A case of metageria with a review of literature

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Progeroid syndromes, one of which is metageria, are characterized by signs of premature aging with multiple systemic and skin symptoms. Here we describe an 8-year-old girl with no history of specific underlying disease in her family, no hair growth at the scalp since she was born, and taller and thinner than her peers. We noticed diffuse subcutaneous fat atrophy. The patient was referred to Sina Hospital, Tabriz because of the appearance of pseudomilia lesions throughout the body following pulse corticosteroid therapy.

Proper and timely diagnosis of progeroid syndromes is important in preventing undesirable side effects. Introducing this case is important as it prevents other patients from undergoing corticosteroid therapy due to misdiagnoses, such as alopecia areata.

Keywords: acrogeria, metageria, progeroid syndromes, Werner syndrome

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INTRODUCTION

Progeroid syndromes comprise of heterogeneous medical conditions with a variety of systemic and skin etiologies that lead to premature aging [1]. Gilchrest identified the cutaneous features of progeroid syndromes as follows: loss of subcutaneous fat, dermal atrophy, alopecia, premature graying of the hair, poikiloderma, persistent cutaneous ulceration, pigmentary aberrations, wrinkling, cutaneous sclerosis, and nail dystrophy. The syndromes are more often than not characterized by these cutaneous findings in dermatology [2–4] none closely mimics the normal aging process. The distribution, specific character, and developmental sequence of pathologic findings diverge from those of normal aging for most organ systems in each syndrome. Furthermore, in each disorder many of the accepted features of normal aging are lacking. These discrepancies are at least as pronounced in the skin as in the other involved organ systems [3].

Progeroid syndromes are divided into several groups based on clinical findings, etiologies, genetic and biochemical markers. The study of progeroid syndromes conduces to a better understanding of the aging process [5].

Metageria is a progeroid syndrome with a high probability of inheritance as an autosomal recessive disease, whose symptoms are observed since birth. These individuals are susceptible to complications, such as atherosclerosis and diabetes mellitus [5].

We present a patient with cutaneous and systemic symptoms mostly consistent with the diagnosis of metageria, although a definite diagnosis occurs with time.

CASE PRESENTATION

An 8-year-old girl, the second child of healthy parents without a family relationship, and the result of a normal full-term delivery, with a normal mental

capacity was referred to our clinic. The first child of the family did not have any diseases. The second child had no hair growth on her scalp or eyebrows from birth. The patient underwent triamcinolone 20 mg therapy per month for six months, following a diagnosis of alopecia areata universalis prior to referral to the dermatology clinic at Sina Hospital. Pseudomilia lesions appeared around the body and corticosteroid use was discontinued, resulting in her referral to the clinic. The child was taller and thinner than her age group.

Clinical Findings

In the examination, her height was 132cm and her weight was 24kg. The patient had prominent eyes, a normal nose, and a normal voice. However, there was a remarkable generalized loss of subcutaneous fat, leading to prominent subcutaneous vasculature through the skin, especially on the scalp. There was no hair on the scalp, and fine and scattered hair in the eyebrows and eyelashes. There were pseudomilia lesions throughout the body with a larger number on the face. Telangiectasias were located behind the patient's neck (Figure 1).

In examining her teeth, there were mild cavities in the milk teeth, but the growing permanent teeth in the maxillary and mandible were normal. No heart murmur was found in the cardiovascular examination, blood pressure was normal, and the pulses of all four limbs were found with no abnormal findings. The thyroid gland was not examined, but the genital examination was normal for the age. Moreover, there was no deformity in the organs or joints of the fingers and no evidence of ulceration.

There were no positive findings in the paraclinical studies. Complete blood count, fasting blood sugar (FBS), 2 hours post prandial blood sugar (2hpp), insulin level and erythrocyte sedimentation rate were all normal.

Her lipid profile, tyroid function tests, and liver

Table 1. Clinical manifestations of metageria, acrogeria and pangeria (Werner syndrome) compared to our patient's signs and symptoms [6,13]

