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SUBCUTANEOUS GRANULOMA ANNULARE AND IgA – IgG2 DEFICIENCY*

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Subcutaneous granuloma annulare (SGA) is a benign granulomatous disease occurring in childhood, with lesions most commonly located about the elbow, knee and scalp. The etiology of SGA remains obscure. We present a typical case with SGA also showing laboratory findings of IgA and IgG2 deficiency.

Histologic findings of the lesions on the scalp were characterized by multiple large foci of complete collagen degeneration with a peripheral palisade of histiocytes; the foci of degeneration was edematous basophilic. In contrast to current literature, an abnormality in the cellular immune system was not found. However, immune defects (IgA and IgG2 deficiency) related to the humoral immune system were observed.
Key words: subcutaneous granuloma annulare, IgA-IgG2 deficiency.

Subcutaneous granuloma annulare (SGA) is a benign inflammatory granulomatous disease occurring in childhood, with lesions most commonly located about the elbow, knee and scalp[1,2]. SGA is one of the four clinically distinct subtypes of granuloma annulare[1]. Although trauma and immune complex vasculitis have been considered, the etiology of SGA remains obscure and the disease is generally considered to be idiopathic[3]. In recent dermatology and pathology literature, there are some reports and letters noting the association of granuloma annulare and sarcoidosis[4], cervical adenocarcinoma[5], herpes zoster infection[6], and aberrant cell-mediated immune response[7]. An association between SGA and humoral immunity has not been reported. This case report relates two rare entities: SGA, and IgA (immunoglobulin A) and IgG2 deficiency occurring in the same patient.

Case Report

A four-year-old girl, with a one-year history of recurrent, rapidly growing, and spontaneously resolving painless masses on the scalp, had been presented to different physicians because of parental concerns of malignancy and lack of

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specific and definitive diagnostic tests, except biopsy. Her past medical history was remarkable for recurrent upper respiratory tract infections. On admission, four lesions (firm, nontender and immobile, the largest 2 cm in diameter, located on the occipital region of the scalp) were found on physical examination. Cranial x-ray revealed a soft-tissue mass without direct osseous involvement. Complete blood count, erythrocyte sedimentation rate, renal and hepatic function tests, prothrombin time, and blood sugar were all normal.

Excisional biopsy was performed and the lesion was described as located in the subcutaneous tissue, attached to the periosteum over the bone. Histologic findings were characterized by multiple large foci of complete collagen degeneration with a peripheral palisade of histiocytes (Fig. 1). The foci of degeneration was edematous basophilic with hematoxylin-eosin that stained positively with Alcian blue. There were inflammatory cells, mostly lymphocytic, around the granulomatous areas (Fig. 1).

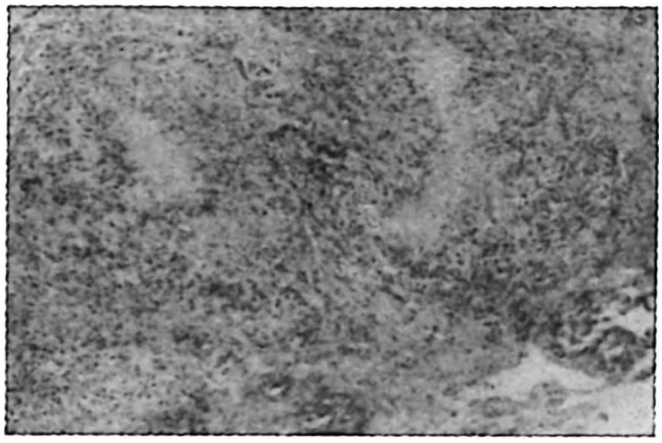

Fig. 1: The two granulamatous areas, with central complete collagen degeneration, which are surrounded by palisading histiocytes (H.E.x100).

After the diagnosis of SGA, some investigations related with autoimmune diseases, such as: antinuclear antibody (ANA), anti-ds-DNA, rheumatoid factor (RF), complement components (C3 and C4), C-reactive protein (CRP), serum haptoglobin, and ferritin and immunoglobulin (Ig) concentrations, were performed. All tests were within the normal reference intervals except the serum IgA and IgG2 levels. Serum immunoglobulins were investigated three times by nephelometry, and serum IgG subclass values by ELISA. Serum IgA and IgG2 values were found to be decreased when compared with values in healthy Turkish children[8] (IgG: 678-604-690 mg/dl, IgM: 122-97-141 mg/dl, IgA: 24.3-22.4-21.7 mg/dl (normal 66-120 mg/dl), IgG1: 5.0 g/L, IgG2: 0.2 g/L (normal 0.8-3.6 g/L), IgG3: 1.86 g/L, IgG4: 0.07 g/L). There was a slight decrease of gamma-globulin fraction (9.5%) (normal 12-22%) in protein electrophoresis. On the other

hand, the percentages and absolute counts of lymphocyte subsets by flow cytometry were normal when compared with normal age-related values[9]. Delayed-type skin reaction to purified protein derivative (PPD) due to previous vaccination with BCG (Bacillus-Calmette-Guerin) was observed.

The child was diagnosed with "subcutaneous granuloma annulare and IgA-IgG2 deficiency", and the lesions resolved spontaneously after three months. Only one recurrence has been observed during the follow-up period of one year.

Discussion

SGA is a benign inflammatory disorder that occurs in children. The mean age at initial presentation of lesions is 3.9 years[1]. Our case was three years old at initial presentation of SGA, and the lesions were located on the scalp, as mentioned in different series.

The etiology of SGA remains unclear. Early reports implicated tuberculosis, but this has never been confirmed[10]. More recently, it has been hypothesized that vasculitis and cellular immunity play a role in SGA. Direct immunofluorescence studies have shown blood vessel deposits of IgM, IgG and C3 complement, leading some investigators to question the significance of an immune complex vasculitis[11]. Immunologic studies of lymphocyte subsets support the hypothesis that SGA is the result of an aberrant cell-mediated immune response[7]. Despite years of investigation and application of the latest technology, the specific cause of SGA remains unknown.

In our case, the laboratory investigations related to the cellular immune system were all found to be normal and the patient had no other signs and symptoms of an immune complex disease.

Selective deficiency of the IgG2 subclass commonly accompanies IgA deficiency[12]. IgA deficiency and granuloma annulare are associated with many autoimmune diseases[1, 12]. However, our patient did not have any laboratory or clinical signs of an autoimmune disease.

No other case showing concurrent SGA and IgA-IgG2 deficiency has been found in the literature. Because of the questionability of immunologic abnormalities in the pathogenesis, this illustrative case is of interest.

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