CHRONIC MUCOCUTANEOUS CANDIDIASIS WITH CANDIDAL GRANULOMA

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Summary

A case of candidal granuloma is described in a 32 year old female suffering from chronic muco-cutaneous candidiasis since the age of 10 years. Immunological tests revealed a defect in cell-mediated immunity. The disease was resistant to various known local anticandidal agents. Levamisole and B.C G. vaccination given as immunostimulants did not give any relief to the patient.

Chronic mucocutaneous candidiaiss is a distinct clinical syndrome wherein there is persistent infection of the skin, mucosa and nails by candida albicans. Candidal granuloma is the term used to describe those cases of chronic muco cutaneous candidiasis in which the skin lesions are granulomatous and marked by hyperkeratois.

Review of the literature

Hauser and Rothman in 1950 made the first attempt to characterise and define the entity of candidal granuloma[1]. They described a typical case of candidal granuloma and assembled 13 previous reports which they felt, had similar features. Later, Nityananda[2] and Warin[3] reported similar cases in female children. Lehner[4] classified it as a separate type of cutaneous candidiasis. According to Kugel, Harrel and Cripps[5], the features distinguishing this from other types of disseminated candidiasis were, 1. onset in childhood 2. extreme chronicity with recurrence following therapy 3. profound tissue response evidenced by cutaneous granuloma and 4. absence of involvement of internal organs and other constitutional diseases. Associated diabetes and widespread pancreatic fibrosis were reported in some cases.[6] Though previously candidal granuloma was considered as a specific entity[1,2,3] recent tendency is to regard it as only one variety of chronic mucocutaneous candidiasis, belonging to group 2b of Higg & Well's classification[7] of Chronic mucocutaneous candidiasis.

Pathogenicity of candidal granuloma is not well understood. A variety of ichthyosis with secondary colonisation of retained epidermal products by C. albicans was postulated by Maibach & Kligman[8]. This was later contradicted by others[5]. An altered host response rather than unusual virulence of the organism is important in pathogenesis. Normally serum has the capacity to inhibit growth of C. albicans[9]. Decrea-

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sed ability of patients' serum to inhibit conversion of yeasts to invasive mycelia has been suggested[5]. A defect in immune function may be noted in some cases. Associated hypergammaglobulinemia can occur[10]. On the basis of absence of delayed hypersensitivity but the normal production of migration inhibition factor (MIF), Valdimarrsson[11] has suggested that in these patients candida antigen attracts macrophages normally but they are then unable to deal with the organisms because of defective phagocytosis or killing so that there is progressive accumulation of this impotent infiltrate leading secondarily to pronounced epidermal changes. At present it is not possible to correlate precisely the different immunological defects with the different clinical forms[12]. Histology reveals hyperkeratosis, acanthosis and a chronic granulomatous infiltrate in the dermis. PAS positive filaments will be seen in the horny layer and the viable epidermis[2,10].

Case Report

An unmarried 32 years old female nurse attended the department of Dermatology, Medical College Hospital, Trivandrum in July 1979 with complaints of whitish patches, multiple erosions on the mucosa of the mouth and vagina and swelling of the nail folds of toes and fingers since the age of 10 years. She noticed a keratotic, verrucous growth of the big toe of the left foot for 2 years and thick crusted plaques on the left side of the face for 6 months. She had received repeated courses of penicillin injections, and had been applying various anti candidal agents like 1% gentian violet, nystatin cream, etc., without much symptomatic relief. Two years before admission she was on antituberculous drugs (INH, PAS and streptomycin) for 18 months for respiratory complaints. She attained menarche at the age of 16 and her menstrual periods were regular and normal. She refused to marry due to her chronic illness. She was the 6th child of a nonconsanguinous marriage. Nobody in her family suffered from similar disease or any other chronic ailment.

Examination revealed diffuse, thick, whitish plaques with fissuring and erosions on the mucosa of the whole oral cavity (Fig. 1) and vagina. Forcible removal of the plaques caused much pain and bleeding and exposed the underlying granular surface on the mucosa. There was maceration and fissuring of the corners of the mouth. There was curdy white discharge from the vagina. Skin on the central part of the face showed diffuse infiltration with knob like projections especially on the tip of the nose. There were multiple dry, thick, scaly keratotic plaques on left side of the face (Fig. 2). The nail folds of fingers and toes were red, swollen and tender. The nail plates of some of the fingers and toes were thick, crumbled and dystrophic. On the dorsum of left big toe there was a keratotic verrucous lesion 4 x 3 cm size (Fig. 3). Other systems were clinically normal.

The patient was treated with clotrimazole solution (Lotril-Gufic), nystatin vaginal tables (Mycostatin-Sarabhai) and B. Complex group of Vitamins. Repeated avulsion of nails and paring of the keratotic lesion of the big toe was done. There was no appreciable response to the above lines of treatment even after 6 weeks. She was then given B.C.G. Vaccination and a course of Vermisol (Levamisole-Khandelwal Lab) for 6 weeks as an immunostimulant. There was no significant improvement in patient's condition even after 5 months. The patient is lost to follow up as she was transferred to Delhi.

