeks later we received a letter from him that he was still cured of his skin eruption.

Case 2

A 13-year-old Italian girl developed a strongly itching papular eruption 2 weeks before admission to the clinic. The eruption was initially restricted to the face but subsequently spread to the trunk and extremities. There were no other accompanying symptoms or previous signs of infection.

There was a generalized eruption of red, slightly scaly papules on the face, trunk and extremities (Fig. 2). Epidermis showed acanthosis and parakeratosis. There was marked edema of the stratum papillare and a mild non-epidermotropic perivascular infiltrate by lymphocytes and macrophages.

The papules occurred along the skin tension lines, giving a pityriasis rosea-like impression but there was no herald patch. Scalp, palms, soles and oral mucosa were not affected. The lymph nodes were not enlarged. The differential blood count showed eosinophils 11%. The concentration of IgE in serum was 133 kU/l. Other routine laboratory tests including syphilis serology and blood levels of vitamin B₁₂, folic acid and zinc were within the normal range. There was no pathological reaction in the recall antigen test. No pathological increase in relevant virus titres was detected, even at later stages. Worm eggs could not be found in the faeces. An adhesive strip applied to the outer anal ring revealed masses of mostly embryonated eggs of *Enterobius vermicularis*.

Therapy with 2×100 mg mebendazole (Vermox®) given orally for one day aggravated the pruritus for a short time and caused the skin eruption to spread. Subsequently, pruritus and skin eruption subsided completely within one week. At check-up, the concentration of eosinophils in the blood had fallen to 3%, and the IgE was 112 kU/l. Pinworm eggs could not be detected than or any time thereafter.

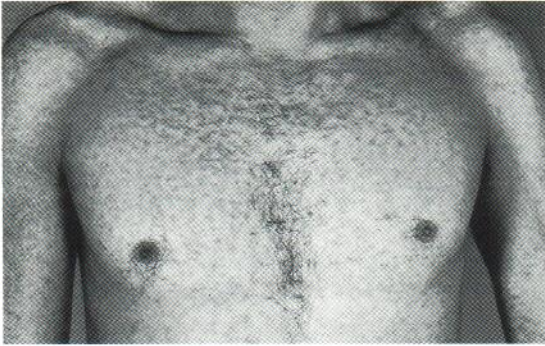


Fig. 1. Papular eruption in dwarf tapeworm infestation (case 1): partly red, partly flesh-coloured, intensely pruritic papules on the trunk and extremities.

Case 3

A one-and-a-half-year-old boy from Eritrea had had a papular skin eruption for 2 weeks. The pruritus was only mild. Apart from a recent gastro-intestinal infection he was in good health.

The generalized eruption showed small dense reddish papules, particularly on his forehead. Over the extensor side of the left wrist there was a firm, flesh-coloured annular infiltration with a scaly central crust. Scalp, palms, soles and oral mucosa were spared. The lymph nodes were not enlarged.

The haemogram showed haemoglobin 95 g/l, the erythrocytes were $4 \times 10^{12}/l$, the haematocrit 28.6%, the MCV 71 fl and the leukocytes $12.9 \times 10^9/l$. The differential blood count showed neutrophils 14%, lymphocytes 76% and eosinophils 10%. There was hypoferric anaemia (iron 0.32 mg/l). The IgE in serum was 30 kU/l. Other routine laboratory test results were within the normal range. There was repeated evidence of whipworm eggs in the faeces.

Internal therapy with 2×50 mg mebendazole (Vermox®) given orally for 3 days initially aggravated the skin eruption, and pruritus became more intense. Papules and pruritus then subsided within a week and the blood eosinophilia disappeared. The annular infiltration on the wrist was only slightly regressive. After 3 weeks the exanthem relapsed. Eggs of *Trichuris trichiura* were again detected in the faeces and also in the mother's faeces. Reinitiated therapy with mebendazole at the specified dosage and duration brought a regression of both the papules and the wrist infiltration within 10 days. The mother was also treated with mebendazole for 3 days. The child has since shown no skin abnormalities and check-up examinations of the faeces have not revealed any worm eggs.

Case 4

A 7-year-old refugee child from Somalia had been suffering from intensely itching papules for more than 8 months. On the trunk and extremities there were multiple, small, flesh-coloured lichenoid papules (Fig. 3). Lichenification and hyperpigmentation were seen on cubital flexures but there were no other signs of atopy. Palms and soles showed small pustules and yellow crusts. The axillary lymph nodes were enlarged and sensitive to pressure. WBC showed leuko-

cytes $9.3 \times 10^9/l$. The differential blood count showed eosinophils 8%. There were no other abnormalities in the routine laboratory tests or in the urine examination. Serum-IgE was 500 kU/l. The serum zinc concentration was 0.77 mg/l. *Staphylococcus aureus* was detected in smears taken from pustules on the hands. Eggs of *Trichuris trichiura* were found repeatedly in the faeces.

The staphylodermia was treated by administration of 3×500 mg flucloxacillin (Staphylex®) given orally for 10 days. This was accompanied by oral zinc substitution (200 mg zinc sulfate (Solvezink®) per day and by local treatment with fusidine acid (Fucidine® Creme). The exanthem response to hydrocortisone and coal tar cream was poor. Internal therapy with 2×100 mg mebendazole (Vermox®) for 3 days initially aggravated the itching for a short time and caused the skin eruption to spread. Pruritus and papules then subsided within 10 days. Check-up examination for helminth eggs were negative and the eosinophils in the blood as well as the IgE had dropped to normal.

