

A RARE CASE OF PRECOCIOUS PUBERTY IN GIRLS; MCCUNE-ALBRIGHT SYNDROME

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ABSTRACT**BACKGROUND**

Pubertal changes before the age of 8 years in girls are regarded as precocious puberty. McCune-Albright Syndrome is a genetic disorder and accounts for 5% of female precocity. It consists of multiple, disseminated, cystic bone lesions, café-au-lait skin spots and sexual precocity.^[1] Sexual precocity is due to autonomous early production of oestrogen by the ovary. McCune-Albright syndrome (MAS) is classically defined by the clinical triad of fibrous dysplasia of bone (FD), café-au-lait skin spots, and precocious puberty (PP). It is a rare disease with estimated prevalence between 1/100,000 and 1/1,000,000.^[1] FD can involve a single or multiple skeletal sites and presents with a limp and/or pain, and occasionally a pathologic fracture. Scoliosis is common and may be progressive. In addition to PP (vaginal bleeding or spotting and development of breast tissue in girls, testicular and penile enlargement and precocious sexual behaviour in boys), other hyperfunctioning endocrinopathies may be involved including hyperthyroidism, growth hormone excess, Cushing syndrome, and renal phosphate wasting. Café-au-lait spots usually appear in the neonatal period, but it is most often PP or FD that brings the child to medical attention. Renal involvement is seen in approximately 50% of the patients with MAS. The disease results from somatic mutations of the GNAS gene, specifically mutations in the cAMP regulating protein, G_s alpha. The extent of the disease is determined by the proliferation, migration and survival of the cell in which the mutation spontaneously occurs during embryonic development. Diagnosis of MAS is usually established on clinical grounds. Plain radiographs are often sufficient to make the diagnosis of FD and biopsy of FD lesions can confirm the diagnosis. The evaluation of patients with MAS should be guided by knowledge of the spectrum of tissues that may be involved, with specific testing for each. Genetic testing is possible, but is not routinely available. Genetic counselling; however, should be offered. Differential diagnoses include neurofibromatosis, osteofibrous dysplasia, non-ossifying fibromas, idiopathic central precocious puberty, and ovarian neoplasm. Treatment is dictated by the tissues affected, and the extent to which they are affected. Generally, some form of surgical intervention is recommended. Bisphosphonates are frequently used in the treatment of FD. Strengthening exercises are recommended to help maintaining the musculature around the FD bone and minimise the risk for fracture. Treatment of all endocrinopathies is required. Malignancies associated with MAS are distinctly rare occurrences. Malignant transformation of FD lesions occurs in probably less than 1% of the cases of MAS.

KEYWORDS

Puberty, Precocious, McCune.

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BACKGROUND

Pubertal changes before the age of 8 years in girls are regarded as precocious puberty. In peripheral or incomplete precocity, also known as precocious pseudopuberty, there is no stimulation from hypothalamo-pituitary gonadotropin. It may be due to adrenal feminising or masculinising tumours, ovarian cysts or tumours or McCune-Albright Syndrome. McCune-Albright Syndrome is a genetic disorder and accounts for 5% of female precocity.^[1] It consists of multiple, disseminated, cystic bone lesions, café-au-lait skin spots and sexual precocity. Sexual precocity is due to autonomous early production of oestrogen by the ovary. Here, we are presenting a case of McCune-Albright Syndrome in a 10-year-old girl who presented with spotting since 3 years and premature thelarche since 1 year.

