FAMILIAL MUCOCUTANEOUS CANDIDIASIS – A CASE REPORT

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Chronic mucocutaneous candidiasis is an immune-deficiency disorder primarily due to T- cell dysfunction characterized by persistent candidal infection of mucous membrane, skin, scalp and nails. A familial occurrence has been reported in some instances suggesting a genetic predisposition. Chronic mucous membrane candidiasis has an onset in infancy or childhood; the primary affected site is the oral cavity; however, lesions may occur on trunk, hands, feet and scalp. This paper describes two siblings with candidial infection of the oral mucosa associated with cutaneous bacterial infection.

Chronic mucocutaneous candidiasis (CMC) is a primary T- cell immunodeficiency characterized by persistent or recurrent candidal infections of the skin, nails and mucous membrane without Candida sepsis.(1) CMC does not represent a specific disease, but rather a phenotypic presentation of a spectrum of immunologic, endocrinologic, and autoimmune disorders. The unifying feature of these heterogeneous disorders is impaired T-cell-mediated immunity against Candida species. (2)

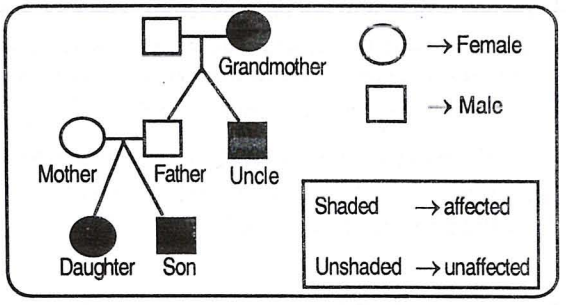
CMC is associated with defect in cell-mediated immunity that may either be limited to Candida antigens or be part of a more general immune abnormality. Recent data suggests alterations in cytokine production in response to Candida antigens. Patients who lack T-cell immunity (those with severe combined immune deficiency syndrome or DiGeorge syndrome) or patients with severely impaired T-cell function (eg, patients with AIDS) are susceptible to chronic candidal infections. (2)

Although, these disorders are confined to the cutaneous surface, they display little propensity for systemic dissemination. Oral lesions appear first, followed by perleche, lip fissures, nail and cutaneous involvement. When presenting in childhood, the lesions are detected before the age of 3 years. [3] Children with CMC usually have the appearance of other disorders, including non-candidal infections (81%), idiopathic endocrinopathies (44%) & autoimmune diseases (32%). (1)

To the best of our knowledge, there are no reports to suggest any other dermatological condition co-existing with CMC to date. Thus, we report a case of CMC with Ecthyma, in 2 siblings.

Case report

A 16 year old female patient visited the outpatient department of Oral Medicine and Radiology of Oxford Dental College; Bangalore, India with a chief complaint of proclined upper front teeth. Her past medical history, patient revealed consulting a physician 1 year ago for weakness, dizziness and for skin, mouth lesions which aggravated during summer season. Her investigations revealed hemoglobin of 11gms % and she was prescribed oral iron supplements and topical applications, for her skin and mouth lesions. Occurrences of similar skin and oral lesions were present in other family member's particularly paternal grandmother, paternal uncle and patient's brother. Patient's mother gave a history of noticing the lesions at the age of 3 years for both siblings.



Family tree illustrating an Autosomal recessive inheritance of CMC in our patients (Table I)

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On general examination, the patient was hypersthenic and moderately nourished with mild pallor. Hyperpigmented areas of the healed skin lesions were noticed over the upper and lower extremities. No abnormalities were noticed with nails and scalp. On intra-oral examination a diffuse white curdy lesion was present on the dorsal surface of the tongue and on the middle 3rd region of the hard palate which was surrounded by an erythematous area. Both the lesions were non-tender and scrapable. (Fig-1)

The patient's brother showed similar oral lesions (Fig-1) and other cutaneous lesions on the upper and lower extremities, on the back and nape of the neck. Dry scaly lesions were present on the scalp. (Fig-2) Laboratory investigations of both siblings revealed the following results.

