The Fifth Phakomatosis – A Case Report

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ABSTRACT
The Fifth Phakomatosis shows the presence of multiple cutaneous, skeletal, ophthalmic and neurologic abnormalities. It is an autosomal dominant trait caused due to mutations in the Patched Tumour Suppressor Gene (PTCH), found on the long arm of chromosome 9. The case report highlights the importance of prompt diagnosis which will lead to proper treatment and counselling of the patient. This is a case report of a 26 year old male patient who presented with the characteristic clinical, radiologic and histologic features of the Fifth Phakomatosis.

Keywords: Phakomatosis, Gorlin-Goltz syndrome, Odontogenic keratocyst.

INTRODUCTION
Phakomatoses are a group of hereditary disseminated hamartomas characterized by systemic hamartomas of the brain, skin, bones and eyes. The term “phakoma” was first used by Van der Hoeve in 1932 to indicate a mother spot, or birthmark, a characteristic finding seen in many conditions like retinal and cerebellar hemangiomatosis (von Hippel–Lindau syndrome), neurofibromatosis (von Recklinghausen syndrome), and tuberous sclerosis complex (Bourneville syndrome) which were all classified as phakomatoses.

In 1960, Gorlin and Goltz first described the spectrum of features which are associated with the fifth phakomatosis. It included the presence of multiple odontogenic cysts, cutaneous, skeletal, ophthalmic and neurologic abnormalities. In cases of Gorlin-Goltz syndrome, it is of great importance to make an early diagnosis since the severity of complications, such as malignant skin and brain tumors can be reduced and maxillofacial deformities related to the jaw cysts can be avoided.

CASE REPORT
A 26 year-old male patient reported to the Department of Oral Medicine and Radiology, Dr. DY Patil Dental College and Hospital, Pune. He presented with a swelling in the front region of the lower jaw since 7 years. The swelling had gradually increased to the current size of 6x3 cm and had been consistent since 1 year. There was no pain/pus discharge associated with the swelling. He had tobacco and gutkha chewing habit since 5-6 years, 2-3 times a day and an unremarkable medical and dental history.

On Extra-oral examination, facial asymmetry was noted. The swelling was diffuse, firm, non tender and extended from the parasymphyseal region on one side to the other side. Pronounced depression was seen on...
the right cheek, overlying the right body of mandible. Overlying skin was normal in appearance and colour. TMJ movements were normal. Mouth opening was reduced to approximately 20 mm. Multiple palmar pits measuring approximately 1-2 mm in diameter were seen.

On Intraoral examination, buccal cortical plate expansion was seen in the mandible extending from 33 to 36 and 43 to 46 region. No carious lesion was noted.

Generalized blanching of buccal mucosa was seen giving a marble like appearance. Fibrous bands were palpable bilaterally on buccal mucosa, circumoral region and in the retromolar area.

The Orthopantomogram (OPG) revealed well defined, **multilocular radiolucency** in close association with 48 having corticated borders, extending till the **angle and ramus of the mandible** posteriorly and inferiorly till the lower border of mandible. Inferior nerve canal was not traceable. A well defined multilocular radiolucency with corticated borders was seen extending from midline to the middle one-third of the right side of the body of mandible and till the lower border of mandible, inferiorly. A diffuse radiolucency with ill defined borders was seen on the left body of the mandible in close association with impacted 35, extending till 37. A mixed radiopacity-radiolucency was seen in the left maxillary sinus associated with impacted 28.

Fine Needle Aspiration Cytology (FNAC) from the right mandibular posterior region yielded yellowish white, thin watery fluid. Cytological examination revealed RBC’s, PMN’s, cholesterol crystals. Cytological impression was of an infected odontogenic lesion.

Based on the clinical, radiographic findings and FNAC report, a provisional diagnosis of multiple Odontogenic Keratocysts was given. This raised a suspicion of Gorlin-Goltz syndrome and thus the patient was subjected for further investigations.

Chest x-ray revealed bifid posterior aspect of right 3rd rib and hypertrophied pedicle and transverse process of D3 vertebral body on right side. Spine x-ray revealed fusion of the T2 and T3 vertebral body. Hand-wrist x-ray revealed flame shaped radiolucencies on the proximal aspects of radius and ulna.

