CASE 5

Patient: A 12-year-old Thai girl from Ayutthaya

Chief Complaint: Scaly erythematous patches at periorificial, ears and fingers for 5 years.

Present Illness: She had recurrent scaly erythematous patches on various skin sites, mucous membrane and nail which had been diagnosed as cutaneous candidiasis. She had been treated with antifungal agents which showed clinical improvement. However, relapse usually occurred after treatment cessation.

Past History: The patient's general health was good except her height and weight were below 3 percentile.

Family History: None of the family members experienced similar skin lesions.

Physical Examination:

GA: A healthy girl patient.
HEENT: Normal teeth, hair and eye examination,
No thyroid enlargement.
Heart & Lungs: WNL
Abdomen: No hepatosplenomegaly
Breast and genital development: Normal development

Dermatological Examination (Figure 5.1-4)**:** There are well defined scaly erythemetous patches at periorificial, both ears and hands with mutilated of 1^{st}-3^{rd} left fingers and 4^{th} right finger and dystrophic nail. Mucous membrane showed whitish patches at tongue and buccal mucosa.

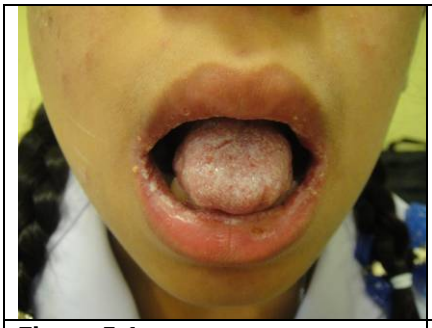

Figure 5.1

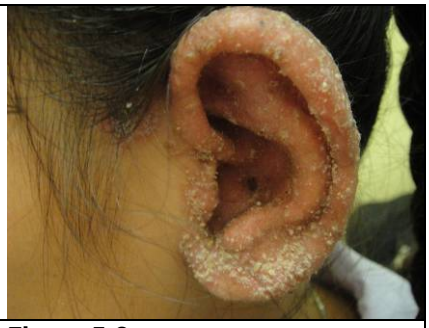

Figure 5.2

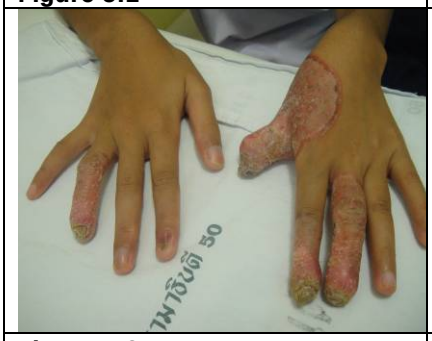

Figure 5.3

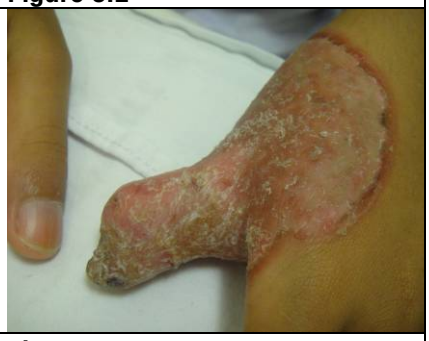

Figure 5.4

Investigations:

CBC: Hb 12 g/dl, Hct 35.1%,
WBC 7290 N 38.4% L 53.4% M 5.6%, E 1.6%
platelet 213,000

LFT: AST 30 ALT 35 ALP 177

Chemistry: Glucose 77 mg/dL,
Ca 8.6 mg/dL, Albumin 36.7 g/L
INP 4.5 mg/dL Mg 2.0 mg/dL

Hormone: PTH 31.15 pg/ml (15-65) Cortisol 2.4 ug/dl
Estradiol 10.94 pg/ml (7.1-24.7)
FSH 1.47 mIU/ml LH <0.07 mIU/ml

KOH: positive finding

Skin culture: Candida albicans

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Consultant: Amornsri Chunharas

Discussion:

Chronic mucocutaneous candidiasis was first described by Thorpe and Hadley in 1929[1], known as a spectrum of disorders in which patients have persistent or recurrent infections of the skin, nails and mucous membranes with *Candida spp. C. albicans* is the species that responsible for majority of case[2]. CMC may be sporadic or familial and affects both sexes with a discrete predominance of females (1.4:1) in the variants associated with endocrinopathies[3].