Tests done	Patient (girl)	Patient's brother	Normal values
Hb%	**11gm%**	**10.8gm%**	M-13.5-18gm% F- 11.5-16gm%
ESR	98mm/hr	35mm/hr	M – 0-15mm/hr F- 0-20mm/hr
Random blood sugar	78 mg/dl	73mg/dl	70-140 mg/dl
TSH	3.06rIU/ml	1.0rIU/ml	0.34-5.6 rIU/ml
Cortisol (7-9 A.M)	15.82µg/dl	12.09µg/dl	6.7-22.6µg/ml
Serum ferritin	**10ng/ml**	**19ng/ml**	M 23.9-336.2ng/dl F-11.0-306.8ng/ml
HIV test	negative	negative	

KOH smears from scrapings of the oral lesion in both patient and patient's brother revealed candidal hyphae (Fig-3), the test was negative for the scrapings obtained from cutaneous and scalp lesions of the patient's brother and hence a provisional diagnosis of Oral candidiasis was given. Further both the siblings were referred to a dermatologist in a medical college for systemic evaluation, the necessary investigations were performed and a final diagnosis of Mucocutaneous Candidiasis without endocrinopathy associated with Ecthyma was given.

DISCUSSION

Several types of chronic mucocutaneous candidiasis have been identified, reflecting a variable clinical presentation, associated disorders and prognosis. No racial predilection is reported for chronic mucocutaneous candidiasis (CMC). Male to female ratio is equal, CMC usually manifests in infancy or early childhood in about 60-80% of cases with mean age of onset being 3 years. (1)

CMC can be broadly classified into familial (inherited) or non-familial (non-inherited) forms. Familial forms are inherited as autosomal dominant or recessive and are associated with or without endocrinopathy. Two other familial subtypes, an autosomal dominant form with nail candidiasis and intercellular adhesion molecule -1 (ICAM-1) deficiency and the other, an autosomal recessive form with hyperimmunoglobulin-E have also been described (3). In our case, patient's illustrate a vertical transmission, of a form of CMC affecting oral mucosa particularly tongue & palate. A review of the family tree indicates typical features of autosomal recessive form of inheritance.

CMC is further classified into several subsets (Tablell) (4)

TYPE	PRINCIPAL OTHER FEATURES	CANDIDIASIS	
		ORAL	CUTANEOUS
Early onset	Occasional iron deficiency	++	+
Diffuse	Granuloma formation , candidal blepharitis,pharyngitis,laryngitis,occasional bacterial & viral infection high prevalence of iron deficiency	+++	+++
With endocrinopathy	Hypoparathyroidism, addison's disease, thyroid disease , diabetes mellitus , vitiligo , other autoimmune disorders	++/+++	++/+++
Late onset	Thymoma , myasthenia gravis , polymyositis , hypogammaglobulinemia, bone marrow changes	+	+

+ =mild; ++= moderate; +++ = severe.

Multiple intrinsic and extrinsic factors contribute to the development of clinical infections. Serum values for various endocrinopathies formulate an important key to diagnose, categorize and to understand the severity of the CMC. (1) In both the siblings' estimation of random blood sugar, thyroid stimulating hormone and cortisol were done, which were within the normal range, by these investigations we could categorize the siblings as CMC without endocrinopathy.

Some patients with CMC have low iron levels, possibly related to decreased iron absorption. This finding can be of importance in the pathology of CMC,

since lack of tissue iron can result in defective epithelium formation. However it is stated that clinical improvement after the use of iron therapy is only proved to be temporary. (5, 6) This facet of CMC, reduction of iron stores resulting in overt or latent iron deficiency anemia was present in both the siblings.

Chronic Mucocutaneous candidiasis can be diagnosed based on clinical findings, KOH preparation & fungus culture. (1) In this case smear test performed from the scrapings of oral lesions for both the siblings showed candidal hypae, suggestive of candidiasis. Scraping obtained from cutaneous and scalp lesions of the patient's brother showed negative results for candidal hypae, suggestive of a non-candidal infection of bacterial origin such as Ecthyma.

