Candida Granuloma

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Candida granuloma is a variant of chronic mucocutaneous candidasis associated with chronic infection mainly by *Candida albicans* in which the skin lesions are rather granulomatous and hyperkeratotic. To date a variety of defects of cell mediated immunity have been shown to be important.

We describe a 2-year-old boy with cutaneous candida granuloma and immunologic dysfunction. (Ann Dermatol 6:(2) 174-178, 1994)

Key Words: Candida grauloma, Immunologic dysfunction

Candida granuloma is a rare form of chronic mucocutaneous candidiasis associated with nonlethal immune deficiency. The lesions are characterized by an inflammatory reaction extending into the dermis and by the development of granuloma similar to the other deep mycoses[1].

Chronic mucocutaneous candidiasis has become a serious problem among patients with impaired host-defense mechanisms[2]. The absence of delayed hypersensitivity, imbalance between cell-mediated and humoral immunity and a defect in phagocytic activity are considered the predisposing factors for the development of candida granuloma[3,4].

In this case immunologic study showed that absence of delayed hypersensitivity, decreased natural killer(NK) and lymphocyte activated killer(LAK) cell activities. They suggest that a defect in immune system may play a role in the development of candida granuloma.

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REPORT OF A CASE

A 2-year-old boy was admitted to the hospital in February 1992 for management of a huge erythematous tumor on his abdomen. This tumor initially developed four months previously on the right lower quadrant of his abdomen with an isolated bean sized nodule.

He was born as a normal full term baby by Cesarean section delivery with body weight of 3.3kg. He has not been taking any medications and his immunization schedules were up to date. There was no history of any illness or trauma. Familial history was noncontributory. On admission, he looked acutely ill and underdeveloped. His body weight was 12.5Kg(25-50th percentile), height 88cm(50-75th percentile), head circumference 48cm(25-50th percentile), chest circumference 52cm(75-90th percentile). His pulse rate was 130/minute, respiratory rate 32/minute, and body tremperature 39°C. The inguinal and axillary lymph nodes were palpable, but there was no hepatosplenomegaly.

Physical examination revealed a firm, immovable, 13x15cm sized mass on the right lower quadrant of the abdomen(Fig. 1). Erythematous scaly patches were also noted on both axillae and inguinal area which developed at the age of one month. Mucous membrane was spared. Complete

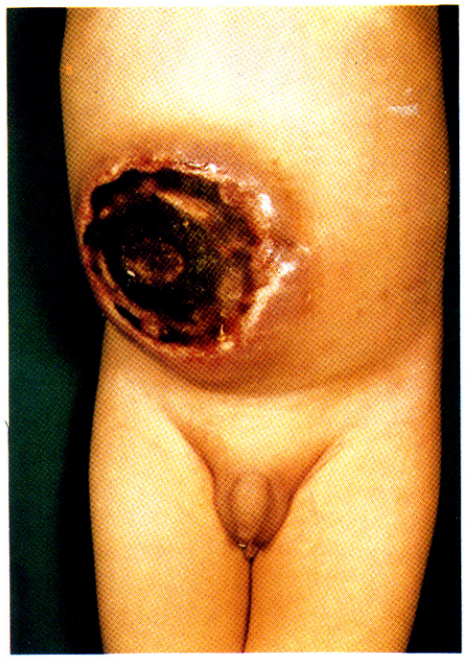

Fig. 1. An erythematous firm, immovable, 13 × 15cm sized mass on the abdominal wall exhibiting central necrosis and crusts.

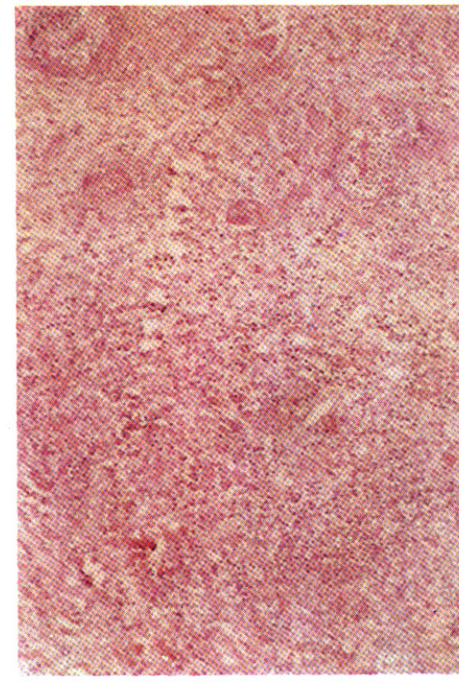

Fig. 2. Histopathologic finding showed granulomatous inflammation of the lesion(H & E stain, × 100).