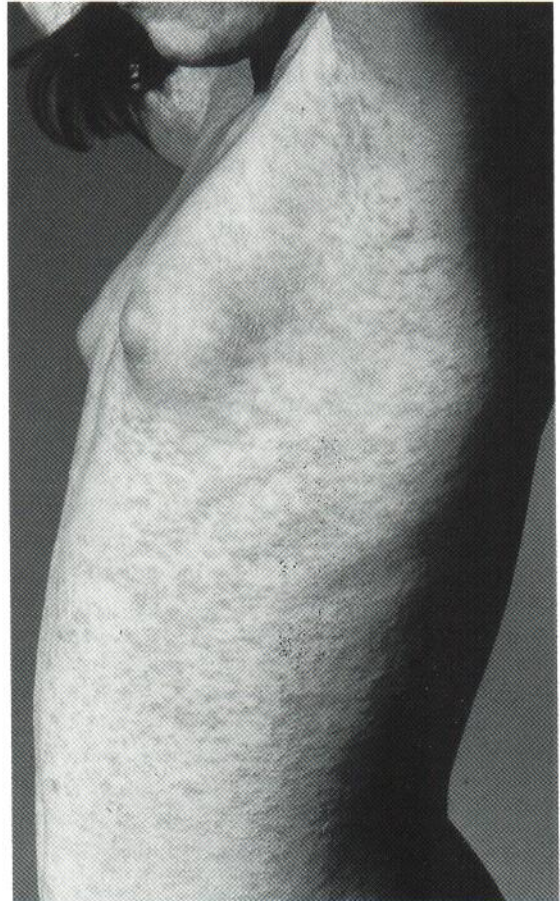


Fig. 2. Papular eruption in pinworm infestation (case 2): reddish scaly pityriasis rosea-like papules on the face, trunk and extremities. A herald patch was not present.



Fig. 3. Papular eruption in whipworm infestation (case 4): multiple small flesh-coloured lichenoid papules on the arms.

DISCUSSION

Dermatological signs of helminth infestation may be the result either of *local skin reaction* at the site of penetration or oviposit, or of *systemic skin reaction* to worm antigens or excretion products (3, 4). Whilst urticaria, facial edema and generalized pruritus are well known in this context, individual reports include a broad spectrum of different clinical features (5). Our cases evidenced papular skin eruptions due to helminth infestation of the gut. Papular skin eruptions may occur with infestation of schistosomes or tissue nematodes (1, 2, 6). To our knowledge, eruptions of this kind coinciding with dwarf tapeworm infestation have not been reported before. Blood and tissue eosinophilia prompted us to suspect a parasitic origin. The evidence of typical eggs of *Hymenolepis nana* in the faeces and the fact that the intense pruritus and the skin eruption subsided completely after antihelminthic therapy confirmed this suspicion.

The chronic course of that skin eruption must be discussed in the context of a permanent antigen stimulus due to autoinfestation by worm eggs originating from dwarf tapeworms in the small intestine. The possibility of internal autoinfection by oncospheres that do not pass out the colon is still a matter of debate (7). In mice, dwarf tapeworm expulsion and subsequent recovery from infestation requires IgG-mediated immunity (8, 9). The extent to which such immunity is necessary for the elimination of *Hymenolepis nana* in Man is not known at the present time but should be taken into account in future cases.

With regard to the skin eruption coinciding with *Enterobius vermicularis*, only early reports are available (10). These speak of a "reflex formation" of dissiminated papules on the trunk and extremities,

which is described as "atopic eczema of oxyuriasis" (11, 12). These skin signs had subsided after antihelminthic therapy and recurred with fresh intestinal worm infestation. A similar connection has been documented with prurigo simplex acuta (strophulus) (13). Furthermore, "anaphylactic skin reaction" and positive cutaneous reaction to pinworm extract have been observed with oxyuriasis (14). The papular eruption with pinworm infestation clinically resembling pityriasis rosea was accompanied by blood and tissue eosinophilia. The IgE in serum was only slightly raised. Pruritus and blood eosinophilia subsided after antihelminthic therapy whereas IgE did not change that much, possibly because of atopy. Although the patient did not complain of anal pruritus (a symptom that is generally considered to be diagnostic in oxyuriasis) the adhesive strip applied to the outer anal ring exhibited masses of pinworm eggs.

Papular skin eruption caused by whipworm infestation has been reported elsewhere (5). Our cases underline the fact that infestation by *Trichuris trichiura* must be considered in infants even in Western Europe due to tourism and refugees. Malnutrition in so-called 'Third World Countries' might encourage chronic infection and possibly autoinfestation. In order to achieve a definite cure, the antihelminthic therapy should be accompanied by measures to counteract malnutrition (e.g. iron deficiency in case 3). In the event of a relapse, the patient must be isolated from carriers (case 4).

With helminth infestation, the thymus-dependent immune mechanisms, which promote the formation of immunoinfiltrate of lymphocytes, mast cells and eosinophils, are stimulated and play a considerable role in the elimination of parasitic antigens (15). This might explain the formation of papules due to mixed cellular infiltrates which are considered to be systemic skin reactions to parasitic antigen stimulus ('id reaction'). In our cases, a particular indication of the present hypersensitivity reaction caused by helminth infestation was the fact that the skin eruption and pruritus subsided after focus of infestation therapy. Other important signs of the assumed allergic-hyperergic pathomechanism were blood and tissue eosinophilia, elevation of serum IgE and the Jarisch-Herxheimer phenomenon at the beginning of tapeworm and whipworm therapy. The detection of helminth antigens in the papules would be final proof of the postulated immunopathological mechanism.

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