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A Case of McCune-Albright Syndrome with Fibrous Dysplasia and Endocrinopathies.

Shilpa Patil[1], Piyush Prajapati[2]*, Shakuntala Prajapati[3], Pramod Shaha[4], Dhanesh Mhaskar[5], Saurabh Gandhi[6], and Aditya Aundhakar[7].

[1]Assistant Professor, Department of Internal Medicine, Krishna Institute of Medical Sciences, Karad.
[2]3rd Year Resident, Department of Internal Medicine, Krishna Institute of Medical Sciences, Karad
[3]Consultant, Department of Pathology, Shanku's Medicity, mehsana
[4]Professor, Department of Radiology , Krishna Institute of Medical Sciences, Karad.
[5]Assistant Professor, Department of Internal Medicine, Krishna Institute of Medical Sciences, Karad.
[6]3rd Year Resident, Department of Internal Medicine, Krishna Institute of Medical Sciences, Karad
[7]2nd Year Resident, Department of Internal Medicine, Krishna Institute of Medical Sciences, Karad

ABSTRACT

Fibrous dysplasia is a benign bone lesion of unknown etiology. Bone involvement usually is solitary (monostotic). Multiple forms (polyostotic) associated with extra skeletal symptoms, particularly cutaneous pigmentation, endocrine dysfunction and precocious puberty is called McCune–Albright syndrome (MAS). McCune Albright is a very rare syndrome which is characterized of minimum two of the three findings: cafe au lait spot, polyosteotic fibrous dysplasia and endocrine disorders. This disease is not inherited. We present a 40 year old man with Polyosteotic fibrous dysplasia and endocrinopathies. Laboratory analysis showed an increased growth horomon, prolactine and Serum alkaline phosphatase.
Keyword: - Fibrous Dysplasia, - Endocrinopathies Mccune-Albright Syndrome

Corresponding author

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INTRODUCTION

McCune-Albright Syndrome (MAS) is a rare, heterogenous, clinical condition caused by a sporadic, somatic, post -zygotic mutation characterized by a triad of polyostotic Fibrous Dysplasia (FD), cafe-au lait maculae and hyperfunctional endocrine glands(1,2). The disorder is more common in females (3) , It is a rare disease with an estimated prevalence between 1/100,000 and 1/1,000,000(4). The café au lait skin pigmentation consist of large hypermelanostic maculae of irregular and serpinginous (coast of maine) borders, which occur mainly on the front , posterior area of the neck, buttocks, thorax, back ,shoulder and pelvis(5,6). FD is a benign condition in which the medullary portion of the bone is replaced by poorly organized fibrous tissue with trabeculae of immature bone(7). it may affect either a single bone (monostotic) or numerous bones (polyostotic)(1) It is caused by embryonic somatic mutation leading to substitution of His or Cys for Arg at amino acid 201 of the Alpha Subunit of the signal transduction protein Gs (Gsalpha) (2). Recent studies have shown a clonal origin for FD, suggesting that this lesion is neoplastic in nature(8). The endocrine disorders associated with this disease may include precocious puberty, hyperthyroidism, pituitary adenomas, adrenal primary hyperplasia, hypophosphatemia, and ovarian cysts(6). "There are no known environmental, ethnic or geographic risk factors for the development of MAS. So far, all cases of MAS are sporadic. The disease did not come from the parents and patients will not transmit it to their children"(9). The symptoms begin during a person's childhood, and the disease is rarely discovered except for unrelated routine radiographic procedures. The history and the physical examination can vary based on a specific person's syndrome.

CASE REPORT:

A 40 year old male, farmer by occupation presented to our hospital with the complaints of polyurea , polydipsia and facial asymmetry . At the age of three year, skull asymmetry became visible, which was more and more pronounced in the following year but no medical opinion was considered.

Physical finding of the patient at the presentation were as follows, height: 178cms, weight: 89 kgs, a prominant acromegalic facial appearance was present. an ophthalmological examination revealed neither diplopia nor any other subjective impairment of his vision. there was a mild paleness of his optic nerve papilla and mild left sided hemianopia. his hearing was normal.

