Original Research Paper Dental Science

A CASE REPORT OF FIBROUS DYSPLASIA WITH ACROMEGALY: MC CUNE ALBRIGHT SYNDROME

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ABSTRACT McCune-Albright syndrome(MAS) is a triad of polyostotic or monostotic fibrous dysplasia, café-au-lait spots and hyperfunctioning endocrinopathies. However, a few cases have been reported by Albright wherein only 2 of the above features were noted. The polyostotic variant occurs more often in subjects with MAS as compared to monostotic/craniofacial forms. The most common endocrine abnormality noted is precocious puberty (in females). The other endrocrinopathies include hyperthyroidism, hyperparathyroidism, hypercortisolism, excessive secretion of growth hormone and prolactin. The association of acromegaly with MAS is rare and affects around 10-20% of subjects. In the present case report, a rare association of craniofacial fibrous dysplasia with pituitary macroadenoma resulting in acromegaly in a 23-year-old male is discussed. The subject did not present with café-au-lait spots. He had undergone surgery and radiotherapy for the pituitary adenoma 5 years prior to reporting to the institution. Patient is currently on somatostatin analogues. Facial recontouring is planned after complete regression of the tumour.

KEYWORDS : Mc-Cune Albright syndrome, Fibrous dysplasia, Acromegaly

Introduction:

McCune-Albright syndrome(MAS) is a triad of polyostotic or monostotic fibrous dysplasia, café-au-lait spots and hyperfunctioning endocrinopathies[1]. However, a few cases have been reported by Albright wherein only 2 of the above features were noted2. The polyostotic variant occurs more often in subjects with MAS as compared to monostotic/craniofacial forms. The most common endocrine abnormality noted is precocious puberty (in females). The other endrocrinopathies include hyperthyroidism, hyperparathyroidism, hypercortisolism, excessive secretion of growth hormone and prolactin[1].

The excessive secretion of growth hormone may be due to the presence of pituitary micro/macro adenoma which may lead to acromegaly. The association of acromegaly with MAS is rare and affects around 10-20% of subjects[3].

In the present case report, a rare association of craniofacial fibrous dysplasia with pituitary macroadenoma which resulted in acromegaly in a 23-year-old male is being discussed.

Case report:

A 23 year old male patient reported with a complaint of swelling in the gums in the upper left back teeth region since 3 months. The swelling was of gradual onset and there was no alteration in the size of the swelling since it was first noticed.

The swelling was asymptomatic except for mild discomfort on chewing.

Medical history revealed that the patient was diagnosed with a growth hormone(GH) secreting pituitary macroadenoma when he was 17 years old for which he underwent surgical removal. A follow up GH level a year later was 8.4ng/ml and MRI revealed peripherally enhancing mass expanding the sella with right parasellar extension into right cavernous sinus suggestive of residual tumor for which he underwent gamma knife radiosurgery.

On general examination, the patient was 6 feet 5 inches tall and his feet and hands were large. The vital signs were in the normal range. There were no signs of pallor, cyanosis, icterus or clubbing. There was no abnormality noted in relation to skin and hair.

On examination of eyes, bilateral ptosis and prominent supraorbital ridges were noted and pupillary reflexes were normal. Examination of ears, nose and cranial nerves did not reveal any abnormality.

The mandible was prognathic. Lips were thick and incompetent. Asymmetry of face noted due to a swelling in the left maxillary region approximately measuring 4 X 3 cm. Superio inferiorly, the swelling extended 4cms inferior to the intraorbital margin. Anterio posteriorly, the swelling extended 3 cms posterior to the ala of the nose. The skin overlying the swelling appeared normal. On palpation, there was no localized rise in temperature and it was non tender and bony hard . On digital palpation, there was no bleeding or discharge.

On intra-oral examination, macroglossia was noted(fig 1).