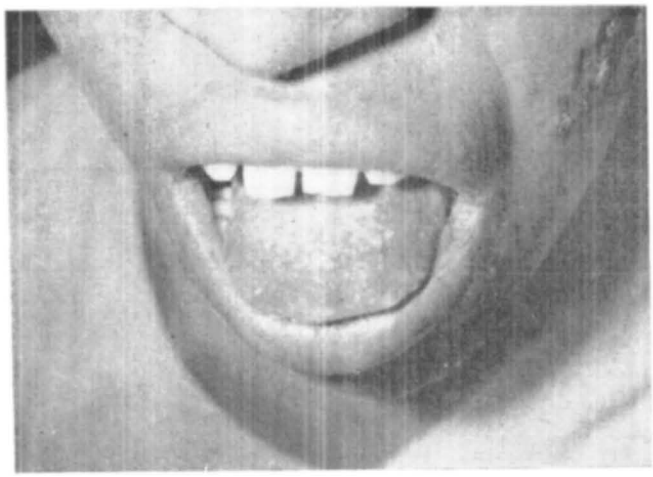

Fig. 1

A case of chronic mucocutaneous candidiasis. Note thick whitish plaques on the tongue, lip and angles of mouth.

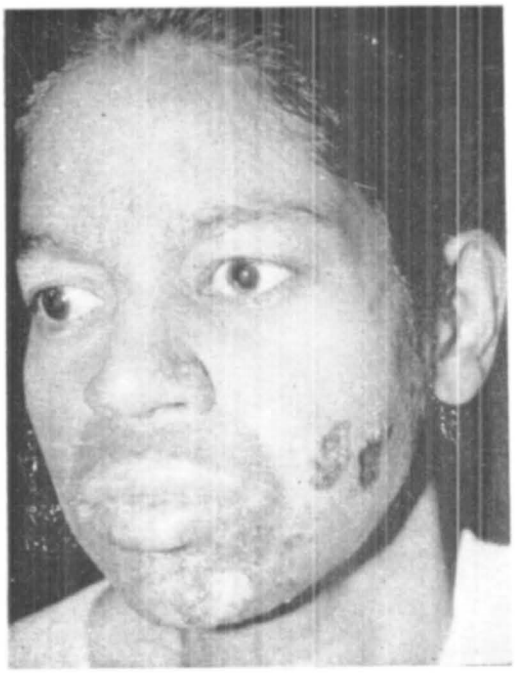

Fig. 2

Note keratotic, verrucous plaques, chin and left side of face.

Investigations : Hb 12.4 gm% WBC T.C. 6800 cells/cmm; DCP58 L34 E8; E.S.R. 80 mm/Ist hr (Westergren) V.D.R.L. non-reactive ; fasting blood sugar 94 mg% and postprandial 124 mg%. Serum Choleserol 125 mg%, Creatinine 1 mg%; Calcium 9.6 mg% ; Protein Total 7 gm% (Albumin 4.2 gm% ; Globulin 2.8 gm%).

X-Ray chest :- PA view : Normal

Sputum for AFB : Negative.

B. M. R. : Within normal limits.

Scrapings in 10% KOH for Candida was positive from the lesions in the mouth, vagina, nails and toes, but negative from the face lesions.

Cultures on Sabouraud's dextrose agar were done with specimens from lesions at the following sites. 1. mouth

2. vagina 3. face 4. nails 5. toe. These yielded flat, smooth, whitish colonies with yeasty odour. The organism fermented glucose and maltose with the formation of acid and gas, and lactose with the formation of acid only. Fermentation of sucrose was negative.

Histological examination of the big toe lesion revealed marked hyperkeratosis, parakeratosis, acanthosis and papillomatosis. The upper and mid dermis was infiltrated densely by lymphocytes, histiocytes and few plasma cells. PAS stained sections revealed a number of hyphae in horny layer and in the uppermost part of the epidermis. No fungal element was seen in the dermis. Similar histological features were noted in face lesions also.

The patient could not be sensitised to DNCB. The test was performed as described by Canales et al[12]. Total T cell count was 20% (E. Rosette Method[13].) Mantoux test was negative.

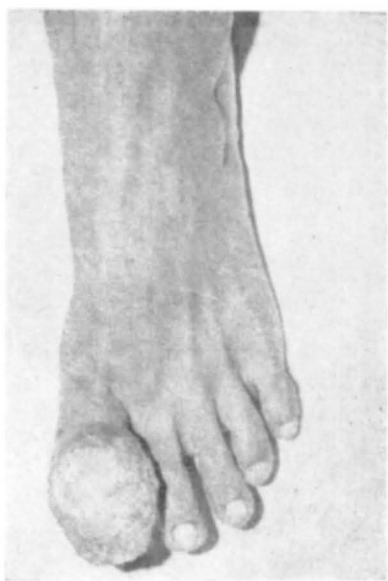

Fig. 3
Keratotic verrucous growth left big toe. Nail plate is crumbled.

