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CASE REPORT

TUBEROUS SCLEROSIS- A CASE REPORT

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Abstract
Tuberous sclerosis was first described by von Recklinghausen, in 1862, in a newborn child with multiple cardiac and brain tumors. However, the term Tuberous Sclerosis was coined years later by Bourneville and Pringle who described the association of renal and cerebral lesions, but without cutaneous manifestations. This interesting condition has usually been classified among the diseases of the nervous system and has been given only casual attention by general clinicians and dentists. Since the term tuberous sclerosis refers primarily to the changes in the brain, the broader term tuberous sclerosis complex is therefore employed to denote the coexistence of homologous changes in other organs, notably the heart, kidneys and skin. This is a rare genetic disorder with low prevalence in Indian population. We present to you a case report of a patient who came to the department with a chief complaint of foul smell from the mouth and was later diagnosed as having tuberous sclerosis on the basis of her clinical features and further imaging studies.

KEY WORDS: Hamartomas, Angiofibromas, Koenen tumors, Subependymal nodule, Astrocytomas

INTRODUCTION

Tuberous Sclerosis (also known as Bournville-Pringle syndrome) is a rare disorder, usually linked to a triad of conditions comprising epilepsy, mental retardation, and angiofibromas, as well as to oral and skin manifestations, though all the 3 signs are rarely present. A partial form of the condition is usually observed. The disease develops as an abnormal growth of ectodermic and mesodermic cells producing benign tumors that extend to areas of the head, heart, brain, and kidneys.[1]

Tuberous sclerosis is an autosomal dominant multisystem disorder arising from mutations in either chromosome 16 or chromosome 9. About one third of all cases of TS are inherited from an affected parent. All other cases are due to sporadic new mutations of the tuberin protein gene occurring in the early stages of life.[3] Mutations are so frequent that almost two thirds of all cases are sporadic.[1]

People of all races and sex may be affected. The condition may become apparent any time from infancy to adulthood but usually occurs between 2-6 years of age.

The prevalence is estimated to be between 1/5000 and 1/15000 individuals. Tuberous sclerosis is still a clinical diagnosis.

CLINICAL PRESENTATION OF THE DISEASE:

Clinical manifestations have been divided into major and minor criteria.[2,3] The presence of two major characteristics or of one major criterion and two minor criteria confirms the diagnosis.[4]

Major criteria[4]

- Facial angiofibromas
- Multiple ungual fibromas (Koenen tumors)
- Cortical tubercle
- Subependymal nodule
- Multiple astrocytomas
- Renal angiolipomas
- Hypomelanocytic maculae (3 or more)
- Cardiorhabdomyomas

Minor criteria[4]

- Cerebral tubercles
- Non-calcified subependymal nodules
- Hamartomatous rectal polyps
- Gingival fibromas
- Non-renal hamartomas
- Multiple renal cysts
- Retinal hamartomas
- Enamel hypoplasia

The most common oral manifestations of Tuberous Sclerosis Complex are fibromas, gingival hyperplasia and enamel hypoplasia. Other less frequent findings in the oral cavity are a high arched palate, bifid uvula, harelip and/or cleft palate, delayed dental eruption and the presence of diastemas.[4]

Tuberous Sclerosis is usually diagnosed in the first year of life, due to the presence of epileptic patterns or to deterioration in the locomotor system that leads to the search for ash leaf macules on the skin.[5] However sometimes due to absence of common features the diagnosis becomes difficult.