- The Laboratory Finding Were As Follows:

Parameter	Observed Value	Normal Range
Human Growth Hormone	25 Ng/Ml	Up To 3
Prolactin:	75.6 Miu/Ml	2.1-17.7
Alkaline Phosphatase	308 IU/Lit	37-47
Leutinising Hormone	4.08 Miu/Ml	1.5-9.3
Follicle Stimulating Hormone	11.57 Miu/Ml	13-70
Cortisol Free 24 Hour Urine	181 ≥µg/24 Hour	28.50-213.70
Total T3	166ng/Dl	60-200
Total T4	10.7 µg/Dl	4.5-12
TSH	1.76 µiu/Ml	0.30-5.5
BSL FASTING	219 mg/dl	70-100 mg/dl
BSL-PP	267 mg/dl	100-150 mg/dl
GLYCOSYLATED Hb%	8.3	
Serum elctrolytes	wnl	
Complete blood count	Wnl	
RFT	Wnl	

Mri Brain Plain & Contrast:

- Lobulated enhancing lesion in the sellar region causing expansion of sella turcica bulging anteriorly in to sphenoid sinus s/o Macro- Adenoma.
- Gross expansion of occipital bone (right side), squamous part/mastoid part/petrous part of temporal bone on right side & clivus (predominantly right half) showing varying signal intensity with area of

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heterogenous iso to hypointensity on all sequences, likely to be sclerosis with adjacent ill defined hypointense on T1W1, hyperintensity on T2WI, likely to be cystic spaces..... features s/o polyostotic fibrous Dysplasia.

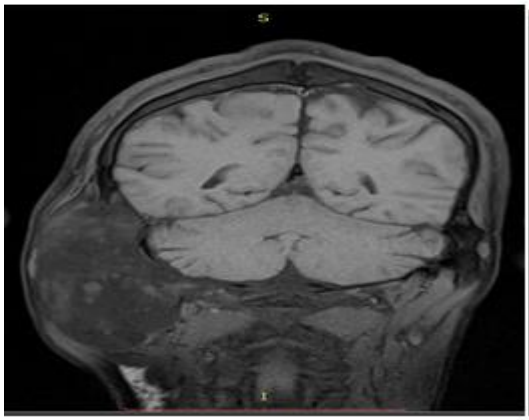

Fig 1: Gross expansion of right occipital bone and temporal bone, heteroginous signal intensity

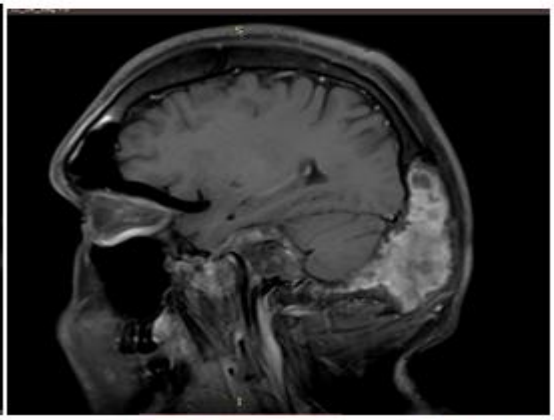

Fig 2: Expansion of frontal and occipital

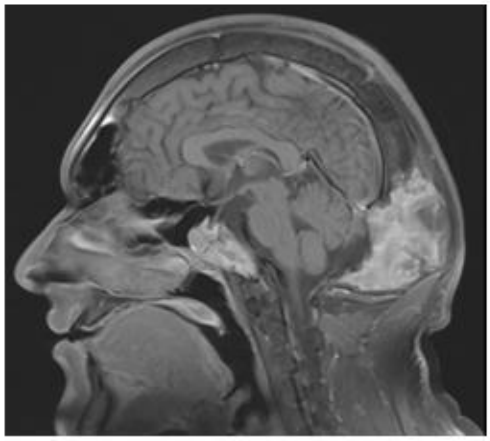

Fig 3: Expansil, Heterogenous enhancing lesion involving occipital and clivus intensity