	Our Patient	Metageria	Acrogeria	Werner syndrome
Inheritance	Cannot exclude new mutation	AR	AR, AD	AR, AD
Gender ratio	.....	F=M	F>M	F=M
Onset	Birth	Birth	Birth	Second decade
Stature	Tall and thin	Tall and thin	Normal	Small stature
Face	Normal	Beaked nose, pinched face	Micrognathia, atrophy of skin on tip of nose	Beaked nose
Skin	Generalized atrophy, telangiectasias	Atrophy on limbs, mottled hyper-pigmentation, telangiectasia	Atrophic with telangiectasias and mottled hyper-pigmentation on extremities	Dry atrophic skin, Mottled hyper-pigmentation, telangiectasia
Scalp hair	Alopecia	Fine and thin	Normal	Premature graying ~20 yr, loss of hair ~20-25yr
Eyes	Prominent	Prominent	Normal	Bilateral juvenile cataracts, keratopathy, glaucoma
Nails	Normal	Normal	Dystrophic, thickening	±Dystrophy
Limbs	Loss of sub-cutaneous fat	Generalized loss of subcutaneous fat, one case of leg ulcers	No leg ulcers	Lower limb ulcers, generalized loss of subcutaneous fat
Cardio-vascular	N/A	premature atherosclerosis	Normal	Atherosclerosis, vascular calcification, CAD
Skeletal	Normal	Normal	Normal	Osteoporosis, soft tissue calcification
Metabolic	N/A	Early onset of diabetes mellitus	Normal	Mild mature onset diabetes mellitus
Prognosis	.....	Dependent on severity of diabetes mellitus and atherosclerosis	Normal lifespan	Hypogonadism

N/A =not applicable, F= female, M= male, CAD= coronary artery disease, AR= autosomal recessive, AD= autosomal dominant

