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INTRODUCTION

McCune-Albright syndrome (MAS) is a sporadic disease characterised by polyostotic fibrous dysplasia, cutaneous pigmented spots and autonomous hyperfunction of multiple endocrine systems(1). Somatic activating mutations in the gene (GNASI) for the alpha subunit of Gs, the protein that stimulates cyclic adenosine monophosphate (cAMP) formation, has been identified in affected tissue of individuals with MAS(2). The activation of adenyl cyclase is part of a signal transduction pathway that generates cAMP which is an intracellular second messenger causing permeability changes and hormone secretion on cells with features of MAS.

An example is secretion of thyroid stimulating hormone (TSH) by the anterior pituitary, when this hormone reaches altered thyroid acini cells, with resultant increase in iodine uptake and increased production of T3 and t4, hence hyperthyroidism. A rare case of MAS, presenting as an autosomal dominant trait through four generations in a family is presented.

CASE REPORT

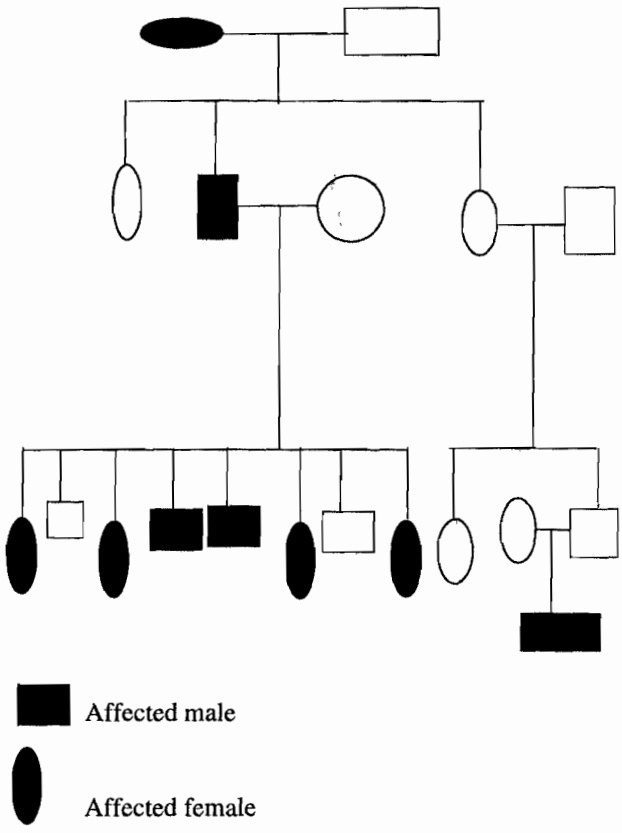
In 1997, a fifteen-year old female with a painless slow-growing grotesque mandibular swelling of a year's duration presented at the University of Nairobi, Dental Hospital. A similar lesion in her upper face (maxilla) had been surgically excised a few years back. All save for two brothers in her family had 'fragile bones' and were on treatment and follow up in Kenyatta National Hospital's orthopaedic unit.

As a result of the frequent fractures associated with the 'fragile bones' our patient had lower limb deformity necessitating the use of crutches. On further questioning of the proband's parent a pedigree of the affliction in the family was drawn (Figure 1).

There was a notable absence of precocious puberty in all affected females. A sister to the proband at 20-years had hyperthyroidism and subsequently hypertension. The hyperthyroidism was conservatively managed with medication. All the sisters to the proband were invalid and on wheelchairs. One of the afflicted brothers exhibited acromegalic features.

Figure 1

Pedigree of autosomal dominant trait of MAS in the family.



Examination of the proband revealed obvious facial asymmetry with a left mandibular painless and bony hard swelling in addition to a scar on the upper lip (Figure 2). The lower limbs were thickened and deformed with cafe-au-lait and spots (Figure 3). Serum calcium and phosphorous were normal with slight elevation of serum alkaline phosphatase to 129 IU/L (with a laboratory reference range of 42-126 IU/L). An orthopantomogram revealed pagetoid opacities and luscencies (Figure 4). An incisional biopsy with histologial examination of the mandibular swelling was consistent with a picture of calcification (Figure 5).

