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McCune Albright Syndrome: A Case Report & Review of Literature

Richard Mario Lurshay	DNB Pediatrics, Senior Resident, Nazareth Hospital, Shillong, Meghalaya, India.
Pramod Paharia	MBBS, Senior Pediatric Medical Officer, Nazareth Hospital, Shillong, Meghalaya, India.
Santanu Deb	MD, Senior Consultant & HOD, Dept. of Pediatrics, Nazareth Hospital, Shillong, Meghalaya, India.
Indrani Roy	MS, Senior Consultant & HOD, Dept. of Obstetrics &Gynaecology, Nazareth Hospital, Shillong, Meghalaya, India.
Sabrina Yesmin	DCH, Consultant Pediatrician, Nazareth Hospital, Shillong, Meghalaya, India.

ABSTRACT

McCune Albright syndrome (MAS) is characterized by the classical triad of polyostotic fibrous dysplasia (FD), skin hyperpigmentation (café-au-lait spots), and endocrine dysfunction. We report a 21 month girl with MAS, who presented with vaginal bleeding and recurrent fractures. Physical examination revealed multiple café-au-lait spots and features of advanced breast development for age. What makes this case unusual was the radiography findings of polyostotic fibrous dysplasia in all the long bones and skull, an unusually early feature in this child. Ultrasonography revealed bilateral ovarian cysts with a bulky uterus. Hormonal studies revealed very high estradiol levels, as well as elevated serum levels of progesterone, prolactin, adrenocorticotrophic (ACTH), free thyroxine (FT4) and triiodothyronine (FT3). Severe deficiency of Vitamin D was also noted.

KEYWORDS : McCune-Albright syndrome, precocious puberty, polyostotic fibrous dysplasia, Café-au-Lait spots, hyperprolactinoma

INTRODUCTION

McCuneAlbright syndrome (MAS) was defined by the triad of polyostotic fibrous dysplasia of bone (FD), caféaulait skin pigmentation, and precocious puberty (PP) (McCune, 1936; Albright, 1937). Autonomous hyperfunctioning of other endocrine organs causing hyperthyrodism, occult thyrotoxicosis, hypercortisolism, GH excess, hyperprolactinemia, are also described (Rao, Colaco & Desai, 2003). Therefore, a more clinically relevant definition of MAS, broader than the original triad of FD + PP + café au-lait is: MAS = FD + at least one of the typical hyperfunctioning endocrinopathies and/or caféau-lait spots, with almost any combination possible (Collins & Shenker, 1999; Collins, 2006). MAS is a rare disorder and its prevalence is estimated to be between 1/100 000 and 1/1 000000 (Siadati & Shafigh, 2010).

CASE REPORT

This patient, a 21 month old girl, presented to our out-patient department with chief complaints of vaginal bleeding since 3 days. She had also suffered from a fracture of her left humerus 4 days back, following a low energy fall. There was a past history of similar fracture of her right femur that had also occurred following a trivial fall. There was no history of fever, convulsions, headache, visual disturbances or sexual assault.

The girl was the second-born of a non-consanguineous marriage, born of a full term pregnancy, delivered vaginally, with immediate cry. She was developmentally normal. Her elder sister who was 3 years of age, was normal and healthy. Her mother had attained menarche at the age of 12 years.

Examination revealed that the child weighed 9.5 Kg (< 3rd percentile as per WHO growth chart). Her height was 75cms (< 3rd percentile as per WHO growth chart). There were hyperpigmented, non pruritic macular lesions (caféaulait spots) with irregular borders, on the neck, chest, abdomen and back (Fig. 1). There was no lymphadenopathy or goiter. Cardiovascular and respiratory system examination did not reveal any abnormalities. Her left upper limb was in a sling (as was advised by the orthopedic surgeon), to treat the fracture. Axillary and pubic hair had not yet developed (Tanner stage 1). Bilateral breasts were developed (Tanner stage 2) (Fig 2). Labia minora and majora were enlarged. There was no clitoromegaly. There was a bloody discharge from the vagina.