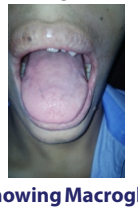

Fig 1: Intra oral picture showing Macroglossia

Cortical expansion was noted in relation to maxillary left posterior region with respect to 24, 25, 26 and 27 involving both buccal and palatal aspects(fig 2). The overlying mucosa appeared normal. On palpation, the swelling was non tender and bony hard. No bleeding or discharge was noted on digital palpation.

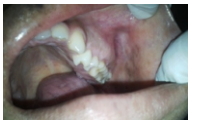

Fig 2: Bicortical expansion in the left maxillary posterior region

Examination of 24, 25, 26, 27, 28 revealed no abnormality. The teeth

were vital on electric pulp testing. Class III molar relation was noted on both sides with left posterior cross bite(fig 3) and anterior open bite(fig 4). Maxillary and mandibular anterior spacing and midline shift was noted.

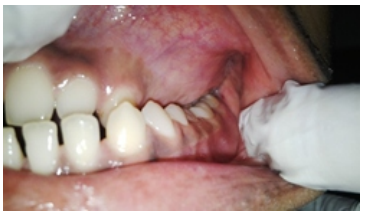

Fig 3: Posterior crossbite

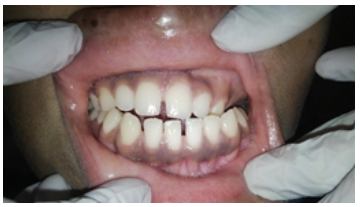

Fig 4: Anterior openbite

A provisional diagnosis of fibrous dysplasia in relation to the maxillary left posterior region with acromegaly was given.

The following differential diagnoses were considered, Juvenile ossifying fibroma was considered as it is generally asymptomatic and occurs in a younger age group and has equal predilection in both maxilla and mandible. Further the expansion is bicortical with intact cortical plates. However, the expansion is bulbous. CGCG was considered as it usually occurs in young adults as a painless, slow growing swelling with bicortical expansion.

The radiographic Investigations included IOPAR, panoramic radiograph, Lateral cephalograph and paranasal sinus view.

IOPAR of 24,25,26,27 showed increased density of the bone in the alveolar bone region with obliteration of the marrow spaces. Loss of lamina dura was noted wrt 24,25,26,27 with narrowing of the periodontal ligament space wrt 25,26.

OPG showed increased radiopacity(ground glass appearance) in the left maxillary posterior region(fig 5). Anterio posteriorly, it extended from the distal aspect of 23 up to 28, Superio inferiorly it extended from the alveolar crest in relation to 23, 24, 25, 26, 27, 28 obliterating the maxillary antrum. The periphery was ill defined. Displacement of 25 noted.

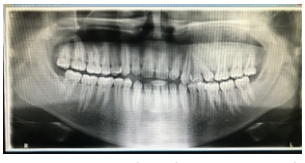

Fig 5: OPG showing increased radiopacity in the left maxillary posterior region irt 23 to 28 and displaced 25.

PNS radiograph showed increased radiopacity of maxillary bone on the left side , obliteration of the left maxillary sinus with elevation of the floor of the orbit(fig 6). Increased radiopacity and enlargement of zygomatic bone was also evident.

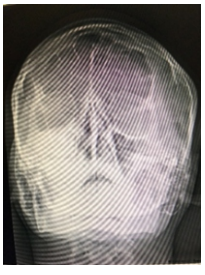

Fig 6: PNS view showing obliteration of the maxillary sinus with elevation of floor of the orbit.

The following radiographic differential diagnoses were considered- Craniofacial fibrous dysplasia ranked high in the differential diagnosis as ground glass appearance with ill-defined periphery is its most characteristic feature. Expansion into the maxillary sinus, displacement of teeth without root resorption are common findings.

Paget's disease may also present as a diffuse radiopacity, however, it occurs in an older age group and is bilateral in involvement.

Hyperparathyroidism may present in a similar fashion but it is generally polyostotic, bilateral and does not cause bone expansion. Based on the history, clinical and radiographic examinations, a final diagnosis of Mc Cune Albright syndrome was made.

