Case Report

Radioiodine treatment in McCune–Albright syndrome with hyperthyroidism

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ABSTRACT

McCune–Albright syndrome (MAS) is a sporadic disease characterized by polyostotic fibrous dysplasia, "café-au-lait" spots and hyperfunctional endocrinopathies. Pathophysiological basis is activating mutation of the gene that encodes the alpha subunit of Gs membrane protein that stimulates the intracellular production of cAMP, conferring autonomous secretion of the gland in particular. One of the uncommon endocrine manifestations is hyperthyroidism. We present a patient who had café-au-lait spots, polyostotic fibrous dysplasia and hyperthyroidism. She was treated with radioactive iodine for the symptoms of hyperthyroidism and subsequently relieved from hyperthyroid features.

Key words: Fibrous dysplasia, hyperthyroidism, McCune–Albright syndrome, radioiodine

Introduction

McCune–Albright syndrome (MAS) is a rare sporadic disorder with an estimated prevalence between 1/100,000 and 1/1,000,000,[1] characterized by the triad of polyostotic fibrous dysplasia (FD), café-au-lait maculae and hyperfunctional endocrinopathies.[2,3] Hyperfunctioning endocrinopathies include hypercortisolism, hypersomatotropism, hypophosphatemic rickets and hyperthyroidism. The association of hyperthyroidism with polyostotic FD is uncommon.[4] We report another rare case who had FD and precocious puberty with hyperthyroidism and was treated with radioiodine, adding to the existing literature[5] that documents only six instances of radioablation in MAS.

Case Report

A 7-year-old female child presented with precocious menstruation, café-au-lait spots and breast development since last 2 years. She had complaints of sweating, palpitation, heat intolerance. No family history of such disorder was found. On examination, apart from café-au-lait spots, prominent breasts and mild facial asymmetry, she had raised pulse rate of 110/min and diffuse enlargement of both lobes of the thyroid gland. There was no history of headache or loss of vision. On investigation, serum biochemistry and hemogram were within normal limits. Thyroid function tests showed the following results: T3: 221 ng/dl (normal 60–181 ng/dl); T4: 7.9 μg/dl (normal 4.5–12.6 μg/dl) and thyroid stimulating hormone (TSH): 0.12 μIU/ml. TSH at the time of radioiodine treatment was 0.01 μIU/ml. Thyoird microsomal antibody (TMA) was negative. Serum prolactin was 44.91 ng/ml (normal 4.79–23.3 ng/ml), testosterone 43.65 pg/ml (normal 12.5–166 pg/ml), luteinizing hormone (LH) ≤0.07 μIU/ml (normal 0.1–6 μIU/ml), follicle stimulating hormone (FSH) ≤0.1 mIU/ml (normal 3.5–12.4), estradiol 43.65 pg/ml (normal 12.5–16.6 pg/ml), and parathormone (PTH) 42 pg/ml (normal 15–68 pg/ml). Growth hormone (GH) measured 4.98 ng/ml (normal up to 13 ng/ml), insulin-like growth factor 1 (IGF-1) was 460 ng/ml (normal 57–316 ng/ml), and serum 25(OH)2 vitamin D3 level was 48.54 nmol/l (normal 47–144 nmol/l).

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Serum cortisol at 0800 hours was 569 nmol/l (normal 171–536 nmol/l) and adrenocorticotropic hormone (ACTH; taken at the same time) was <1.35 pg/ml. X-ray showed multiple ground glass opacities with lytic and sclerotic areas in long bones and skull bones [Figure 1]. Ultrasonography (USG) of the abdomen revealed left-sided ovarian cyst. Computed tomography (CT) of the abdomen revealed mesenteric lymphadenopathy, with no abnormality in adrenal glands. Magnetic resonance imaging (MRI) showed altered signal intensity lesion expanding the sphenoid bone, bilateral frontal and left maxilla with normal pituitary gland. Tc99m-Methylene Diphosphonate (MDP) bone scan revealed intensely increased tracer uptake in the frontal bone, left maxilla, left side of mandible, left humerus, radius, shaft of both femur and tibia [Figure 1]. Radioactive iodine-131 uptake (RAIU) by the thyroid gland at 24 hours was 44.3% and Tc99m-pertechnetate scan revealed diffusely enlarged thyroid gland with increased trapping function [Figure 2]. She was treated with 5 mCi of radioiodine (empirical dose) along with Inj. Zoledronic acid, Depoprovera and tab. letrozole. On follow-up at 3 months, the patient improved symptomatically and the thyroid function tests were within normal limit: T3: 1.74 ng/ml (normal 0.8–2 ng/ml); T4: 8.92 μg/dl (normal 4.8–12.7 μg/dl) and TSH: 2.9 μIU/ml (normal 0.27–4.2 μIU/ml).