CASE REPORT:

A 45-year-old woman reported to the department of oral medicine and radiology of our institution with a chief complaint of foul smell from the mouth. On general examination, she was having small multiple brown fleshy overgrowths of variable diameter present over the entire face extending upto the neck. She was anemic in appearance and the skin was having a yellowish tint. **(Figure 1)**

There were smooth, firm, flesh-coloured lumps emerging from the nail folds of hand **(Figure 2)** and feet **(Figure 3)** (Periungual fibromas). Also there was flesh coloured orange-peel

connective tissue naevi of varying sizes, present on the anterior portion of clavicular region on left side (Shagreen patch). **(Figure 4)**

A solitary fleshy overgrowth was present on the right toe which was pinkish white in color, measuring approximately 5 X 3 cm in diameter with rough and irregular surface. **(Figure 3)**

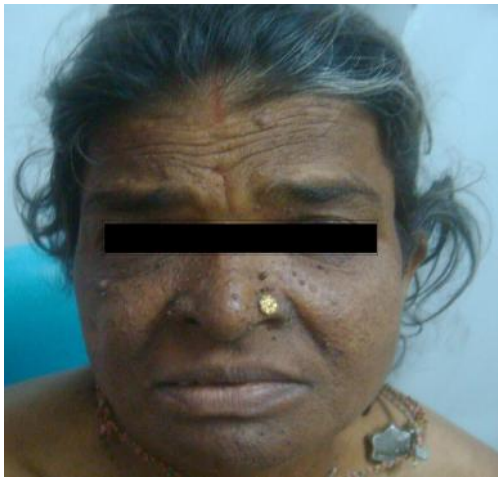

Figure 1: Clinical picture showing small multiple brown fleshy overgrowths of variable diameter present over the entire face extending up to the neck (Facial Angiofibromas)

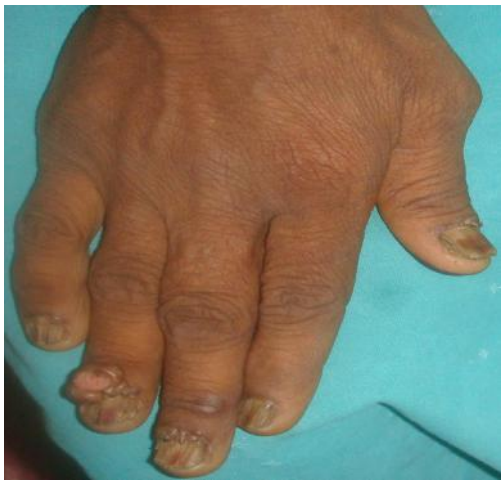

Figure 2 Flesh coloured -peel tissue naevi of variable diameter present in relation to left side of anterior portion of clavicular region (shagreen patch)

On intraoral examination, patient was having a poor oral hygiene. There was presence of multiple pin headed nodules on both sides of the buccal mucosa. They were grayish black in color and round in shape. **(Figure 5)** On dorsal surface of tongue there was presence of grayish pigmentation. **(Figure 6)**

A panoramic radiograph was taken to evaluate any bony changes. The radiograph revealed presence of multiple radiolucencies in the mandible along the mandibular canal. **(Figure 7)**

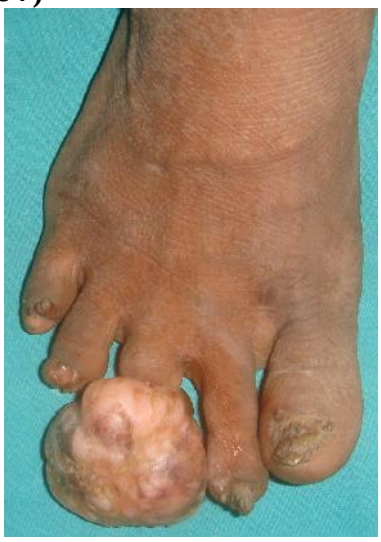

Figure 3 Smooth firm flesh -co loured lumps (Periungual fibromas)emerging from the nail folds of feet.

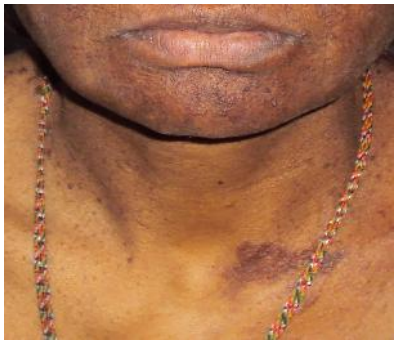

Figure 4 Multiple pin headed nodules present bilaterally on the buccal mucosa.