Discussion:

MAS is a triad of fibrous dysplasia, café au lait spots and hyper functioning endocrinopathies. The signaling pathway of G protein, cAMP and adenylate cyclase is altered in MAS. G protein is comprised of alpha, beta and gamma subunits, and in MAS, the alpha subunit, encoded by the GNAS gene is mutated[4]. The GNAS mutation at codon 227 results in the constitutive activation of adenylate cyclase and high levels of intracellular cAMP resulting in endocrinopathies, such as hyperthyroidism, growth hormone excess, renal phosphate wasting and Cushing syndrome.

The original description of McCune Albright syndrome includes fibrous dysplasia, café-au-lait macules and precocious puberty2,5. Although , MAS includes the triad of these features, any of two of the above findings are sufficient to make the diagnosis of Mc Cune Albright syndrome1. In the present case report, only 2 of the above pathognomonic findings namely, craniofacial fibrous dysplasia and acromegaly were noted. Similar findings were noted in an Indian case series of 3 cases where in none of the 3 patients had café-au-lait pigmentation, one patient presented with craniofacial form (skull and maxilla) and two patients presented with monostotic form1. However, this is in contrast to most cases reported in literature, wherein majority of the patients had café au lait macules and polyostotic form of fibrous dysplasia. In the present case, no other endocrine abnormality apart from GH secreting pituitary macroadenoma was found. This is in contrast to cases reported in the literature where in the multiple endocrine abnormalities have been reported.

Acromegaly in Mc Cune Albright syndrome differs from classical acromegaly in several aspects[6]. Acromegaly patients with MAS are usually younger (around 20 years) at the time of diagnosis whereas in classical acromegaly, the patients are around 30-40 years at the time of diagnosis. MAS with acromegaly is usually diagnosed based on accelerated growth rather than facial dysmorphism in classic acromegaly. Similar findings were noted in the present case, the patient was diagnosed at the age of [17]. The obvious clinical signs were increased height and increase in size of hands and feet. 80-90% of classic acromegaly patients present with pituitary tumor, where as only few patients of MAS with acromegaly present with pituitary tumor. Visual disturbances are common in subjects with MAS and acromegaly. In contrast to the above mentioned findings, in the present case, acromegaly was result of pituitary macroadenoma, and he did not have any visual disturbances which is in similarity with the above mentioned Indian case series. Classical Acromegaly is known to be associated with hyperphosphatemia, however hypophosphotemia has been found in some MAS patients with acromegaly as well. This has been attributed to increased levels of serum FGF23 (fibroblast growth factor 23). Hence the levels of serum calcium (Ca), phosphate, vitamin D, and FGF23 levels should be monitored in MAS with acromegaly.

Management mainly aims at removal of the tumor and esthetic recontouring. This can be attained by surgery, radiotherapy and

medical management. Surgical removal of the tumor can be done by trans-sphenoidal, trans-ethmoidal and trans-frontal routes, of which trans-sphenoidal route is the preferred route. In MAS associated with craniofacial forms of fibrous dysplasia, surgery is difficult because of the increased thickness of the cranial bones.

Also, there is risk of hemorrhage because of the high vascularity of the fibrous dysplasia lesions. Radiotherapy has been used for treating the pituitary tumors, alone or in combination with surgery. However, development of sarcomas in irradiated fibrous dysplasia lesions have been reported. Hence, it is preferable to avoid radiation therapy in patients with craniofacial form of fibrous dysplasia.

Medical management is the preferred modality of treatment[3]. Dopamine agonists or somatostatin analogues can be used alone or in combination. Recently, with the advent of GH receptor antagonist, pegvisomant, the treatment of MAS associated acromegaly has greatly improved. The present patient is currently under somatostatin analogues, (on monthly basis). Correction of malocclusion and recontouring will be done at a later date when there are no residues of tumor left.

Conclusion:

To conclude, the role of oral physician is to recognize the correlation of bony lesions along with other systemic conditions and hormonal imbalances. An interdisciplinary approach will help improve the quality of life such individuals.

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