Our Dermatology Online

Case Report

A case report of Apert syndrome with review of literatures

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ABSTRACT

Apert syndrome is a rare syndrome which presents with craniosynostosis, severe syndactyly, and dysmorphic facial features. It is mainly caused by a new mutation in fibroblast growth factor receptor-2 gene. Up-regulation of this gene results in bone fusion and nuclear deficiency of the transcription factor FoxO1 which is a key transcription factor in the pathogenesis of acne. We present herein a 19-year-old man with nodulocystic acne associated with acrocephaly, prominent forehead, ocular hypertelorism, short and broad nose, high arched palate, maxillary hypoplasia, dental crowding and ectopia, severe bilateral syndactyly of the hands and feet. Apert syndrome was diagnosed for him based on mentioned clinical findings. Isotretinoin 20 mg/day was prescribed for nodulocystic acne with significant improvement two months later. Severe acne in early puberty associated with synostosis is the hallmark of Apert syndrome and we should mindful of these syndromic cases in dermatology clinic.

Key words: Apert syndrome; Syndactyly; Acne

INTRODUCTION

Apert syndrome (AS) is a rare acrocephalosyndactyly syndrome presented with craniosynostosis, severe syndactyly, and dysmorphic facial features. It is mainly caused by a new mutation in fibroblast growth factor receptor-2 (FGFR-2) gene on chromosome 10q26 but it may have an autosomal dominant inheritance pattern as well [1-3]. Older fathers have a higher chance of having a child with AS. FGFR2 is transmembrane receptor that mediates single transduction from the extracellular to the intracellular environment. Downstream signaling is important for proliferation, differentiation, and apoptosis. Mutation in FGFR-2 gene could affect the bone formation. FGFR2 gene directs the bones to join together at the right time [3,4].

CASE REPORT

A 19-year-old man with acrocephaly, prominent forehead, ocular hypertelorism, short and broad nose, high arched palate, maxillary hypoplasia, dental crowding and ectopia, severe bilateral syndactyly of hands and feet was referred to our clinic due to severe nodulocystic acne (Figs. 1a – 1d). He had history of recurrent ear infection, sleep apnea and 17 surgeries for his deformities. Family history for syndromic disease was negative. His father was 25 years old at the time of his birth. Diagnosis of AS was confirmed based on physical examination. Isotretinoin 20mg/day was prescribed for treatment of nodulocystic acne. Truncal acne was significantly improved two months later but resolution on the other parts was slower. Laboratory evaluations remained within normal limits throughout the treatment period during six months follow up.

DISCUSSION

Most adolescents with AS are prone to the development of severe facial and truncal pustular acne with extension to the upper limbs. Acne lesions in AS may be resulted from increased sensitivity of sebaceous glands to

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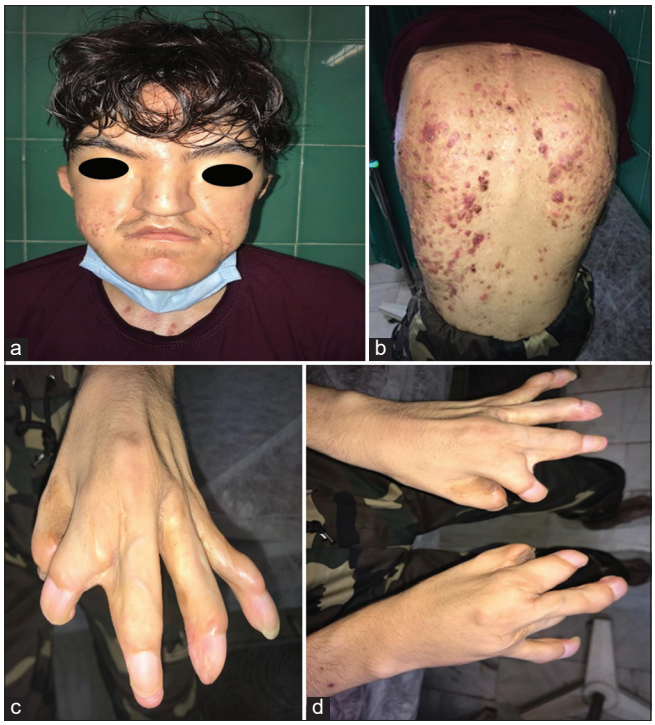

Figure 1: (a) Characteristic face, Craniosynostosis due to premature fusing of skull bones results in skull growing parallel to the suture lines instead of perpendicular growing which causes deformity of skull and face. (b) Truncal nodulocystic acne. (c and d) Fusion of the 2nd, 3rd fingers (Mitten Hands)

normal levels of circulating androgens. There is a hyper-responsibility to androgens, perhaps mediated by keratinocyte growth factor receptors, which also explains premature epiphyseal fusion in AS [5,6].

We found several reports of successful treatment of acne with isotretinoin in AS and it is the treatment of choice for acne in these patients [5-8]. Different dosages have been used and prolonged treatment or repeated drug courses have been necessary in some cases. Occasionally the daily dose of 1 mg/kg or even 1.5 mg/kg is necessary [9-11]. In some other cases, good results were achieved using a daily dose of approximately 0.8mg/kg. Lower therapeutic dosage of isotretinoin should be continued for a longer period of time [11,12] but some authors believe that severe acne in patients with AS should be treated aggressively from the onset. A total dose of at least 120 mg/kg is thought to be necessary in order to minimize post-treatment relapse, but depending on the clinical efficacy of the drug, the treatment must be adjusted in each patient [9-11].

The use of lower dosage is recommended especially for teen-aged patients with AS, but long-term complications of this treatment should be evaluated carefully. Long-term low dose isotretinoin is the treatment of choice for acne in these patients. Retinoids have a counter-balancing role for nuclear deficiency of the transcription factor FoxO1 [10-12].

Our case had sleep apnea and recurrent ear infection which could be caused by mid facial hypoplasia and upper air-way abnormalities [13]. Unfortunately, up to now there has not been a definitive cure for AS and common interventions are surgical procedures for skeletal deformities. The main goal of craniofacial surgery is to allow sufficient brain growing for minimizing proptosis and improving cosmetic appearance [1-3].

In conclusion, severe acne in early puberty associated with synostosis is the hallmark of AS and we should be mindful of these syndromic cases in dermatology clinic. Investigation of incriminated genes involved in these syndromic cases could help for better understanding of acne pathogenesis.

Consent

The examination of the patient was conducted according to the principles of the Declaration of Helsinki. This case report was approved by ethics committee of Guilan University of medical sciences (IR.GUMS.REC.1400.018).

The authors certify that they have obtained all appropriate patient consent forms, in which the patients gave their consent for images and other clinical information to be included in the journal. The patients understand that their names and initials will not be published and due effort will be made to conceal their identity, but that anonymity cannot be guaranteed.

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