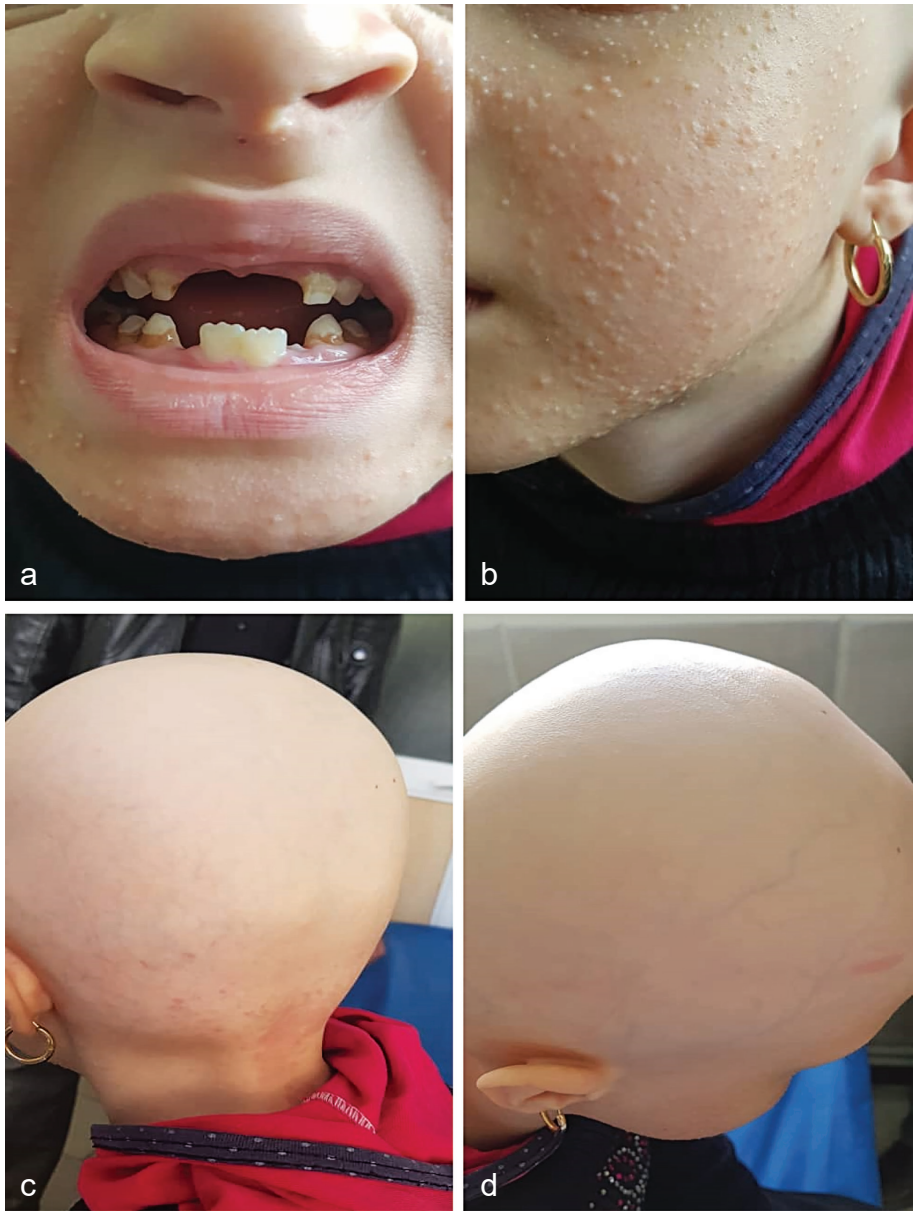

Figure 1. (a) Shape of the teeth, (b) Pseudomilia lesions on the face and fine hair of eyebrows and eyelashes, (c) Telangiectasias behind the neck (d) Prominent subcutaneous vasculature through the skin, especially on the scalp as a result of subcutaneous fat loss.

function tests were also normal.

The corticosteroid was discontinued to resolve the patient's current problem, and topical tretinoin with sunscreen was prescribed for her skin lesions.

DISCUSSION

Metageria was first identified as a premature aging syndrome by Gilkes et al, in 1974, who described two patients with the following characteristics: thin birdlike faces, beaked noses, staring eyes, acral cutaneous atrophy, generalized absence of subcutaneous fat, telangiectasias and mottled hyperpigmentation, fine scalp hair, normal sexual maturity, and early-onset diabetes, all observed from birth [6]. To date, patients suspected of having a premature aging syndrome have been diagnosed on the basis of criteria such as skin morphology, age of onset, metabolic disorders (diabetes mellitus, accelerated atherosclerosis, hypogonadism), and height [6]. Based on these criteria, our patient is compatible with a metageria diagnosis due to skin changes in the form of subcutaneous fat loss, cutaneous atrophy,

telangiectasias, alopecia and symptoms from birth. Progeroid syndromes have certain symptoms in common that can be confused in differential diagnoses. In Werner syndrome, such symptoms as cutaneous atrophy, loss of subcutaneous fat, loss of hair, premature atherosclerosis, diabetes mellitus, and hypogonadism are observed.

Acrogeria is one of the differential diagnoses of metageria reported as acrometageria in some cases due to the lack of differentiation between the two [10]. Symptoms that differentiate metageria from acrometageria [11] are generalized skin changes and lack of subcutaneous fat due to diabetes mellitus and early atherosclerosis. In our patient, skin changes were generalized. Due to her age, metabolic changes had not yet appeared in the patient, hence the fact that not all criteria were observable. Another differential diagnosis is hypohidrotic ectodermal dysplasia (HED), a hereditary X-linked condition with a phenotype that includes sparse scalp hair, deficiency of the eccrine sweat glands and anodontia or oligodontia with teeth [12]. This differential diagnosis was made in our patient with regards to alopecia and fine hair on eyebrows and eyelashes. However, in metageria, genetic inheritance is of an autosomal recessive type. Our patient had no issue with sweating or the shape and number of teeth. The patient's pseudomilia lesions may be considered as a side effect of corticosteroid pulse treatment.

In metageria, the inheritance of the disease is unknown, yet is thought to be autosomal recessive [13]. There was no history of the same problem and no particular diseases running in the family of our patient.

Ophthalmologic examinations should be performed in cases of metageria. A certain study found hyperopia and vitreous body adherence in the right eye of the patient [14].

There was no thyroid abnormality in our patient, whereas late hypothyroidism was diagnosed in a patient with features consistent with metageria reported by Kaufmann et al. [11]. Therefore, thyroid function tests should be considered for future follow-up examination.

Patients with metageria have a higher risk of developing diabetes mellitus, and since the prognosis of the disease depends on the severity of diabetes and atherosclerosis [6,13] periodic tests in terms of FBS and 2hpp have to be done at specified intervals. Regarding the possibility of treatment-resistant ulceration in metageria, which has even led to amputation in some cases [6], it is important to pay attention to the presence of any wound in pressure areas and to provide adequate care and use appropriate shoe pads to prevent progeroid complications [15].

CONCLUSION

Introducing our patient conduces to preventing similar patients from corticosteroid therapy due to misdiagnoses, such as alopecia areata. Proper and timely diagnosis of progeroid syndromes is important for preventing subsequent adverse effects. Further recommended are periodic cardiovascular, neurological and ocular examinations and periodic tests to enable an early treatment of aging symptoms in all patients. In addition to family education, possible complications and required follow-up, children should be psychologically supported. Adhering to a balanced diet and regular use of appropriate sunscreens will help reduce complications. It is recommended that parents undergo genetic counseling prior to another pregnancy.

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Conflict of Interest: None declared.

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