The precise molecular defect is not known for most forms of primary CMC, with the exception of the autoimmune polyendocrinopathy-candidiasis-ectodermal dystrophy (APECED) syndrome which mutation in the AIRE(autoimmune regulator) gene have been well established.[4] A common immunologic abnormality is failure of the patient's T lymphocytes to produce cytokines that are essential for expression of cell-mediated immunity to *Candida.* CMC patients have shown general dysregulation of IL-12, IL-6 and IFN gamma, resulting in an inability to clear candidal organisms. In addition chronic infections result in production of high levels of inflammatory cytokines (IL-6) followed by anti-inflammatory cytokines (IL-10) that further reduce the production of T helper 1-inducing cytokines via a positive feedback loop. Furthermore, to date there is increasing evidence suggests that this inefficient defence is reflected by a DC/T cell defect which results in an impaired Th17 and Th1 immune response and consecutively, a failed immune instruction of tissue cells.[5]

Several unique syndromes are part of this entity based on the extent and locations of the Candida infections and characteristic associated findings such as polyendocrinopathies,

autoimmune disorders, thymoma, and interstitial keratitis (Table1). The skin manifestation ranges from recurrent recalcitrant thrush to mild erythematous scaling plaques with dystrophic nail to severe generalized, crusted granulomatous plaques. The cutaneous plaques usually occur on the scalp and periorificial and intertriginous sites. Scalp infections may lead to scarring alopecia. The nails are thickened, brittle, and discolored with associated paronychia. Mucosal involvement is usually limited to oral thrush, however esophageal, genital and laryngeal mucosa involvement have been reported. The other features that accompanied with CMC which occur more commonly in childhood onset candidiasis and APECED syndrome including alopecia, vitiligo, keratoconjunctivitis, enamel dysplasia, autoimmnune hepatitis, malabsorption, alopecia and nail dystrophy.[6] Of these dental enamel dysplasia is the most common associated finding which can be severe, and some of patients were edentulous or nearly so by the end of the second decade.[6]

In APECED syndrome, the most common endocrinopathies were hypoparathyroidism (79%), hypoadrenalism (72%) and ovarian failure (60%). Sixty percent of the patients had 2 or more endocrinopathies. Development of endocrinopathies usually occurred during the fourth and fifth decades of life therefore annual evaluations of endocrine functions in CMC patient are recommended.

Patients with CMC rarely develop invasive disease or disseminated Candida infection. However, Candida brain abscess after dental procedure in a patient with oral candidiasis has been reported. Fifty percent of these patients may develop other bacterial, viral or fungal infections[2]. Dermatophyte infections of the skin and nails are common, which could be misinterpreted as candidiasis refractory to antifungal treatment. Invasive or disseminated infections

caused by H. capsulatum and C. neoformans also have been reported.[2]

Azole antifungal agents are mainstay of treatment for CMC also prevention of relapses. However, emerging resistant strains of Candida spp. to azoles may impede long-term prophylaxis in CMC. Several immunomodulatory approaches also have been evaluated, with inconsistent results and moderate success.

References

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6. Ahonen P, Mylla¨rniemi S, Sipila I, Perheentupa J. Clinical variation of autoimmune polyendocrinopathy-candidiasisectodermal dystrophy (APECED) in a series of 68 patients. N Engl J Med 1990; 322:1829–36.

Table 1: Classification of Chronic Mucocutaneous Candidiasis

CMC Type	Inheritance	Onset	Clinical Features	Associated Disorders	Non-candidal Infection
Chronic oral candidiasis	No	Middle-aged	Candidiasis of tongue and buccal mucosa. No esophageal, skin and nail involvement.	Fe^{2+} deficiency	No
Familial CMC	AR, AD	Before 2 yr	Oral candidiasis. Limited skin and nail involvement.	No endocrinopathies	Yes
APECED	AR, AIRE gene	Before 5 yr	Oral, diaper, skin and nail involvement. Endocrinopathies and autoimmnune disorder	Most common endocrinopathies: Hypoparathyroidism, Hypoadrenalism Other associated: Thyroid disease,1°hypogonadism, Hepatitis,Malabsorption, Vitiligo Pernicious anemia, Alopecia areata	Yes
CMC with thymoma	No	Adult onset	Mucous membrane and cutaneous candidiasis	Benign/Malignant thymoma Aplastic anemia, Myasthenia gravis, Hypogammaglobulinemia	No
Candida granuloma	No	Before 5 yr	Thick, adherent candidal crusts on scalp and face	None	Yes
CMC with keratitis	AD	Early childhood	Candidiasis of oral cavity, diaper area	Keratoconjunctivitis, Alopecia Endocrine abnormalities	Yes