Figure 2

Proband with a left mandibular grotesque swelling

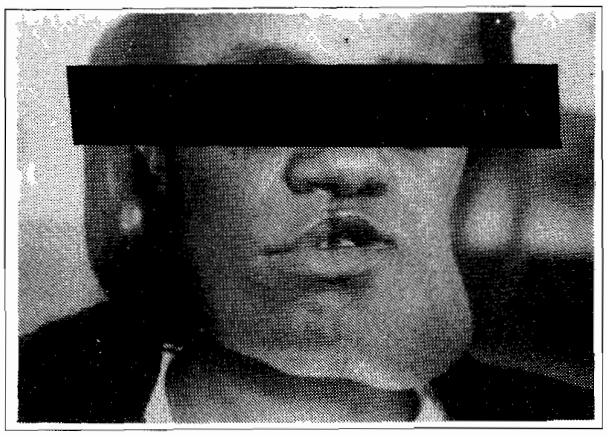


Figure 3

Proband's lower limbs showing deformity and cafe-au lau pigmentation

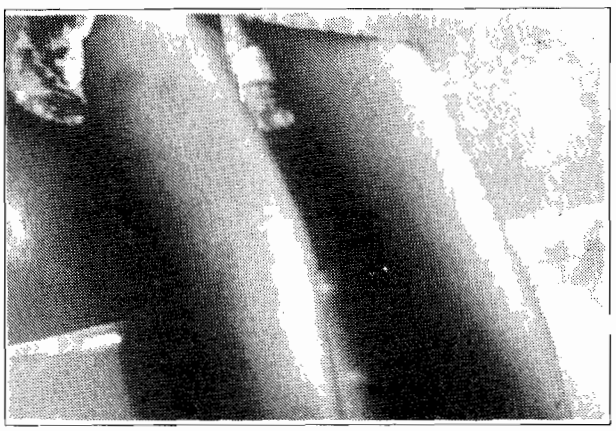


Figure 4

Orthopantomogram of the proband with pagetoid features

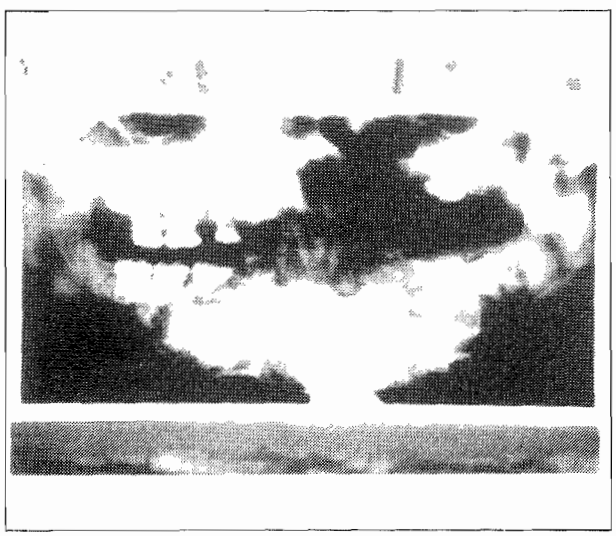


Figure 5

Histopathologic picture X100 H E. of lesion showing predominantly spheroidal calcifications

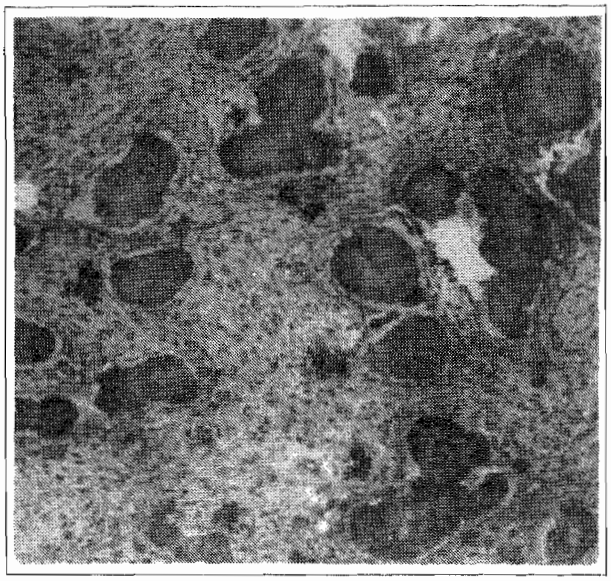
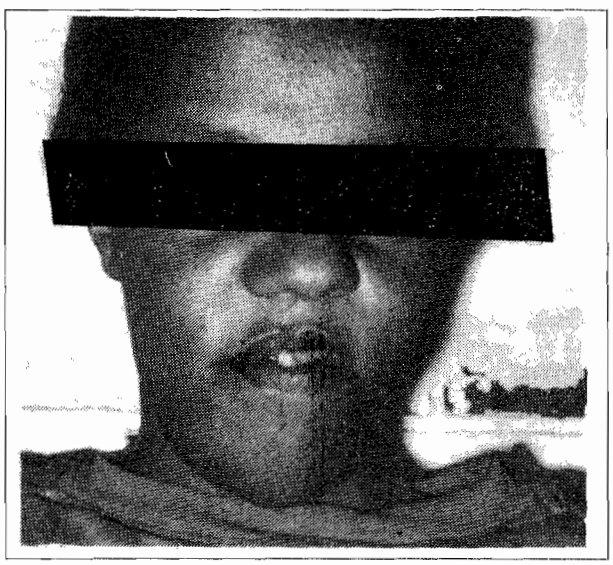


Figure 6

Proband following mandibular recontouring



A diagnosis of MAS transmitted as an autosomal dominant trait through four generations was made.

DISCUSSION

MAS is a sporadic disease in which a mutation in the GNASI gene occurs post-zygotically in a somatic cell(2). The only case of hereditary MAS we found in the literature is that reported by O'Halloran and Shalet (3). In that case, MAS is not familial but is associated with familial multiple

endocrine neoplasia (MEN) type 1 in a female. Hereditary MAS as it seems is rare and indicates the possibility of the involvement of more than just a post-zygomatic somatic mutation of the cells involved. Due to limitations in terms of equipment it was not possible to do molecular genetic studies for this family. Precocious puberty, a consistent finding in MAS, was notably absent in the entire family. This seems to emphasise the variable expressivity of this condition(4).

The frequency of 'maxillo mandibular' involvement in polyostotic fibrous dysplasia is difficult to determine(5). In the present case the affliction was on three females in the immediate family of the proband and the onset was during the second and third decade. The proband was managed by surgical recontouring of the mandibular lesion with good aesthetic results and no recurrence in two years (Figure 6). The need to report cases of MAS as an important aspect in understanding its biologic nature cannot be overemphasised.

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