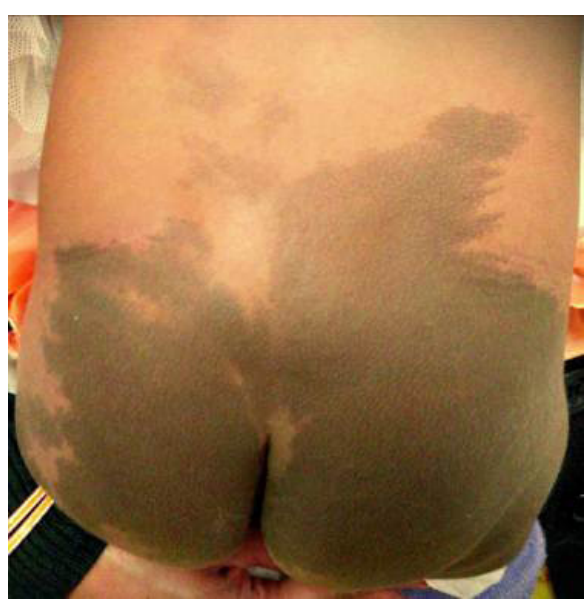

Figure 1: Caféaulait spots on the buttocks; Note the jagged «coast of Maine» borders, and the tendency for the lesions to both respect the midline and follow the developmental lines of Blashko

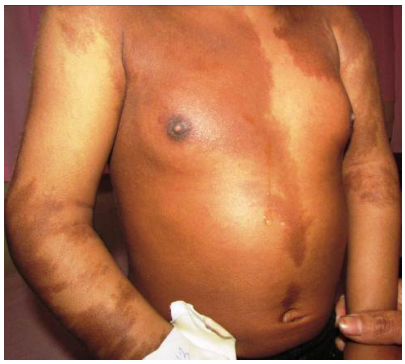

Figure 2: Showing the Caféaulait spots on the trunk. Also note the thelarche (Tanner's stage II of breast development).

Pelvic ultrasonography showed that her uterus was enlarged for her age. Her endometrium was 5.6mm in thickness and was in the secretory phase. Bilateral asymmetric ovarian cysts were also detected. The right ovarian cyst was 1.6cm X 1.5cm in size and the left ovarian cyst was 2.6cm X 1.8cm in size.

Radiography of skull and long bones showed polyostotic fibrous dysplasia. X-ray of the skull showed sclerosis of left frontal bone, left ethmoid sinus and sphenoid bone.

Upper limb X-rays showed lytic expansile lesions in the proximal shaft of humerus and ulna bilaterally and in the right radius. Lower limb X-rays also showed expansile lytic lesions in the proximal femur bilaterally (Fig 3) and in the mid-portion of the tibia. Laboratory reports are given in Table I.

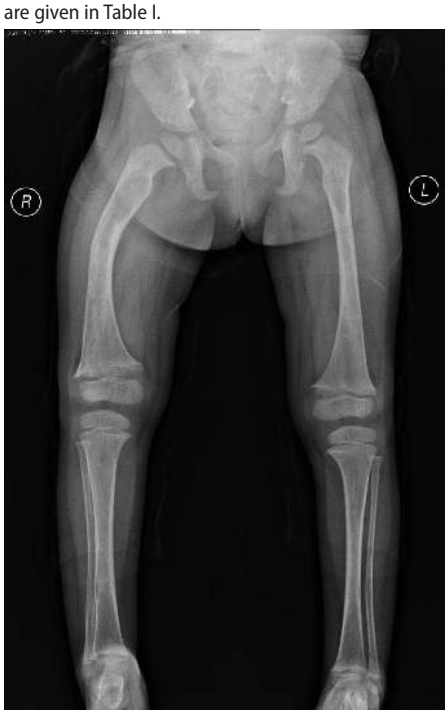

Figure 3: Radiological evidence of fibrous dysplasia seen in the proximal shafts of both femurs with the classic "shepherd's crook" deformity of the right proximal femur.

Table I: Laboratory Investigations

TEST	RESULT	REFERENCE VALUE
Serum Estradiol (E2)	595.23 pg/mL	5.00 – 10.
Serum Luteinising Hormone	< 0.07 mIU/mL	0.02 – 0.18 mIU/mL
Serum Follicle Stimulating Hormone (FSH)	< 0.05 mIU/mL	1.00 – 4.20 mIU/mL
Serum Progesterone	0.40 ng/mL	< 0.33 ng/mL
Serum Prolactin	24.56 ng/mL	3.6 – 12 ng/mL
Plasma ACTH	68.50 pg/mL	< 46.00 pg/mL
TSH	0.05 µIU/mL	0.27 – 4.2 µIU/mL
FT3	15.14 pmol/L	3.1 – 6.8 pmol/L
FT4	29.71 pmol/L	12 -22 pmol/L
Alkaline phosphatase	1091 U/L	145 – 320 U/L
Vitamin D	7.33 ng/mL	> 25 ng/mL

In view of hyperthyroidism, child was started on carbimazole. Vitamin D deficiency was treated with Stoss therapy of 600,000 IU of vitamin D, administered intramuscularly in 4 divided doses over 1 day. This was followed by daily vitamin D therapy of 600 IU/day. In order to reduce the excessive gonadal steroid exposure, the aromatase inhibitor, letrozole, was also started. Further follow-up was advised.