Discussion

Chronic mucocutaneous candidiasis is a progressive candidal infection which is usually associated with some constitutional defects especially congenital thymic disorders affecting lymphocyte function[14]. Defective cutaneous expressions of CMI are observed consistently[12]. Candidal granuloma, though previously considered as a specific entity[2,4] is only one variety of chronic mucocutaneous candidiasis and it fits into type 2b of Higg and Wells' classification[7]. Our patient has all the clinical features of chronic mucocutaneous candidiasis. The hypertrophic horny lesions on the big toe made us first to think of other possibilities like, tuberculosis verrucosa cutis, chromomycosis etc. The cultural and histological studies excluded these possibilities. Further, the antituberculous drugs she had taken for her lung complaints did not have any effect on the toe lesion. Later possibility of candidal granuloma was considered. Repeated examination in KOH of the crusts taken from the big toe lesion revealed the fungi. Culture on Sabouraud's agar and histological study of the tissue taken from the face and big toe lesion confirmed our clinical diagnosis of candidal ganuloma. Our patient started suffering from this chronic infection from the age of ten years though granulomatous reaction of the skin developed many years later. Throughout the course of her illness the skin lesions were resistant to various local anticandidal agents. Our investigations – failure to sensitise with DNCB, negative Mantoux test and low T. Cell count – revealed a defect in cell mediated immunity in this patient. So our patient definitely suffered from some constitutional defect affecting lymphocyte function and thereby defective cutaneous expression of delayed hypersensitivity. At present it is not possible to correlate precisely

the differing immunogical aspects with the different clinical forms. A genetic basis has been suggested by the occasional finding of cutaneous candidiasis and cutaneous anergy in siblings. We could not perform tests to assess delayed hypersensitivity in the siblings of our patient, though, there was nobody suffering from any chronic disease in her family. Other possible causes which can predispose to the development of chronic mucocutaneous candidiasis have been ruled out in our patient. B. C. G. vaccination[15] and Levamisole[16] which are known immunostimulants did not give any relief to the patient.

References

1. Hauser FV and Rothman S: Monilial granuloma, Arch Derm Syph 1950, 61 : 297.
2. Nityananda K: Monilial granuloma, Brit Med J 1959, 1 : 690.
3. Warin RP: Monilial granuloma, Brit Med J 1959, 1 : 1121.
4. Lehner T: Trans a Resp St John's Hosp derm SOC Lond 1964, 50 : 8. Quoted by Beare JM, Gentles JC, Mackenzie DWR: Mycology, Text Book of Dermatology Vol. I, Rook A, Wilkinson DS, Ebling FJG, Blackwell Scientific Publications, Oxford 1968, p 809.
5. Kugelman TP, Cripps DJ & Harrell ER: Candida granuloma with epidermophytosis, Arch Derma 1963, 88 : 150.
6. Rothman S: Some unusual forms of cutaneous moniliasis, Arch Derm 1959, 79 : 598.
7. Higgs JM & Wells RS: Mucocutaneous Candidiasis, Brit J Derm 1972, 86 : 88.
8. Maibach HI and Kligmon AM: The Biology of Experimental Human moniliasis, Arch Derm 1962, 85 : 233.
9. Roth FJ and Gold Sterin MI: Inhibition of growth of pathogenic yeasts by human serum. J Invest Derm 1961, 36 : 383.
10. Engel MF and Brunsuic GA: Monilial Granuloma with hypergamma globulinemia, Arch Derm 1961, 84 : 192.
11. Valdimarsson H et al: Clin Exper Immunolo 1972, 1 : 151. (Quoted by Roberts SOB and Mackenzie DWR: Mycology, Text Book of Dermatology Vol. I, 3rd Edition, Rook A, Wilkinson DS, Ebling FJG, Blackwell Scientific publications, Oxford 1979, p 767.
12. Canales L, Middleman RO and Louro JM et al: Immunological observations in chronic mucocutaneous candidiasis, Lancet 1969, 2 : 267.
13. Wybran J and Fuddenberg HH: Thymus designed Rosette forming cells in various human disease states, J Clin Invest 1973, 52 : 1026.
14. Chilgren RA, Quie PG & Meuwissen HJ et al: Chronic mucocutaneous candidiasis, deficiency of delayed hypersensitivity and selective local antibody defect, Lancet 1967, 2 : 688.
15. Gutterman JU, Mc Bride C and Freireich EJ et al: Active immunotherapy with BCG for recurrent malignant melanoma, Lancet 1973, 1 : 1208.
16. Huskisson EC, Scott J and Balme HW et al: Immunotherapy with Levamisole for rheumatoid arthritis, Lancet 1976, 1 : 393.