

McCune-Albright Syndrome: A Case Report and Literature Review

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Abstract:

McCune-Albright Syndrome (MAS) is a rare, heterogenous, clinical condition caused by a rare genetic mutation. The disorder is more common in females and is characterized by a triad of cutaneous, bone and endocrine abnormalities. We describe a girl patient with MAS having precocious puberty and multiple café-au-lait macules and deforming polyostotic fibrous dysplasia of bone. Clinical presentation and X-ray finding were strongly diagnostic for MAS. Patients with McCune-Albright Syndrome reach the adult age with a significant burden of the disease that continuously reduces their quality of life. Skeletal deformities, fractures, hyperthyroidism, and hyperestrogenism are just few of the many challenges in the management of these patients. These disorders with close observation and early detection can be controlled.

Keywords:

Albright Syndrome, Fibrous Dysplasia, McCune, Polyostotic.

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), café-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 hypermelanotic maculae of irregular and serpiginous (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 (G α) (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).

Precocious puberty is the common clinical presentation and girls are affected more than boys (1,5). The non-classical form consists of only two of these three conditions.

Gonadotropin-independent precocious puberty is the most common endocrine involvement described. A number of other endocrine and non-endocrine organs may be involved, including the adrenal, thyroid,

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pituitary, liver and heart. Here we report a case of MAS with this triad of symptoms.

Case Presentation

The discussed patient first has been referred to department of pediatric Endocrinology and Metabolism, Mashhad university of Medical Sciences-Iran, with a complaint of breast enlargement, at the age of 6 years old.

At the time of admission the patient weighed 25 kg (W-Z score=1.21) with a height of 128cm (H-Z score= 2.35), therefore having a Body Mass Index (BMI) of 15.3 kg/m². On physical examination, she had enlarged breasts (Tanner stage 2–3) with pigmentation of the areola (fig.1).



Fig 1: Breast enlargement in 6 years old girl with precocious puberty.

A pelvic ultrasound revealed a left ovarian cysts measuring 3.70×3.4 cm. The uterus was enlarged with a length of 4.6 cm (normal ≤ 3 cm) and had a prominent endometrium.

The patient's bone age in radiographic evaluation, was measured 8 according to Greulich and Pyle atlas of skeletal maturation (9).

Hormonal analysis revealed an elevated level of estradiol 113pg/mL (normal < 36 pg/mL) and luteinizing_hormone (LH) 1.7 mlu/ml (normal < 1mlu/ml); dehydroepiandrosteron sulphate (DHEA-SO₄) and follicle stimulating hormone

(FSH) were all in their normal range. The patient was diagnosed with central precocious puberty, and therefore went under treatment with gonadotropin-releasing hormone agonist (GnRH) agonists.

At third month follow-up, the patient complained of pain in lower limb area and Radiographic evaluations revealed a series of fibro dysplastic changes (fig.2).

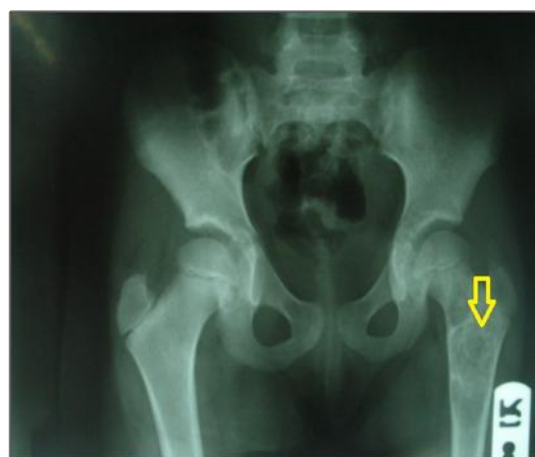


Fig. 2: Fibrodysplastic changes of femur in 6 years old girl present with precocious puberty

After re evaluation, she was diagnosed with McCune-Albright syndrome according to precocious puberty, bone changes and café-au-lait maculae observed (fig.3).