DISCUSSION

The child that presented to us had the classical triad of symptoms similar to observations made by Albright in 1936. However, what stands out in this child is the vast extent of bony involvement in the form of fibrous dysplasia, at such a young age.

MAS is predominantly characterized by multiple bony lesions (polyostotic fibrous dysplasia) (Nager, Kennedy & Kopstein, 1982) Fibrous dysplasia in the appendicular skeleton usually presents with a limp and/or pain (sometimes reported by children as being "tired"), but occasionally a pathologic fracture may be the presenting sign (Dumitrescu & Collins, 2008). Our patient also had similar complaints of two previous fractures involving the extremities. FD has a typical appearance on radiographs described as "ground glass." In general, lesions in the long bones have a "lytic" appearance (Dumitrescu & Collins, 2008).

FD in the craniofacial bones tends to have a "sclerotic" appearance on plain radiographs. This is due to the relatively greater degree of mineralization of FD tissue in the craniofacial bones (Riminucci et al, 1999). These typical characteristic features were also demonstrable in our patient. Hart et al have investigated the onset and presentation of different FD lesions according to their location and accordingly have reported that FD onset has a region-specific pattern, 90% of craniofacial, extremities, and axial skeleton lesions were present by 3.4 years, 13.7 years, and 15.5 years, respectively (Leet et al, 2004). But, overall, the median age for onset of FD lesions is 6-10 years (Leet et al, 2004). In the current case report, the age of the child presenting with FD in extremities is only 21 months, much earlier than the usual age of onset.

Caféaulait macules are large pigmented spots with irregular borders (coast of Maine). They are of different size, number, morphology, age of appearance, usually affecting one half of the body and may indicate active melanocyte proliferation (de Santis et al, 1999). Previous studies have indicated that caféaulait skin spots occur in approximately 60% of MAS cases (Landau & Krafchik, 1999). The child in our case, had multiple caféaulait spots over the nape of the neck, arms, back and buttocks since birth.

Gonadotropin independent precocious puberty (GIPP) is the commonest endocrine affection described (McCune, 1936). In a case series by Rao et al, five out of six girls presented with bleeding per vaginum (Rao, Colaco & Desai, 2003). Our patient's chief complaint was also bleeding per vaginum, which is the most common presenting feature in girls with precocious puberty. Breast enlargement and pigmentation occurs with the development of follicular cyst and uterine bleeding occurs with their involution (de Santis et al, 1999; Low & Wang, 1998). The child in our case report also showed the presence of ovarian cysts and breast enlargement. Estradiol level was significantly elevated in this child (595.23 pg/mL), much higher in comparison to findings by Rao et al (Rao, Colaco & Desai, 2003), wherein the highest recorded estradiol level was 65 pg/mL. The prepubertal levels of LH and FSH in the presence of pubertal levels of estradiol confirm the presence of GIPP.

Autonomous hyperfunctioning of other endocrine organs causing hyperthyrodism, occult

thyrotoxicosis, hypercortisolism, GH excess, hyperprolactinemia, are described. Thyroid disorder is the second commonest affection seen. Hyperthyroidism is common (38%) in MAS (Mastorakos, Mitsiades, Doufas, Koutras, 1997) and was also documented in this patient. Hyperprolactinemia was also noted in this child.

CONCLUSION

McCune Albright Syndrome may present at a very early age. MAS must be kept in mind in children with Gonadotropin-independent precocious puberty. In girls, bleeding per vaginum or spotting is a common presenting complaint. Detailed radiographic evaluation to identify fibrous dysplasia is necessary at all ages. Radiographic changes may be detected as early as in the second year of life, as in this case. Ultrasonography is helpful in identifying ovarian cysts. Blood investigations directed at identifying endocrinal disorders is warranted so that appropriate treatment can be initiated at the earliest.

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