

of liver dysfunction was identified. The patient died from multiorgan failure on day 1370.

Chronic GVHD typically involves the skin and the liver. The early phase of chronic GVHD generally appears up to day 100 post-transplant and usually follows acute GVHD. Initially, a slowly progressive erythematous rash on the face, palms and soles becomes lichenoid, with changes resembling lichen planus. Later, scleroderma-like changes occur, which are sometimes widespread. Patchy hyperpigmentation, poikiloderma, vitiligo, erythema, atrophy, alopecia, multiple follicular papules, ulcers of the legs and dystrophic nail changes may occur. Gastrointestinal symptoms, a Sjogren-like syndrome, polymyositis, abnormal liver function, primary biliary cirrhosis and other organ changes also occur in chronic GVHD.⁵ In our case, as irregular-margined hyperpigmentation and mild pityriasis were observed on proximal areas such as the upper arms, trunk, back and face, we diagnosed chronic GVHD. Intriguingly, planar xanthoma also occurred in this patient.

Xanthomas are cutaneous signs of the presence of hyperlipidaemia, defined as an elevated fasting cholesterol level of over 240 mg dL⁻¹ or a triglyceride level of over 200 mg dL⁻¹.⁴ These xanthomas are characteristic of disorders that cause hepatic cholestasis, such as primary biliary cirrhosis, biliary atresia and GVHD. In these conditions, free cholesterol cannot be excreted properly into bile and is instead regurgitated into plasma, where free cholesterol binds with albumin and phospholipids to form an abnormal lipoprotein called lipoprotein X. Affected persons have markedly elevated plasma cholesterol levels (often > 500 mg dL⁻¹). Infiltration of lipoprotein X or its components into dermis and subcutaneous tissue is probably responsible for the development of the planar xanthomas.

In summary, we report a Japanese patient with planar xanthoma due to cholestasis in GVHD following allogeneic bone marrow transplantation.

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Dose-related reduction in allergen-specific T cells associates with clinical response of atopic dermatitis to methotrexate

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SIR, Methotrexate has been reported to be of value in the management of resistant adult atopic dermatitis.^{1–3} We sought to investigate whether clinical improvement associates with changes in peripheral blood antigen-specific T-cell responses. Of our three adult patients with atopic dermatitis on methotrexate, we have followed one individual who expresses HLA-DRB1*0101. This patient is thus amenable to longitudinal analysis of allergen-specific CD4⁺ T-cell responses using a class II tetrameric complex based on a DRB1*0101-restricted peptide from Fel d 1, a major cat allergen.^{4,5} Under local ethical approval, we used a class II tetrameric complex (Beckman Coulter, San Diego, CA, U.S.A.) combined with ELISpot (Mabtech AB, SE-131 28 Nacka Strand, Sweden) to track the frequency and function of allergen-specific CD4⁺ T cells during 10 months of methotrexate therapy. Figure 1 shows the frequency of T-cell responses *ex vivo* and after culture for 10 days in the presence of Fel d 1-specific peptide and interleukin (IL) -2. The frequency of the *ex vivo* allergen-specific CD4⁺

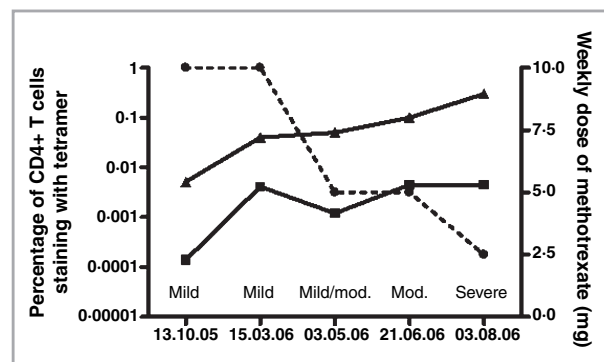


Fig 1. *Ex vivo* (squares) and cultured (triangles) Fel d 1-specific DRB1*0101-restricted CD4⁺ T-cell frequencies during treatment with methotrexate (weekly dose in circles) showing concurrent disease severity.

T cells increased significantly ($P < 0.05$) during methotrexate dose reduction and disease relapse [based on SASSAD (six area, six sign atopic dermatitis) scoring,⁶ listing as mild, moderate and severe]. In addition, the frequency of peptide-stimulated IL-4-producing cells also increased during the disease deterioration and there was a significant positive correlation between the severity score and peptide-specific IL-4 production ($P < 0.05$). We were also able to follow the HLA-DRB1*0101/Fel d 1-specific CD4+ T-cell response in an individual who was not on systemic therapy during the same period, which showed that the ex vivo frequencies over 12 months did not differ significantly in the absence of therapy.

Methotrexate is a potent inhibitor of the enzyme dihydrofolate reductase leading to the inhibition of *de novo* purine and pyrimidine synthesis and reduction in cell proliferation. In addition it is believed that the anti-inflammatory action of methotrexate is also mediated by the accumulation of extracellular adenosine which may be pro-apoptotic for different cells.^{7,8} Furthermore, methotrexate has been reported to modify cytokine and adhesion molecule expression within various lesional tissues including the skin.^{9,10} However, we are not aware of any studies investigating the influence of methotrexate on antigen-specific T cells in a human disease setting. We observed a selective reduction in both ex vivo effector cells and those memory cells that retain the capacity to proliferate in vitro. Our data would therefore support a model where methotrexate exerts its effects via reduction in the circulating frequency of T cells through preferential apoptosis within the activated population.⁸

Although it is clearly important to increase patient numbers, we are currently limited to studying the relatively rare individuals with HLA-DRB1*0101 as this is the only allele with a defined perennial allergen-specific T-cell epitope for which we can use class II tetrameric complexes. However, our data fit with predictions in nonantigen-specific systems⁸ and show that successful treatment of atopic dermatitis with methotrexate is accompanied by a selective loss of activated allergen-specific T cells.

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Annular elastolytic giant cell granuloma: a prodromal stage of mid-dermal elastolysis?

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SIR, Annular elastolytic giant cell granuloma (AEGCG) is a rare granulomatous dermatosis characterized by annular plaques with central atrophy and raised erythematous margins and usually located on the facial and neck areas of middle-aged women. However, some cases of AEGCG involve body regions not exposed to ultraviolet (UV) radiation and generalized forms have been described.^{1,2}

Here we report a case of AEGCG resolving with clinical and histological features of generalized mid-dermal elastolysis (MDE) suggesting that AEGCG might represent an inflammatory variant or prodromal stage of MDE.

A 36-year-old woman presented with a 3-month history of an extensive, slightly pruritic, skin eruption involving extremities, abdomen, lower back, axillary regions and décolleté and to a lesser extent both cheeks, covering about 50% of the skin surface. In the past, the patient had suffered from prurigo-type atopic dermatitis and recurring dyshidrotic palmar eczema. Apart from oral contraception no medication was taken. The patient smoked about 10 cigarettes a day. Except for a raised serum IgE of 648 kU L⁻¹ (normal < 100) and polyvalent type-I allergies in prick testing no abnormal laboratory findings were found.

Physical examination revealed irregular and annular erythematous plaques with elevated borders. The centres of the