Ecthyma is an ulcerative pyoderma of the skin caused by group A beta-hemolytic streptococci. Because ecthyma extends into the dermis, it is often referred to as a deeper form of impetigo. Ecthyma begins as a vesicle or pustule overlying an inflamed area of skin that deepens into a dermal ulceration with overlying crust. The crust of ecthyma lesions is gray-yellow and is thicker and harder than the crust of impetigo. A shallow, punched-out ulceration is apparent when adherent crust is removed. The deep dermal ulcer has a raised and indurated surrounding margin. Important factors that contribute to the development of streptococcal pyodermas or ecthyma are high temperature and humidity, crowded living conditions, poor hygiene. (7) Like CMC, the expression of pyogenic infection is also variable, and in our case more severe affliction of Ecthyma was seen in patient's brother. In this case, both the siblings were diagnosed having CMC (diffuse type) without endocrinopathy associated with Ecthyma.

Topical therapies are not usually effective in patients with CMC. Oral involvement in CMC can be aided by clotrimazole troches or oral nystatin solution. (1) Our patient was prescribed with candid mouth paint (clotrimazole 1%) to be applied 3 times daily (Fig- 4) .Oral administration of systemic antifungal drugs are effective and Pulse therapy (100mg/week of fluconazole) as maintainance therapy for up to 9 months, can improve the quality of life. However, most patients have a relapse within a few weeks or months after the antifungal treatment is stopped and the underlying immunologic defect often cannot be corrected. (3) Treatment with cimetidine and zinc sulphate may be an alternative, for patients with CMC who fail to respond for long term antifungal therapy. (1) Terbinafine has been used effectively in ketoconazole resistant chronic mucocutaneous candidiasis. (6)

Topical therapy with mupirocin ointment (Bactroban) for localized ecthyma was considered in both the siblings. More extensive ecthyma lesions may require oral antibiotics; the duration of treatment varies because ecthyma may require several weeks of therapy to completely resolve. Penicillin should be adequate to treat ecthyma. Oral antistaphylococcal agents (eg, dicloxacillin, cephalexin, erythromycin, clindamycin) have been used to cover possible secondary Staphylococcus aureus infections.

CONCLUSION

Clinical significance of CMC lies in the fact that it may present with varies clinical manifestations. A detailed immunologic study should be performed and the possibility of accompanying disorders, such as endocrinopathy or autoimmune diseases should be investigated. Once the diagnosis is made, long- term follow up is needed because of the high likelihood that many accompanying disorders may occur in the years after CMC is diagnosed. Parents should be alerted regarding the recurrent nature of disease and current paucity of effective long term therapies. Early diagnosis of CMC is of great importance as prompt treatment of CMC can prevent the spread of Candida and oral lesions. This case report emphasizes the importance of dentists for early diagnosis of mucosal lesions in children to achieve the best treatment plan.

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and rotation can be best done by reconstruction through osseous grafting. When surgical reconstruction is not possible, training flange or mandibular resection guidance prostheses followed by removable prosthesis is an option. Early post resection physical therapy is indicated to reposition the mandibular fragment towards a more normal position and to minimize the effect of scar formation. Delaying the physical therapy during the healing phase results in scar contracture which will lead to difficulty in repositioning of the mandible.

The training flange is fabricated depending upon the severity of mandibular deviation. The problem of training flange is further complicated in edentulous patients.

In the above case the training flange in the form of interlocking rims was fabricated for the edentulous jaws and held by circum mandibular wiring and per-alveolar wiring in maxillary arch, followed by interarch fixation with the help of stainless steel hooks at the time of the surgery. As no time was lost post surgical, the mandibular deviation was minimized. Early intervention by the prosthodontist at the treatment planning phase and the team approach helped to rehabilitate the patient with mandibular defect satisfactorily.

CONCLUSION

The success of maxillofacial prosthodontic treatment involves a team approach. The complete rehabilitation of the patient with intraoral defect is only possible when the prosthodontist is involved at the initial stage of the treatment planning.

In developing country where these patients are generally left untreated or partially treated the prosthodontist needs to create awareness amongst the other speciality & finding methods to rehabilitate these patients with minimum material & facilities.

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