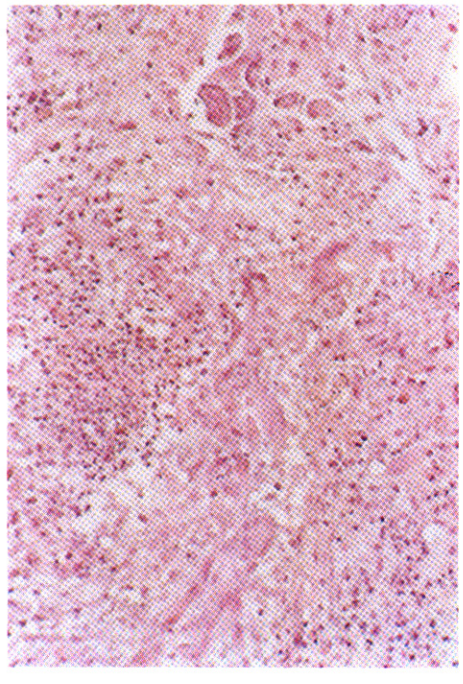

Fig. 3. A high power view revealed granulomatous inflammation composed of lymphocytes, eosinophils, epithelioild cells and giant cells(H & E stain, × 400).

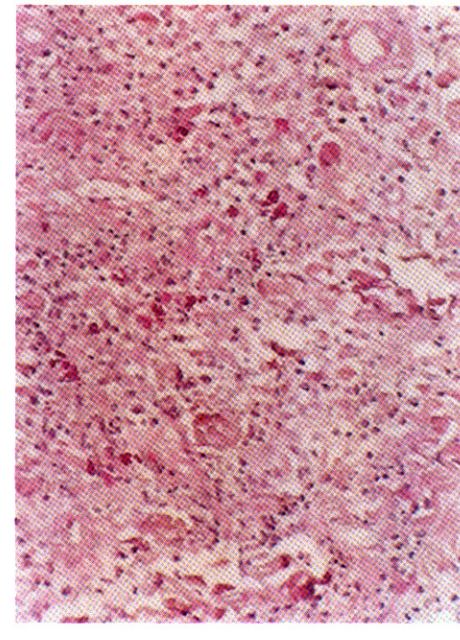

Fig. 4. PAS stain demonstrated many fungal elements (× 400).

Fig. 5. On eosin methylene blue(EMB) agar *Candida albicans* was identified by production of germ tubes.

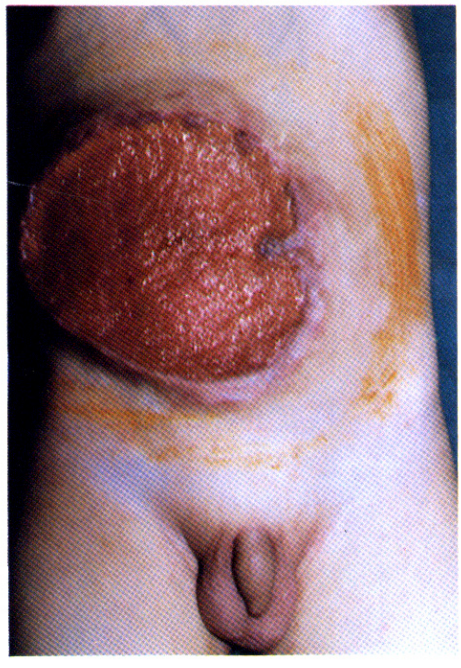

Fig. 6. Two months after the operation the lesion was much improved.

blood count revealed leukocytosis and eosinophilia. Other laboratory tests including urinalysis, liver and renal function test, chest roentgenogram, serum iron level, total iron binding capacity, transferrin saturation, and zinc level were normal or negative. Results of immunologic tests were normal including proportions of T lymphocytes and immunoglobulin levels. NK and LAK activities were decreased. Multi-CMI skin tests using Merieux Multi-Test CMI revealed no response to tetanus, diphtheria, streptococcal, tuberculin, candidal, trichophyton and proteus antigens. A biopsy specimen was obtained at the margin of the mass. Histologic examination showed granulomatous inflammation composed of epithelioid cells, lymphocytes and multinucleated giant cells in mid- and lower dermis(Fig. 2, 3). PAS stain demonstrated many fungal spores and some of them were within giant cells(Fig. 4).

