CASE REPORT

Postpubertal Cherubism with Noonan Syndrome

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ABSTRACT

Cherubism is a self limiting, autosomal dominant, fibro-osseous lesion of the maxillo facial region affecting the young adults. The etiology is considered to be a mutation of the SH3BP2 gene from chromosome 4p16.3. Sporadic non-familial cases have also been reported. The affected subjects usually present with simultaneous, bilateral swellings of the maxillae and/or mandible, premature loss of primary teeth, malocclusion due to disturbed eruption pattern of permanent teeth and a characteristic chubby faced angelic eyed appearance. This usually presents as an isolated finding, however, it can exist in association with syndromes like Noonan's syndrome, Jaffe syndrome, Gardener syndrome and Ollier's disease. Treatment is focused on the exact genetic diagnosis and management of symptomatic conditions utilizing cosmetic surgery and orthodontics. Genetic counselling of the affected families may help to decrease its incidence. This report presents a rare case of cherubism with associated features of Noonan syndrome.

Key Words: *Cherubism. Noonan syndrome. Benign fibro-osseous lesions.*

INTRODUCTION

Cherubism is an autosomal dominant, benign fibro-osseous lesion of the jaws involving more than one quadrant that usually stabilizes after the growth period, leaving some facial deformity and malocclusion.[1] This name is derived from the temporary chubby-cheeked resemblance to putti, often confused with cherubs, in Renaissance paintings of the Romanesque art.[2]

The etiology had been traced to a mutation of the SH3BP2 gene from chromosome 4p16.3 but had also been associated with other syndromes including Noonan syndrome, Ramon syndrome, and Fragile X syndrome.[3] This mutation increases production of proteins involved in chemical signaling to macrophages, B-cells and osteoclasts with resultant bone resorption.[3]

Cherubism with prevalence of 1 in 2500 children usually appears around age of 7 years and continues through puberty.[4] The disease also affects the orbital area creating an upturned eye appearance. The fibers and cysts will be found among the trabecula of the coronoid process, the ramus of mandible, the body of mandible and the maxilla regions. The affects of cherubism may also interfere with normal jaw motion, speech and vision.[4] Cherubism associated with Noonan syndrome presents additional features of dwarfism (short stature), webbed neck configuration, chronic otitis media, hyperemia and deeply grooved philtrum.[5]

Routine dental radiographs can be extremely helpful in the initial diagnosis of the extent of the bone damage with definitive diagnosis by sequencing of the SH3BP2 gene to verify mutation in axon 9.[4]

The present report describes this rare occurrence in a postpuberal girl.

CASE REPORT

A 16 years old girl was referred complaining of bilateral swellings of the mandible and maxillae. The condition had started 6 years ago nearly at the age of 10 years. The lesion had a history of expansion and regression in different phases with associated localized hyperemia. There was no complaining of pain, tenderness or crepitation. However, there was difficulty in mouth opening and chewing. The patient also complained of short stature and reduced growth. The neck was small with averted shoulders. Patient also complained of ear problems with persistent discharge of pus from right ear. She had also undergone multiple ENT surgical procedures for this problem but not completely satisfied.

On examination, lesion on both sides was hard and smooth in texture with no irregularities (Figure 1). There were no soft tissue lumps or ulceration. There was no tenderness and no associated lymphadenopathy. Peripheral integrity of the mandibular borders was intact. On intra-oral examination, there was no soft tissue or dental pathology except missing lower posterior teeth.

On radiographic examination, there were marked radiolucencies in the posterior part of mandible involving angle of the mouth, posterior borders of ramus and even neck of the condyle as marked by arrows (Figure 2). This represented characteristic ground glass appearance of the jaw bones with irregular radiolucencies and radiopacities (Figure 2). The complete blood examination revealed raised blood calcium levels characteristic of marked osteoclastic osteoblastic activity.

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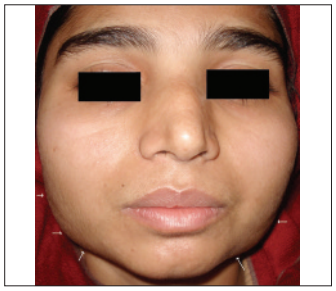

Figure 1: Frontal view with marked bilateral posterior mandibular overgrowth.

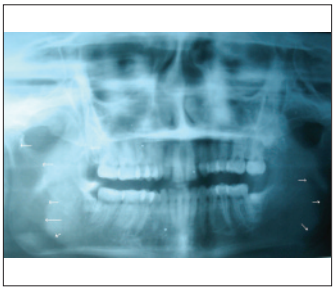

Figure 2: Radiographic view showing marked radiolucencies in the posterior mandibular areas.

The treatment offered was cosmetic surgical procedure involving the bone shaving from the affected areas but the patient refused to opt for this modality. However, she consented to go for genetic DNA sequencing analysis. The patient and the family were explained about the pattern of inheritance of this condition and were referred to a genetic counselling centre.

DISCUSSION

Cherubism pose physical, psychological and personality deficits in the affected subjects and families. Severe cases may become even life threatening disorders. The recommended treatment modalities mainly focus on the multidisciplinary approach and referral to the concerned departments, where it should be a symptomatic relieve planning and rehabilitation. These are mainly developmental genetic disturbances, so treatment plans should incorporate the detailed family history.

Cherubism mainly affects the oral and maxillofacial region, so dental professional may be the first one to interact with this condition. A detailed history, investigations and proper diagnosis are of utmost importance. However, treatment planning should always be made in consultation with Oral Maxillofacial Surgeon, Oral Pathologist, Paedodontist, Orthodontist and Genetic Specialist. Because this disease is associated with the time of tooth eruption, the disease may be helpful in discovering what factors of tooth eruption contribute to cherubism.[6]

Mutations in the SH3BP2 gene lead to the production of an overly active version of this protein. The effects of SH3BP2 mutations are still under study, but researchers believe that the abnormal protein disrupts critical signaling pathways in cells associated with the maintenance of bone tissue and in some immune system cells. The overactive protein likely causes inflammation in the jaw bones and triggers the production of osteoclasts, which are cells that break down bone tissue during bone remodelling.[3]

This disease is also one of the few self-limiting conditions that unexpectedly stops and withdraws. Normal bone remodelling activity may resume after puberty. Since this disease is genetically linked, genetic counselling may be the only way to decrease occurrence of cherubism. The optimal time to be tested for mutations is prior to having children. The disease results from a genetic mutation and this gene has been found to spontaneously mutate. Therefore, there may be no prevention techniques available.[7] Generally, moderate cases are watched until they subside or progress into the more severe range. Severe cases may require surgery to eliminate bulk cysts and fibrous growth of the maxilla and mandible. Special consideration should be taken when operating on the face to avoid the marginal mandibular branch of the facial nerve as well as the zygomatic branch of the facial nerve. Unintentional damage to these nerves can decrease neuromuscular control and motor activity in the face and mandible region. Orthodontic treatment is generally required to avoid permanent dental problems arising from malocclusion, misplaced, and unerupted permanent teeth. Orthodontic treatment may be used to errupt permanent teeth that have been unable to descend due to lesions and cysts being in their path of eruption. In patients with orbital issues of diplopia, globe displacement, and visual loss will require ophthalmologic treatment.[7]

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