Discussion

In MAS, thyroid diseases range from subclinical hyperthyroidism to frank hyperthyroidism with goiter. Sallum *et al*.,[5] in their review and literature search, reported 85 cases of hyperthyroidism with MAS. Occult T3 toxicosis was also reported by Brogan *et al*.[6] MAS associated thyroidopathies are attributed to post-zygotic activating mutation of cAMP regulating protein, *GNAS1* gene product Gsα, wherein arginine is replaced by another amino acid at position 201.[5,7,8] This leads to constitutive activation of adenylate cyclase, resulting in cAMP overproduction and consequent growth of thyrocytes and hormone hypersecretion.[9] Hyperthyroidism continues unabated as Gsα mutation is persistent. Therefore, preferable mode of treatment for MAS associated hyperthyroidism appears to be total surgical ablation or radioiodine therapy.[4] Literature review[10,11] shows that the remission rates with antithyroid drugs even in Grave's disease are usually less than 30–40% and even lesser (~17%) in pre-pubertal children. Comparatively, 60–90% of children treated with radioiodine therapy are hypothyroid. Children aged 1 year have also been treated with radioiodine.[11] Besides, no case of second malignancy has been reported in the literature so far following treatment with iodine for thyrotoxicosis. Therefore, optimal therapy is either radioiodine therapy or surgery. This child did not have clinical goiter. Therefore, keeping in view the above aspects, radioiodine was advocated for this child.

Hyperthyroidism with or without goiter in the context of MAS is considered rare, but is well described. Thyroid dysfunction here is non-autoimmune. Hyperthyroidism may be initially treated medically with antithyroid drugs. Increased morbidity due to recurrent hyperthyroidism after withdrawal of antithyroid drugs and complications during surgical removal necessitate ablation with radioactive iodine, the option which is most suitable for definitive management.

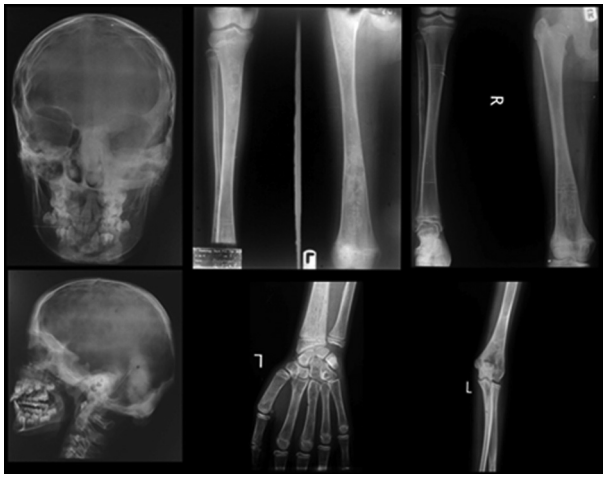

Figure 1: Radiographs of the described patient showing expansion of the diploic space of the left greater wing of sphenoid, body of sphenoid, occiput and the left frontal bone, along with expansion of the meta-diaphyseal region and mixed lytic–sclerotic lesions in the femur and tibia on the left side, expansion of the first metacarpal on the left side, and also in the left humerus and the radius

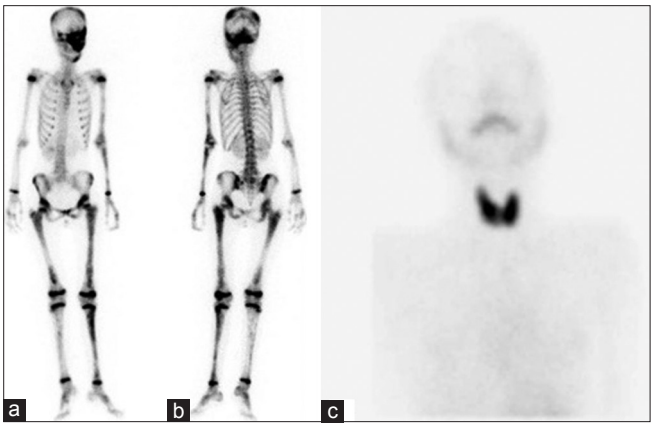

Figure 2: Tc99m-MDP whole body bone scan in (a) anterior and (b) posterior views showing increased osteoblastic activity in the left frontal, sphenoid, maxillary, occipital and bilateral parietal bones along with left humerus, forearm bones, femur on both sides and left tibia. Tc99m pertechnetate thyroid scan (c) of the same patient showing diffusely increased trapping in both lobes of the thyroids

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