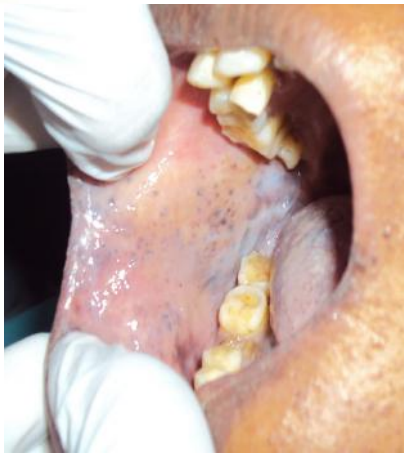

Figure 5 Grayish pigmentation on dorsal surface of tongue

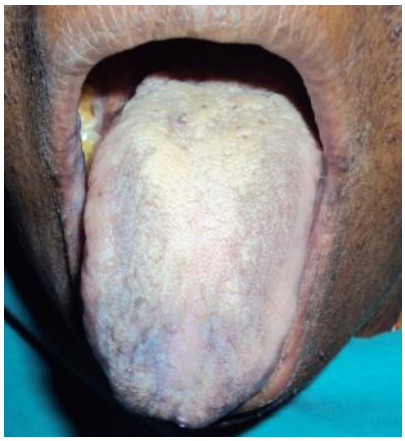

Figure 6 Panoramic radiograph showing presences of multiple radioluncencies in the mndible along the mandibular canal,

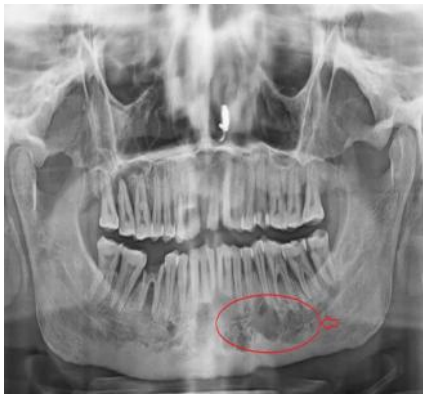

Figure 7 Panoramic radiograph showing presences of multiple radioluncencies in the mndible along the mandibular canal.

On the basis of above findings a provisional diagnosis of Tuberous sclerosis was given. The patient was referred to a physician for further evaluation and to rule out the presence of cysts and tumors in other organs.

The physician conducted an ultrasonographic evaluation to rule out presence of any cysts or tumors elsewhere in the body. In order to evaluate any neurological manifestations, CT and MRI scan was advised. In order to check the malignant potential of the growth on the right toe an excisional biopsy was performed.

No significant finding was obtained by ultrasonographic examination. The CT scan of brain revealed presence of subependymal nodules which were present near the walls of the cerebral ventricles. MRI scans revealed presence of multiple cortical tubercles and giant cell histiocytomas. **(Figure 8 & 9)**

The excisional biopsy done of the right toe confirmed the growth to be fibrosarcoma.

On the basis of clinical and radiographic findings the diagnosis of tuberous sclerosis was confirmed.