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**CASE REPORT**

This child presented with complaints of gradual enlargement of the breasts since 1 year and bleeding per vagina since 3 years. There was no history of convulsions, headache, visual disturbances or sexual assault. The girl was the first child of a non-consanguineously married couple, delivered at full term by vaginal delivery, with immediate cry. Her mother had attained menarche at the age of 13 years. On examination: The child weighed 27.5 Kg (at 50th centile). Her height was 137 cm (between 50th-75th centile). There were brown, pigmented non-pruritic macular lesions on the neck, chest, abdomen and back. There were no papules or vesicles. There was no evidence of acne or hirsutism. There was no goitre, no lymphadenopathy or organomegaly. Cardiovascular and respiratory system were normal. There was no neurological deficit. Ophthalmological examination including perimetry and fundoscopy were normal. SMR staging shows thelarche (stage 3), pubic hair (stage 1) and axillary hair present. Vaginal mucosa appeared pale. On investigations: complete haemogram and urine microscopy were normal. Calcium profile showed increased alkaline phosphatase values. Renal function tests and Thyroid profile were normal. Serum FSH, LH and Prolactin were normal for the age. Estradiol levels were 10.80 pg/mL. Bone age is consistent with 12-15 years of age.

X-ray Skull lateral view showed normal sella turcica and multiple cystic bone lesions. X-Ray Femur- there were multiple, disseminated, cystic bone lesions. Findings were suggestive of fibrous dysplasia of skull bone and femur. USG whole abdomen was normal. USG Pelvis showed bulky uterus, with thick endometrium for age with bulky left ovary which showed 2 cystic lesions with echogenic component.



Figure 1. Cafe-Au-Lait Spots over Back Showing Irregular Border (Coast of Maine Appearance)



Figure 2. Genu Valgum Deformity of Bilateral Knee Joint



Figure 3. Multiple Osseous Lytic Lesions at the Base of Skull



Figure 4. X-ray Knee Joint Showing Osseous Lytic Lesions in Metaphysis of Femur and Genu Valgum Deformity

DISCUSSION

The classical triad of McCune-Albright syndrome (MAS) consists of polyostotic fibrous dysplasia (FD), skin hyperpigmentation (café-au-lait spots), and endocrine dysfunction, frequently seen in females as precocious puberty.^[1] Bone lesions may be solitary (monostotic) or multiple (polyostotic). MAS is a rare disease (the estimated prevalence ranges between 1/100,000 and 1/10,00,000). The skeletal aspect of the disease, Fibrous dysplasia, especially monostotic disease, is not rare. Clinical picture in MAS is related to its mosaic nature, ranging from one or two mild clinical signs with excellent long-term prognosis to a severe life threatening multiorgan disease.^[2] MAS is most commonly confused with neurofibromatosis (NF). The location and shape of the spots usually can help to distinguish between the MAS and NF. The spots in MAS have jagged borders (coast of Maine), whereas those in NF are smooth (coast of California). Café-au lait pigmentation in case of McCune-Albright syndrome does not cross midline. Frequent locations are the nape of the neck and the crease at the apex of the buttocks which had similar presentation in our child. Bisphosphonates are frequently used in the treatment of FD. Strengthening exercises are recommended to help in maintaining the musculature around the FD bone and minimise the risk for fracture. Malignancies associated with MAS are distinctly rare occurrences. Malignant transformation of FD lesions occur in probably less than 1% of the cases of MAS.^[3] Other endocrinopathies, including hyperthyroidism, growth hormone excess, renal phosphate wasting with or without rickets/osteomalacia and Cushing syndrome may be found in association with the original triad. Our child had complaints of bony pain, and screening for rickets showed reduced serum calcium and increased alkaline phosphatase and vit D supplementation was started, now child is clinically better and needs followup for healing rickets. Rarely, other organ systems may be involved (liver, cardiac, parathyroid, pancreas). Treatment of all endocrinopathies is required.

Ultrasonography is very useful in ovarian cyst followup and in the detection of thyroid and adrenal nodules.

CONCLUSION

In summary, McCune Albright's syndrome stems from a Gs-alpha mutation resulting in hyperstimulation effect in the affected cell lines. It is a sporadic somatic mutation during embryogenesis which then manifests in a mosaic fashion and explains the asymmetrical pattern of disease. Two of three characteristics are generally accepted for diagnosis of this syndrome. These include café-au-lait spots which may be faint in early childhood but darken with age, osteitis fibrosa disseminata which can be seen in a mosaic pattern, and multiple endocrine abnormalities, the most common being precocious puberty. Therapy is aimed specifically at the affected organs.

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