Sarcoidosis associated with combined immunodeficiency

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Summary  
The association of multiple non-caseating granulomata  
and a positive Kveim test is normally considered to be  
indicative of a diagnosis of sarcoidosis. However,  
although depressed cell-mediated immunity is  
commonly described, it is extremely rare to find a humoral  
immune paresis.

A patient is reported who had multiple granulomata,  
depressed cellular and humoral immunity and a  
positive Kveim test.

Introduction  
Sarcoidosis is usually accompanied by normal or  
raised serum immunoglobulin levels. We report a  
case of sarcoidosis associated with combined  
immunodeficiency.

Case report  
A 23-year-old housewife was referred to the  
Haematology department of King's College Hospital  
from the ENT department in April 1977, following  
discovery of pancytopenia. There was a history of  
recurrent sinusitis since childhood treated by  
bilateral nasal washouts, and a submucous resection  
for a deviated nasal septum had been performed  
3 months before. There was no other past medical  
history or family history of note.

Clinical examination revealed bilateral cervical  
lymphadenopathy, enlarged tonsils and moderate  
splenomegaly. Results of investigations were as  
follows:

Hb, 9-7 g/dl; WBC, 2-2×10^9/l (neutrophils 6%,  
lymphocytes 85%, eosinophils 2%, monocytes 7%);  
platelets, 74×10^9/l; ESR, 37 min in 1st hr (Westergen);  
Paul Bunnell test, negative; blood group,  
O Rhesus positive; total protein, 60 g/l; albumin,  
35 g/l; IgG, 21-7 g/l; IgM, 1-65 g/l; IgA, none  
detected; autoantibody screen, negative; bilirubin,  
110 µmol/l; AST, 40 i.u./l; alkaline phosphatase,  
200 i.u./l; prothrombin time, 13 sec (control 13 sec);  
calcium, 2-2 mmol/l; chest X-ray, normal; lympho-  
angiogram showed abnormal lymph nodes in left  
para-aortic region; a bone marrow biopsy showed  
hypercellularity only. An exploratory laparotomy  
and splenectomy were performed in May 1977. The  
spleen and para-aortic lymph nodes were enlarged.  
Histological examination of the spleen (wt 450 g),  
Liver and lymph nodes showed numerous histocytic  
non-caseating granulomata with preservation of  
normal follicular structure. Postoperatively a  
Mantoux (1 : 100) test, a Kveim test and tests for  
Brucellosis, toxoplasmosis and tuberculosis were all  
negative. Haematological indices returned to normal.

Between May 1977 and March 1978 the patient  
experienced 3 episodes of pneumonia and developed  
a left pleural effusion which required drainage by  
thoracotomy. Lung biopsy performed at operation  
showed interstitial lymphoid infiltrates and pleural  
changes consistent with pneumonia, but no granuloma.

Further investigations at this time show: IgG  
0-94 g/l, IgA, <0-25 g/l; IgM, 0-17 g/l; urinary  
24-hr calcium excretion, 1-54 mmol/l. Delayed  
hypersensitivity skin tests were negative to  
Candida, PPD and varidase. Total peripheral blood lymphocyte  
count was 2-07×10^9/l, 20% of which formed  
rosettes with sheep erythrocytes and 32% carried  
surface immunoglobulin. Lymphocyte transforma-  
tion with phytohaemagglutinin was markedly  
reduced. Barium meal and follow-through and  
jejunal biopsy were both normal. Repeat Mantoux  
(1 : 100) test was negative. A Kveim test (Kveim  
antigen K19) was positive (Fig. 1).
A diagnosis of sarcoidosis was made and treatment with prednisone, 40 mg daily, was started on 16 March 1978. Regular weekly injections of 1·5 g of human γ-globulin were also given but were stopped

strongly reduced using the preferential B cell mitogen, pokeweed. Suppressor cell activity was measured in 2 different ways: first, the suppressor activity related to production of prostaglandin E₁ and E₂ was measured using indomethacin inhibition (Goodwin, Bankhurst and Messner, 1977) and second, the short-lived suppressor cell activity was measured using an overnight incubation (Bresnihan and Jasim, 1977). With the first technique, a normal suppressor cell activity was found (50% increase, normal range 57±20%), while the short-lived suppressor cell activity was reduced (0·54, normal range >1·2). Repeat Kveim test (Kveim antigen K12) was negative.

Discussion

This patient presented with hypersplenism and initially had a selective IgA deficiency. The past history of repeated respiratory tract infection may have been due to IgA deficiency a deviated nasal septum or neutropenia. Postoperatively, a combined deficiency of IgG, IgA and IgM developed. A cellular immune deficiency was also demonstrated. The possible aetiological role of splenectomy in the development of hypogammaglobulinaemia remains conjectural. A small percentage of selective IgA-deficient subjects has been shown to possess an IgA-specific subset of suppressor cells, while in common variable hypogammaglobulinaemia excess suppressor cell activity appears either as a primary or secondary phenomenon in most patients (Waldman et al., 1978). Suppressor cell activity in the present patient was, however, reduced in the short-lived suppressor cell assay and normal in the prostaglandin mediated suppressor cell activity.

Multiple granulomata have been described from patients with primary acquired agammaglobulinaemia. These patients may also have hypersplenism (Rosen, 1971). However, the association of multiple granulomata and combined immunodeficiency with a positive Kveim test has, as far as the authors are aware, only been reported on one previous occasion (Bronsky and Dunn, 1965). A positive Kveim test has previously been noted in patients with agamaglobulinaemia. These were considered to be false-positive reactions, although one of the 2 patients had splenomegaly (Messerschmitt, Faille and Gonthier, 1975). The occurrence of multiple granulomata in immunodeficiency syndromes may result from macrophage-indigestible antigen interactions (Editorial, 1975). However, in this patient pre-splenectomy levels of IgG were raised with normal levels of IgM, and granulomata were already present. The postoperative development of the IgM and IgG deficiencies could have been related to removal of the spleen in a patient with an already compromised immune system.

Fig. 1. Kveim biopsy from forearm, showing granulomata.
References


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doi: 10.1136/pgmj.56.654.263

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