CT Scan brain revealed multiple falx cerebri calcifications on the axial section.

A well defined extra-axial, CSF density lesion was noted in the posterior cranial fossa, causing scalloping of the occipital bone, likely suggestive of Arachnoid cyst.

Based on the above findings, a clinical diagnosis of Gorlin-Goltz syndrome was given.

**Treatment**

The patient was referred to the department of Oral and Maxillofacial surgery. Nasolabial flaps were raised and transposed intra orally for management of oral submucous fibrosis. Surgical marsupialization and decompression of the mandibular cysts were done, followed by placement of surgical drains. The maxillary cyst was enucleated.

**Histopathology**

Microscopic examination revealed parakeratinized lining epithelium that was 6-8 cell layered and corrugated appearance. Rete ridges were absent. Tombstone appearance of basal cells was evident. Daughter cells were absent. Overall features were suggestive of odontogenic keratocyst.

**DISCUSSION**

The fifth phakomatosis is an autosomal dominant inherited syndrome manifested by multiple defects involving the skin, nervous system, eyes, endocrine system, and bones. It is also known as basal cell nevus syndrome, multiple basal cell carcinoma syndrome, Gorlin syndrome, or hereditary cutaneomandibular polynoecosis, multiple nevoid basal cell epithelioma-jaw cysts or bifid rib syndrome.4

It was first reported by Jarisch and White in 1894, and later in detail by Gorlin and Goltz.

Clinically this condition is characterized by different signs and symptoms. Diagnosis is based on the most frequent and specific features of the syndrome as given by Evans et al. in 1993.6 Diagnosis of Gorlin-Goltz syndrome can be established when two major or one major and two minor criteria are present.5

The major criteria are:

1. Multiple basal cell carcinoma or one occurring under the age of 20 years.
2. Histologically proven OKCs of the jaws.
3. Palmar or plantar pits (three or more).
4. Bilamellar calcification of the falx cerebri.
5. Bifid, fused or markedly splayed ribs.
6. First-degree relative with Nevoid Basal Cell Carcinoma syndrome.

The minor criteria are:
1. Macrocephaly (adjusted for height).
2. Congenital malformation: cleft lip or palate, frontal bossing, coarse face, moderate or severe hypertelorism.
3. Other skeletal abnormalities: sprenkel deformity, marked pectus deformity, marked syndactyly of the digits.
4. Radiological abnormalities: bridging of the sella turcica, vertebral anomalies such as hemivertebrae, fusion or elongation of the vertebral bodies, modeling defects of the hands and feet or flame shaped hands or feet.
5. Ovarian fibroma.

In the present case, the diagnosis of the syndrome was established by the presence of:-

Four Major Criteria:
1. Multiple odontogenic Keratocysts
2. Bifid Rib
3. Falx Cerebri Calcifications
4. Palmar Pits

Three Minor Criteria:
1. Fusion of Verterbral bodies
2. Flame shaped radiolucencies of hand
3. Arachnoid Cyst

CONCLUSION
Early diagnosis, prompt referral and treatment is essential before the case progresses to aggressive basal cell carcinomas and malignant neoplasias.³ This case highlights the importance of the awareness of this rare syndrome.³ It is useful to keep in mind the existence of this syndrome and to recognize the presence of some major criteria that are easily recognizable on thorough clinical examination, CT scan and appropriate radiographs, to thus establish the diagnosis & increase the chances for better overall survival rates. It is important to follow up the patients with diagnosed syndromes for the rest of their lives, as they can produce new odontogenic cysts and new basal cell carcinomas almost continuously. Finally, the whole family of the patients with the fifth phakomatosis, should be examined and genetic counseling should be offered, as it is inherited as an autosomal dominant disorder.
Figure 1: Extra-oral view

Figure 2: Aspirate on FNAC

Figure 3: OPG
Figure 4(a): Chest x-ray revealed bifid 3rd rib (b) Hand-wrist x-ray revealed flame shaped radiolucencies on the proximal aspects of radius and ulna (c) Spine x-ray revealed fusion of the T2 and T3 vertebral body (d) CT Scan brain revealed multiple falx cerebri calcifications on the axial section.

REFERENCES: