CASE REPORT

McCune Albright syndrome: an endocrine medley

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SUMMARY

McCune Albright syndromeis a rare disorder that presents with multiple endocrine abnormalities. We report the case of a 24-year-old woman who presented with right lower limb pain, with no preceding trauma or fracture. On examination she was noted to have coarsened facial features, acral enlargement, bitemporal hemianopia, galactorrhoea and multiple café-au-lait macules. She gave history of precocious puberty, having attained menarche at 7 years of age. Biochemical investigations revealed hyperprolactinaemia, with unsuppressed growth hormone levels following a glucose load and subclinical hyperthyroidism. Technetium-99m methylene diphosphonate bone scan showed polyostotic fibrous dysplasia, MRI of the brain showed a pituitary macroadenoma. Thus she was diagnosed to have McCune Albright syndrome with multiple endocrine manifestations. She was treated with parenteral zoledronate for her bony lesions and initiated on cabergoline for plurihormonal pituitary macroadenoma. She is planned to be on close follow-up to assess for clinical improvement and appearance of other manifestations.

BACKGROUND

McCune Albright syndrome (MAS) is a rare non-inherited condition caused by constitutive activation of Gsa. It presents with café-au-lait macules, precocious puberty and polyostotic fibrous dysplasia (FD).[1] Besides this classic triad, it can also present with other endocrinopathies in the form of acromegaly, hypophosphatemic osteomalacia, hyperthyroidism and Cushing's syndrome. These manifestations can present at different time points; hence, meticulous screening for other organ involvement and long-term follow-up are required.[2]

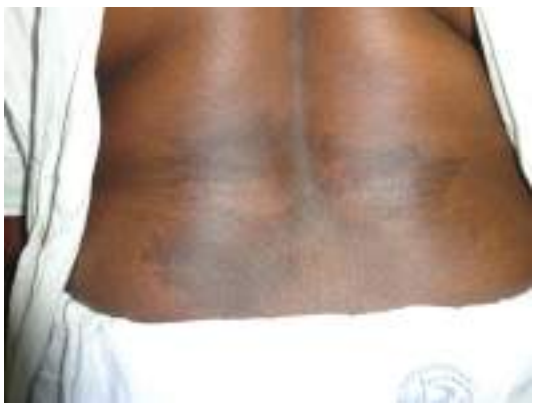

Figure 1 Café-au-lait macules with irregular borders.

CASE PRESENTATION

A 24-year-old woman presented with complaints of pain in her right lower limb for the past 1 year. She had similar complaints in the past and had undergone surgery in her right femur with bone grafting done 10 years back. She also had diminished vision in her right eye since the past 2 years. There was no history of trauma, fracture or growth failure. She had attained menarche at 7 years of age and her cycles were irregular since the past 4–5 years. Her last menstrual period was 2 months prior to her visit. A urine pregnancy test done had excluded pregnancy. On examination, she had hyperpigmented macules with irregular margins over the posterior aspect of her trunk (figure 1) and left forehead, coarse facial features, enlargement of hands and feet (figure 2), thyromegaly with prominent right lobe and galactorrhoea. Her height was 157 cm which was within her target height range (mid-parental height being 158.5 cm). There were no discriminatory features of Cushing's syndrome. There were no bony deformities and visual field examination revealed bitemporal hemianopia.

INVESTIGATIONS

Blood biochemistry showed normal total calcium of 8.6 (N: 8.3–10.4) mg/dL, phosphate of 4.4 (N: 2.5–4.6) mg/dL and high alkaline phosphatase of 216 (N: 40–125) U/L. Her bone turnover markers were elevated, serum beta cross laps being 1934 (N: 137–573) pg/mL and N terminal propeptide of type 1 procollagen being 538 (N:15.1–58.3) ng/mL. Her thyroid function tests showed a suppressed thyroid stimulating hormone (TSH) of 0.004 (normal: 0.3–4.5) uIU/mL, with free T4 of 1.08 (N: 0.8–2) ng/dL and T3 of 146 (N: 90–190) ng/dL. Her insulin-like growth factor 1 was elevated at 809 (N: 66–346) ng/mL and her growth hormone (GH) levels following 75 g glucose load were unsuppressed (basal—10.5 ng/mL, 1 hour—8.78 ng/mL, 2 hours—8.21 ng/mL), thus confirming the presence of acromegaly. Prolactin levels were markedly elevated to 3218 ng/mL (N: 1.9–25). Her post-prandial blood glucose level was 88 mg/dL and her glycated haemoglobin was 5.1%.

X-ray pelvis (figure 3) showed loss of normal trabecular pattern in the femur with typical ground-glass appearance as described in FD, technetium-99m methylene diphosphonate (MDP) bone scan revealed irregular increased tracer activity in

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Figure 2 Acral enlargement.

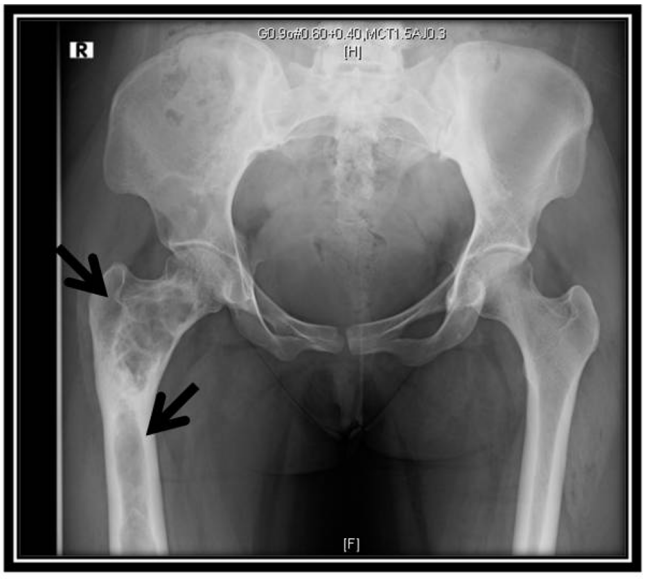

Figure 3 Loss of trabeculae, lytic lesions, ground-glass appearance.

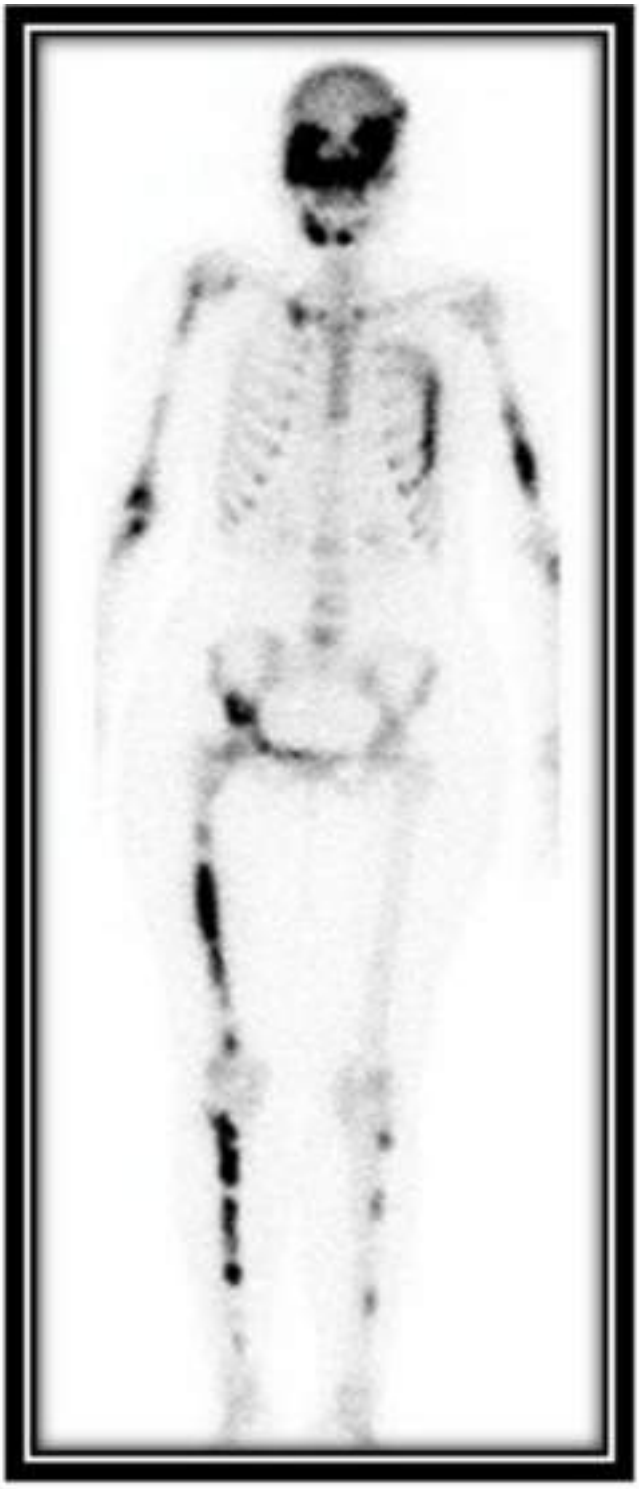

Figure 4 Technetium- 99m methylene diphosponate bone scan showing polyostotic fibrous dysplasia.

the skull, humerii, multiple left-sided ribs, right hemipelvis, right femur and tibiae suggestive of polyostotic nature of the disease (figure 4). Iodine -131 (I-131) thyroid uptake scan (figure 5) showed increased uptake in the right upper and lower poles, and a non-functioning nodule in the middle of right lobe of thyroid. Fine-needle aspiration (FNA) cytology from the non-functioning nodule showed a benign colloid rich lesion. MRI brain with gadolinium contrast (figure 6) showed a pituitary macroadenoma of size $4\times3\times3\,cm^3$ protruding into the lateral ventricle

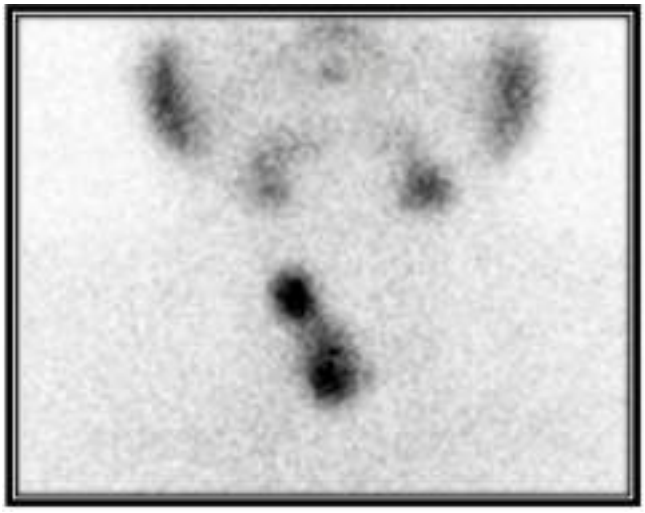

Figure 5 I-131 uptake scan showing two functioning nodules in right lobe and suppressed left lobe.

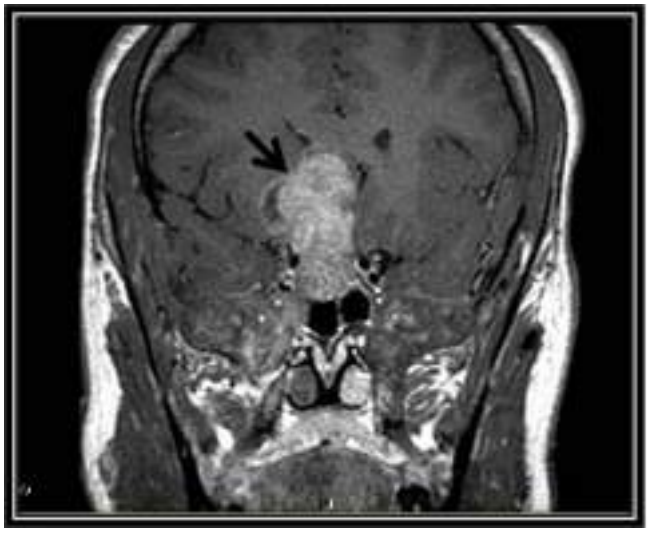

Figure 6 MRI brain showing pituitary macroadenoma.

and causing mass effect on the right basifrontal region. In view of the pituitary macroadenoma, other hormonal axes were assessed as well. Her serum 8 AM cortisol was 13 (N: 7–25) mcg/dL and serum sodium was normal, thus ruling out an adrenocorticotropic hormone (ACTH) deficiency. Her hypothalamo-pituitary-gonadal axis was involved as she had presented with oligomenorrhoea and measurements of serum luteinizing hormone (LH) and follicle stimulating hormone (FSH) were 0.16 and 0.14 mIU/mL, respectively. A meticulous charting of her intake and output revealed that there was no polyuria or polydipsia to suggest diabetes insipidus. A formal visual field assessment was done, which revealed the presence of bi-temporal hemianopia.

DIFFERENTIAL DIAGNOSIS

With the earlier clinical, biochemical and imaging features, our patient was diagnosed to have MAS. She had the typical triad of the disease consisting of precocious puberty, café-au-lait spots and polyostotic FD.[1] In addition, she also had subclinical hyperthyroidism and plurihormonal pituitary macroadenoma secreting GH and prolactin.[3]

TREATMENT

She was administered parenteral zoledronate for treatment of polyostotic fibrous dysplasia. Considering the pleurihormonal (GH and prolactin) nature of pituitary macroadenoma with markedly elevated prolactin levels, she was initiated on cabergoline 0.5 mg two times per week. Although the option of somatostatin analogue therapy was put forward to the patient, she had considerable financial constraints and was not affordable for the same. Therefore, it was decided to continue her on cabergoline two times per week, and reassess her after a period of 3 months. As she was clinically euthyroid and FNA had shown a benign colloid lesion, she was planned to be kept on follow-up for subclinical hyperthyroidism.

OUTCOME AND FOLLOW-UP

She is planned for follow-up after 3 months. At review, her symptomatology will be reassessed. Prolactin and GH levels (post-glucose suppression) will be retested. Thyroid function tests will be repeated. Further, if there is no significant reduction in the size of the pituitary macroadenoma after maximum dose of cabergoline therapy, she will be offered surgery for the same.

DISCUSSION

MAS is typically described by the clinical triad of precocious puberty, café-au-lait spots and polyostotic FD.[1] In addition to the classic triad, our patient also had subclinical hyperthyroidism and plurihormonal pituitary macroadenoma secreting GH and prolactin. Other endocrinopathies described in MAS include Cushing's syndrome and fibroblast growth factor 23 mediated hypophospatemic osteomalacia.[4] MAS, a rare non-inherited disorder, is due to somatic activating mutations in the guanine nucleotide binding protein alpha stimulating (GNAS) gene that codes for the protein guanine nucleotide binding protein subunit alpha (Gsa), which is involved in intracellular cyclic adenosine monophosphate (cAMP) production.[1] Hyperthyroidism is associated with 38%[3] of cases of MAS, although abnormalities detected by ultrasound screening are present in at least two-thirds of these patients.[1] The prevalence of acromegaly in MAS is 20%–30% and is always associated with FD of skull. The vast majority (81%) of patients with acromegaly also have hyperprolactinaemia.[5] Despite precocious puberty, our patient had her height within target range which was probably due to her GH excess state.[1] All features of MAS have varied time of presentation[1] and café-au-lait macules, which are the earliest of the clinical features to appear, are often overlooked as in our case. Hence, meticulous follow-up of patients with MAS is needed to diagnose the different manifestations and for management of the same.

In this patient, medical management in the form of somatostatin analogues were offered; however, due to financial

Learning points

- McCune Albright syndrome (MAS) is a rare non-inherited disorder due to activating mutations of Gsa.
- It is characterised by the triad of precocious puberty, café-au-lait macules and polyostotic fibrous dysplasia.
- Other endocrinopathies include acromegaly, Cushing's syndrome, hyperthyroidism and fibroblast growth factor 23 mediated hypophosphatemic osteomalacia.
- As all features of MAS have a varied time of presentation, a meticulous and long-term follow-up is required.

constraints expressed by the patient in procuring octreotide, she was initiated on cabergoline therapy for medical treatment of acromegaly with hyperprolactinaemia. She is planned for follow-up after 3 months. If it is documented that there is no significant biochemical and anti-tumour response or there is a progression of visual symptoms on maximally tolerated medical therapy, she will be offered surgical excision of the pituitary macroadenoma, with the caveat that surgery may be complicated by bony overgrowth and anatomical distortion of the cranio-facial skeleton.[6]

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