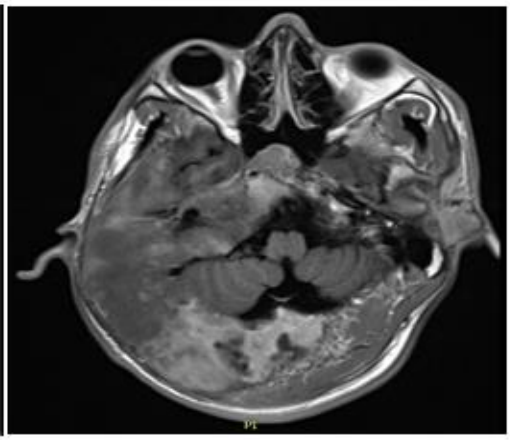

Fig 4: Fibrous Dysplasia with Macro-Adenoma

DISCUSSION

McCune Albright Syndrome is a rare, multisystem disorder with female predilection, first described separately by Donovan McCune and Fuller Albright in 1937, in a group of children presenting with cafe-au-lait maculae, bone deformities and hyperfunctioning endocrinopathies attributed to an activating mutation of Gs gene.[10] The syndrome is caused by a postzygotic somatic mutation in GNAS1 gene located on 20q13-13.29, encoding for the alpha subunit of the stimulatory G protein, resulting in the constitutive activity of the gene products. Normally, on binding of ligands to the receptor, the Gsα gets stimulated and dissociates from the receptor to activate adenylyl cyclase enzyme to increase the production of cAMP which mediates further signaling cascade. On inactivation, Gsα again reattaches with receptor for ligand mediated reactivation.[10,11]

The clinical presentation is heterogeneous with involvement of endocrine & non-endocrine organs depending on the number and the types of cells carrying the GNAS1 mutation.[11] Similarly, the syndrome has varied evolution and progression. Usually the syndrome is diagnosed on the basis of the classic triad of fibrous dysplasia which develops due to the mutation in osteoprogenitor cells without differentiation, hyperfunctioning endocrinopathies along with isosexual precocious puberty and café-au-lait maculae mostly developing between the age of 4 months to 2 years but can be present at birth.[11,12]

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Fig 5: Annormal bony growths seen in the frontal bone and occipital bone

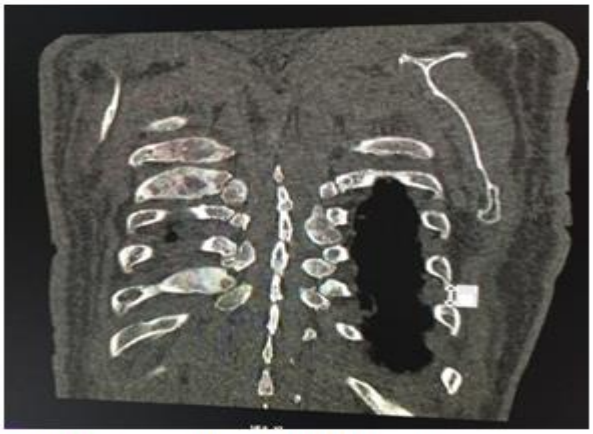

Fig: CT coronal section of thorax (bone window):

Showing diffuse expansion of ribs in which bony tissue is replaced by hypodense ground glass densities with no evidence of periosteal reaction suggestive of fibrous dysplastic change .

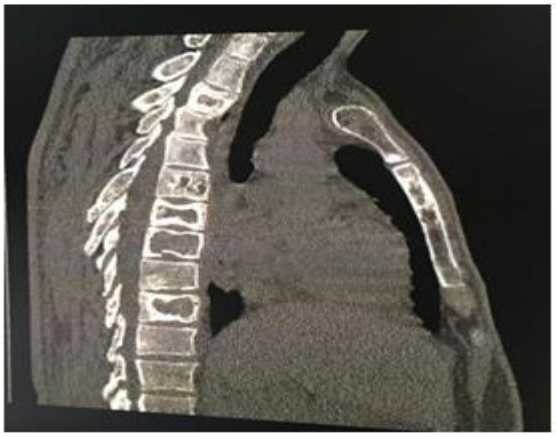

Fig: CT saggital sections of vertebral column Multiple vertebral

Bodies and spinous processes (both cervical and thoracic) show large hypodense homogenous densities replacing normal bony tissue with loss of trabecular patter . No evidence of periosteal reaction suggestive of fibrous dysplastic change