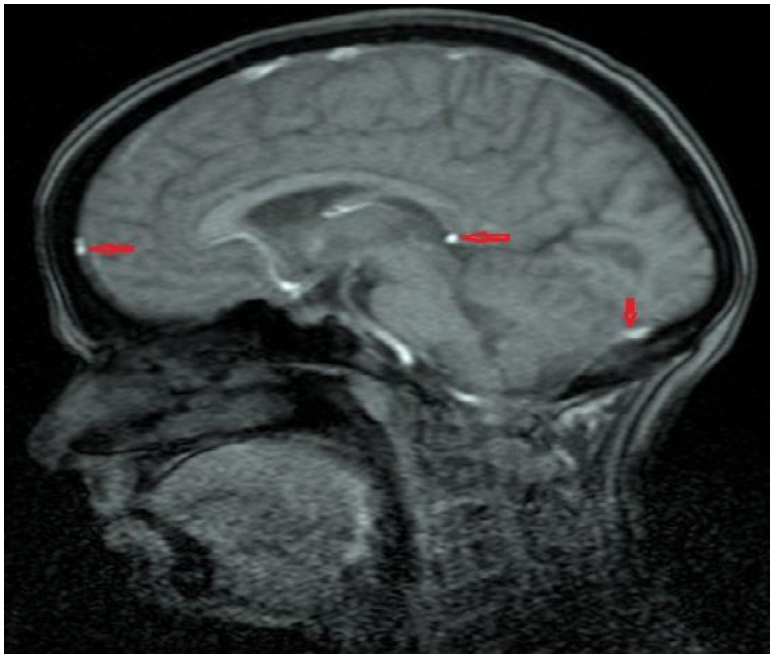

Figure 8 MRI scan revealed presences of multiple cortical tubercles and gaint cells histiocytomas

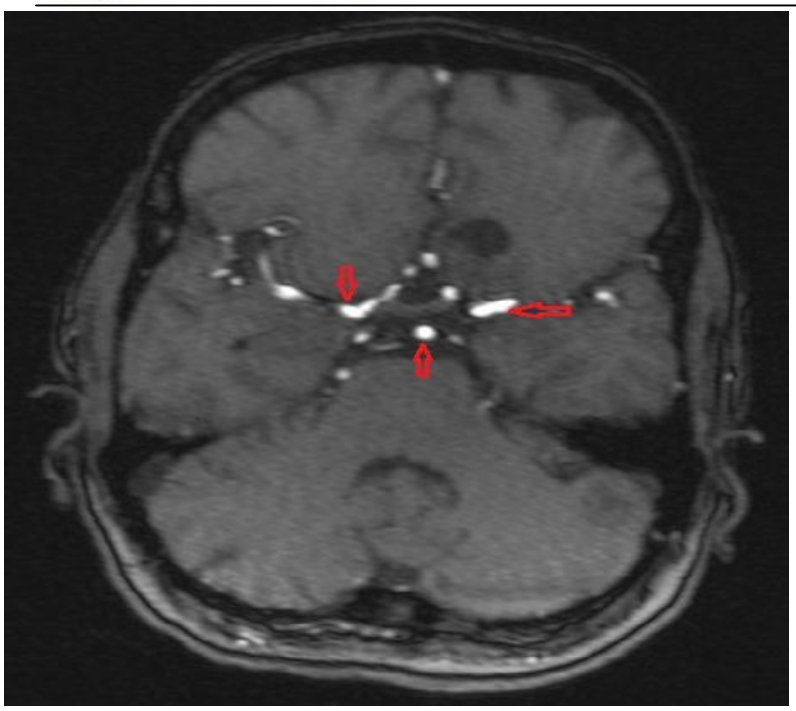

Figure 9 MRI scan revealed presences of multiple cortical tubercles and gaint cells histiocytomas

DISCUSSION:

Tuberous sclerosis complex (TSC) is often associated with mental retardation and epilepsy. Koenen tumors and angiofibromas in turn are observed in 15-20% and 70% of all cases, respectively. Renal angiomyolipomas and cysts affect one-half of patients with TSC and are the cause of chronic renal failure that may prove fatal. Cardiac rhabdomyomas are normally observed before age 25 years in 30-50% of all cases,and are also a cause of early death.[5,6] Our patient presented Angiofibromas, Periungual fibromas, Shagreen patch but no mental retardation or epilepsy.

The most common oral manifestations of TSC are fibrous hyperplasias and enamel hypoplasia.[6] The former are more often found in the gingival zones of the anterior sector, though involvement of the lips, tongue and palate is not unusual. According to some authors, these hyperplasias may be secondary to the medication usually taken by these patients.[7] The incidence of oral fibromas in TSC varies according to the different literature sources between 50-69%, with an average diameter of 5 mm.[8, 9, 10] The aggressivity of the lesions depends on the severity of the local factors. Our patient presented multiple grayish black pin headed nodules on buccal mucosa bilaterally but no gingival fibromas were present.