KOH mount prepared from the abdominal mass, axillary and inguinal lesions were positive for fungal elements. Grossly there formed yellow to cream colored colonies on Sabouraude's medium. Microscopic examination of the colonies showed many hyphae and budding cells. The fungus culture of lesional tissue was performed by use of eosin methylene blue(EMB) agar and *Candida albicans* was identified by production of the germ tubes(Fig. 5).

We treated him with systemic antibiotics and antifungals(fluconazole 50mg/day, nystatin 1.2 million units/day, ketoconazole 3 mg/kg/day). After three months there was no change in the appearance of the lesions. He underwent a debridement and skin graft, and administration of amphotericin B(0.25 mg/kg/day), thymus extract was added to his treatment. After two months the abdominal lesion flattened and became less erythematous(Fig. 6). After six months the patient showed a significantly improved state.

DISCUSSION

Candida granuloma is usually used to describe those cases of chronic mucocutaneous candidiasis in which the skin lesions are rather granulomatous and markedly hyperkeratotic. It is regarded as one variant of chronic mucocutaneous candidiasis. Its predilections are face and scalp but there may be widespread infection of the skin[3]. The features distinguishing this from other types of chronic mucocutaneous candidiasis are: (1) onset of infection in early childhood; (2) extreme chronicity with recurrences following treatment; (3) profound tissue

response evidenced by cutaneous granulomas; and (4) absence of internal involvement or known underlying consititutional disease[5].

Candida granuloma is usually caused by *Candida albicans*, but *Candida guilliermondii* has also been reported to cause it[6].

The etiologies of candida granuloma are still unknown, but some etiologic factors have been reported including endocrinopathies, nutritional and immune deficiencies. It may be associated with endocrinopathies such as hypothyroidism, diabetes mellitus, and with nuteitional deficiencies of pyridoxine, iron, and folate[1,2,4,7,8]. But the role of nutritional deficiencies in the pathogenesis of this disease is unknown.

Some investigators have reported immunologic aspects of the development of candida granuloma. Abnormal humoral immunity, absence of delayed hypersensitivity and activation of alternative complement pathway are well-known[4,9]. First, there is an imbalance between humoral and cell-mediated immunity; high serum humoral anti-candidal response with negative cutaneous delayed hypersensitivity to candida antigen. Three mechanisms have explained this immune imbalance with excess antibody formation and defective cell-mediated immunity; (1) delay in antibody response to the organism may allow rapid multiplication of *Candida albicans* with a subsequent production of excess anti-Candida antibody; (2) high levels of candida antibody may also result from previous infection; and (3) an excess humoral response following the initial candidal infection.[4] Second, candidal cell wall products activat e alternative complement pathway[9]. Immunologic investigations showed negative cutaneous response to candidal antigen, and a defect in our patient in NK and LAK cell activities. But levels of serum immunoglobulins and complements were normal. A specific defect in cell-mediated immunity and killer cell activity may play an important role in the development of candida granuloma.

The diagnosis of candida granuloma is established by the isolation of *Candida* species from the lesional tissue, and by histopathologic findings of fungal granuloma that composed of granulomatous inflammation and fungal spores. We could identify *Candida albicans* from the tissue culture by germ tube test. We also found fungal granuloma histopathologically. The differential diagnosis of this disease includes deep mycosis, foreign body granuloma, and granuloma gluteale. Granuloma gruteale is different from candida granuloma. Histopathologically there are no fungal elements and foreign body giant cells, and the lesion usually occurs over the napkin area and gluteal region in granuloma gluteale[3,4].

Patients with chronic mucocutaneous candidiasis have persistent or recurrent course and treatment of this condition depends on an all-out chemotherapeutic attack on the yeast and on attemps to restore defective immune system[3]. Therefore variable therapeutics have been introduced for the treatment of this disease. Candida granuloma can be treated topically with nystatin, imidazole derivatives and systemically with amphotericin B, ketoconazole, itraconazole and fluconazole. Immunotherapy including thymus extract transfer factor, and immune modulators such as cimetidine and levamisole is also used to treat chronic mucocutaneous candidiasis[4,9-12]. If the patient does not respond to medical treatment, surgical intervention is recommendable.[4] We treated the patient with systemic antibiotics and antifungals for three months but there was no improvement of the lesions. He underwent a debridement and skin graft and amphotericin B immunomodulator(thymus extract) were added to his treatment. After six months the patient showed a significantly improved state.

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