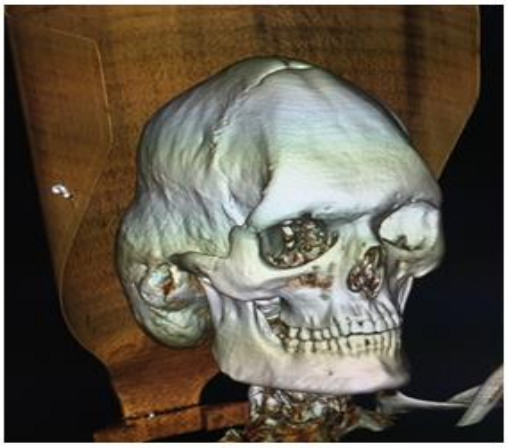

Fig: 3D reconstruction of patients skull showing expansile lesion involving the temporo-occipital region on the right side .

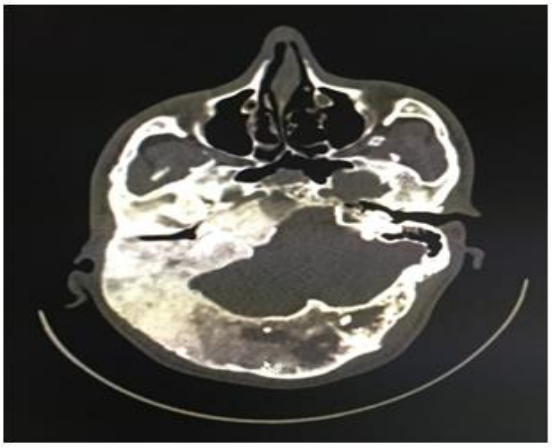

Fig: Axial section of Head Ct (Bone window)

visualised bony elements show widened diploic space with thinning of both , the inner and the outer tables . Normally occuring bony elements are replaced by homogenous ground glass hypodensities (HU) showing extensive haphazard calcification and no evidence of periosteal reaction . orementioned changes are suggestive of fibrous dysplasia

Fibrous dysplasia usually manifests during the first decade of life as aching pain, pathological fractures, limb asymmetry and deformities and is usually polyostotic, commonly involving the long bones, ribs and skull. Involvement varies greatly in severity from small, asymptomatic areas only detected on bone scan to highly disfiguring lesions leading to the pathological fractures and impingement of vital organs.[13]

The endocrine disorders accompanying MAS are precocious puberty, pituitary adenomas secreting growth hormone and/or prolactin, Cushing syndrome, hypophosphatemic osteomalacia, thyroid abnormalities (hyperthyroidism and benign and malignant thyroid nodule) and hyperparathyroidism14, 15, 16). Growth hormone hypersecretion in MAS is common but differs from that observed in classic acromegaly in several aspects.

McCune-Albright syndrome is considered a complex disease because of its varied manifestations and severity. No definite treatment and prenatal diagnosis is possible at present. A recent novel technique of PCR for activating mutation in the peripheral blood cells can help diagnose the disease.[11,13,17] Depending on the number and extent of the endocrine and non-endocrine manifestations, various medical and surgical therapies can be offered.[18]

FD presents a treatment dilemma because there is no proven medical therapy. Bisphosphates have been shown to reduce the incidence of fractures and reduce the intensity of bone pain. However, the only cure for FD is a surgical resection, which is difficult in the skull and facial regions. Surgery is recommended when there is a functional cranial nerve deficit in order to prevent or limit the permanent loss of function15). Medical treatment using a somatostatin or dopamine agonist is often the only option in patients with MAS and an excess of GH because transsphenoidal surgery is not possible due to the massive thickening of the skull base with FD19,20,21). Radiation therapy is not considered to be an option because it is believed to predispose FD to a sarcomatous transformation22,23).

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