It should be noted that these patients present mutations of the TSC1 and TSC2 genes. These genes intervene in cell cycle regulation and are important for avoiding neoplastic processes.[11] No studies have been found associating TSC with an increased risk of oral cancer, though according to Kawaguchi et al[12] TSC2 over-expression could exert an antitumor effect in oral cancer, since

it is an oncosuppressor gene. Fleury et al[13] published a case of undifferentiated pleomorphic sarcoma located in the mandible of a patient with TSC.

Our patient's CT scan of brain revealed presence of subependymal nodules which were present near the walls of the cerebral ventricles. MRI scans revealed presence of multiple cortical tubercles and giant cell histiocytomas. These findings are characteristic of tuberous sclerosis.

CONCLUSION:

Patients with TSC must adopt measures for careful oral and dental hygiene, with regular visits to the dentist, in order to eliminate potential irritative factors and ensure the early diagnosis of any possible lesions. The oral healthcare professional in turn must always request a detailed medical report on the condition of the patient. Effective policies need to be drafted to improve the oral health care standards of these patients.

REFERENCES

1. Antonio Cutando, Jose Antonio and Julian Lopez. Oral health management implications in patients with tuberous sclerosis. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2000; 89: 430-5.
2. Felip Vallmanya, Jose Placer. Tuberous Sclerosis complex. Forty-years of follow-up of a patient affected. Arch. Esp. Urol. 2006; 59(1): 105-107.
3. Tuberous sclerosis. DermNet NZ. Page 1 of 3
4. Karmen Harutunian **1**, Rui Figueiredo **2**, Cosme Gay-Escoda. Tuberous sclerosis complex with oral manifestations: A case report and literature review. Med Oral Patol Oral Cir Bucal. 2011; 16(4): 478-81.
5. Schwartz RA, Fernández G, Kotulska K, Jóźwiak S. Tuberous sclerosis complex: advances in diagnosis,genetics,and management. J Am Acad Dermatol. 2007; 57:189-202.
6. Gupta S, Bhowate R, Degwekar SS. Clinical and radiological findings related to tuberous sclerosis complex: a case report. J Contemp Dent Pract. 2008; 9:85-91.
7. López E, Escovich L, Vigna A. Tuberous sclerosis: presentation of a clinical case with oral manifestations. Med Oral. 2003; 8:122-8.
8. Sparling JD,Hong CH,Brahim JS,Moss J,Darling TN. Oral findings in 58 adults with tuberous sclerosis complex. J Am Acad Dermatol. 2007; 56:786-90.
9. Alvarez Alvarez C, Fernández Sanromán J, Fernández Castilla M, Antón Badiola I. Sporadic oral angiomyolipoma. Case report. Med Oral Patol Oral Cir Bucal. 2007; 12:391-3.
10. Da Silva AA,Carlos R,Contreras E,De Almeida OP,Lopes MA,Vargas PA. Angiomyolipoma of the upper lip: case report and review of the literature. Med Oral Patol Oral Cir Bucal. 2007; 12:101-4.
11. Chakraborty S, Mohiyuddin SM, Gopinath KS, Kumar A. Involvement of TSC genes and differential expression of other members of the mTOR signaling pathway in oral squamous cell carcinoma. BMC Cancer. 2008; 8:163.
12. Kawaguchi S,Harada K,Supriatno,Yoshida H,Sato M. Overexpression of tuberous sclerosis complex2 exerts antitumor effect on oral cancer cell lines. Oral Oncol. 2003; 39:836-41.
13. Fleury RN, Damante JH, Soares CT, Sant'Ana E, Mello EJ Jr, Moreira CR. Malignant fibrous histiocytoma (undifferentiated high-grade pleomorphic sarcoma) occurring in tuberous sclerosis: a case report. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2007; 103:54-9.