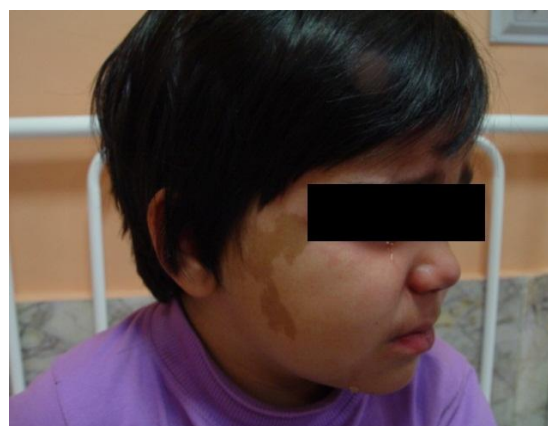


Fig. 3: Café-au-lait maculs in the right side of her face who presented with precocious puberty

In addition to re evaluation of endocrine glands and other organs no abnormal finding was detected, and the patient was prescribed with intravenous pamidronate at a dose of 1-2mg/kg/day for 3 days every 3 months.

In her last visit at the age of 7.5 years old, she weighed 33 kgs, with a height of 127cm, and her Body Mass Index (BMI) was 20.4 kg/m². puberty development was under control and lower limb pain had remitted significantly.

Discussion

MAS is a rare multisystem disorder, first described in 1937 separately by Donovan McCune and Fuller Albright in a group of children, mostly females, with skin pigmentation, bone deformities and endocrinal disorders that develops from an activating mutation in the Gs gene (2,10).

The disorder is the result of post-zygotic somatic mutation in the gene GNAS 1 on chromosome 20q13-13.29 (11), coding for the alpha subunit of stimulatory G protein . G proteins couple cell surface receptors to intracellular proteins to activate or inactivate signaling cascades. The stimulatory G protein is normally activated when a hormone or other ligand binds to the cell surface receptor. The activated Gsa subunit subsequently dissociates from the receptor, binds to adenylyl cyclase and stimulates an increase in the intracellular cyclic adenosine monophosphate (cAMP) levels. The Gsa subunit is then inactivated, which re-associates with the receptor and is again available for hormone-mediated reactivation.

The clinical expression depends on the number of mutated cells and affected organs. Thus, the presentation can be heterogenous, involving various endocrine and non-endocrine organs.

It can be early or late onset or slow or quick evolution. This abnormality lead to

proliferation of osteoprogenitor cells without differentiation, therefore fibrous matrix with woven bone increase. MAS is diagnosed on the triad of FD, endocrinopathy and hyperpigmentation of the skin (12).

The clinical presentation of MAS is highly variable, depending on which of the various potential components of the syndrome predominate. The classical form of MAS is more common in females and is defined by a triad of physical signs as described above.

Café-au-lait macules (CALMs) develop between the age of 4 months and 2 years, but may be present at birth.

Bone dysplasia is revealed during the first decade by aching pain, pathological fractures, limb asymmetry and deformities. Abnormal fibrous tissue growth occurs in many bones, especially in the long bones, ribs and skull bones. Fibrous dysplasia ranges from small asymptomatic areas, detectable only by bone scan, to markedly disfiguring lesions, resulting in pathological fractures and impingement on vital structures. Radiographic appearance can be pagetoid (56%), sclerotic (23%) or cystic (21%) (13). Although once considered a rare finding, fibrous dysplasia of the vertebrae leading to scoliosis is found in 40% of the patients with polyostotic fibrous dysplasia in a study by Leet et al (14).

No definite treatment is available for MAS and, to date, prenatal diagnosis is not possible. But recently, through novel polymerase chain reaction-based techniques, activating mutation in the peripheral blood of patients with MAS has been successfully detected, which might help in diagnostic as well therapeutic areas (11,15).

Various medical and surgical treatments are offered for endocrine and non-endocrine involvement according to signs and symptoms. Corrective surgery can be performed for bone dysplasia. Recently, bisphosphonate therapy has shown promise for fibrous dysplasia patients as it

helps to diminish pain, prevents fracture and leads to partial resolution of fibrous dysplasia lesions (16).

Conclusion

The precocious puberty can also be an early manifestation of McCune-Albright syndrome and the etiologic diagnosis of early sexual precocity is based on careful history and physical examination.

Children with precocious puberty should be evaluated for endocrinopathies and hormonal studies may be necessary in such cases.

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