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BRIEF REPORT

Novel *PTCH1* Gene Mutation in a Patient with Gorlin–Goltz Syndrome

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Dear Editor:

Gorlin–Goltz syndrome (GGS) is a rare hereditary disorder with autosomal dominant (AD) inheritance[1]. Here, we report a de novo novel *PTCH1* gene mutation in a female patient with multiple BCC.

A 21-year-old female patient was admitted to the dermatology outpatient clinic of a tertiary hospital for brown, papular lesions located in the axillary region and back. The lesions started from the right axillary region and spread to the patient's body. Patient's family did not have similar lesions or complaints. The patient had a typical dysmorphic face and mild mandibular prognathism (Fig. 1A). Dermatological examination showed several oval-circular, brown papules, 0.5 to 1 cm in diameter, scattered in both axillary regions and back (Fig. 1B). Full body bone scan revealed cystic lesions in cranial bones. Scapular deformities were also observed (Fig. 1C). Histopathological examination showed ulceration of surface epithelium and groups of basaloid cells with palisading form (Fig. 1D). We received the patient's consent form about publishing all photographic materials. Suprapubic ultrasonography showed fibroma in the ovaries. The central nervous system and skeletal system evaluations were normal. Based on these findings, the patient received the clinical diagnosis of GGS.

Molecular analyses of the patient using whole exome sequencing (Miseq, Illumina, CA, USA) revealed p.Leu852Valfs-Ter54 heterozygous mutation caused by the insertion of 8 nucleotides (c.2553-2554 insGTAAGTCT). The mutation found leads to frameshift mutation and a stop codon at 54th aminoacid position. This mutation is predicted to be probably damaging with a score of 1.000 (sensitivity: 0.00; specificity: 1.00) for HumDiv and with a score of 0.998 (sensitivity: 0.18; specificity: 0.98) at HumVar in silico analyses at Poly-Phen-2[2]. Hence, we for the first time report this mutation in *PTCH1* gene according to genome browsers including Exac browser[3] and dSNP[4], up to the literature. We planned to carry out more comprehensive genetic testing; however, the patient's family refused to participate in further examinations.

GGS is characterized by AD mutations occurring in *PTCH1*, *PTCH2*, and *SUFU* genes at the chromosomal regions of 9q22.32, 1p34.1 and 10q24.32, respectively. PTCH1 is a tumor suppressor gene located on chromosome 9q22.3-q31 and is a receptor for sonic hedgehog which associates with the smoothened protein (SMO) to transduce the hedgehog's proteins signal. Inactivation of the latter is a necessity and insufficient inactivation due to mutations may lead to tumorigenesis[5]. In our patient the represented frameshift mutation has led to stop codon at 54th position after the insertion site (p.Leu582) and hence might produce damaged truncated protein derivative of PTCH1. Therefore, this mutation might be responsible for the malignant clinical findings of the disease in our patient. However, due GGS has an AD trait and variable expressivity is a major feature of the AD diseases we could suggest that

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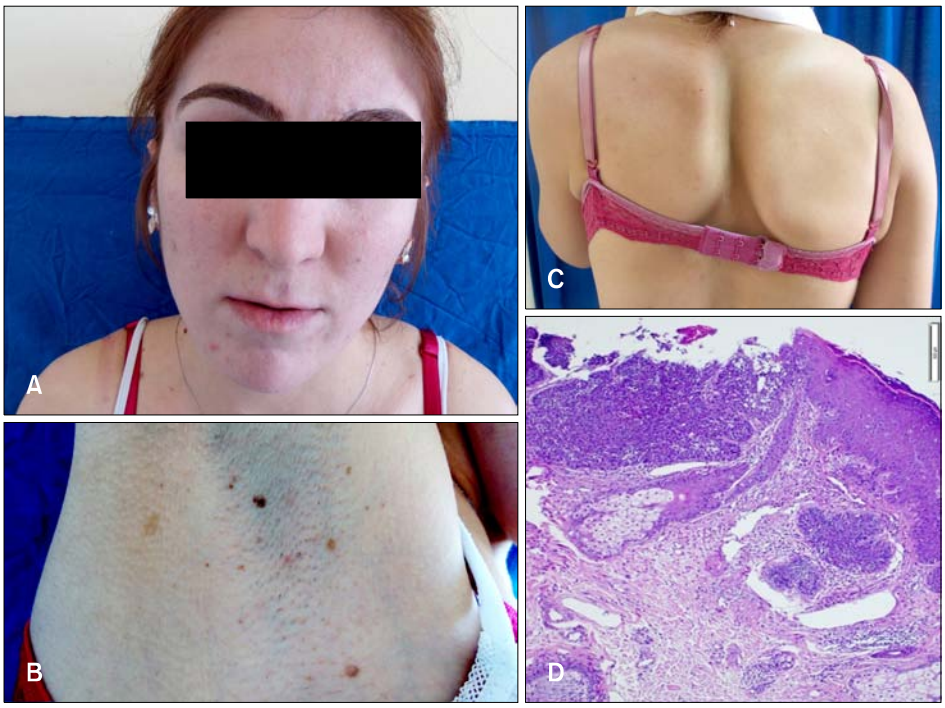

Fig. 1. (A) Dysmorphic face and mild mandibular prognathism. (B) Brown papules in axillary region. (C) Scapular deformity. (D) Ulceration of surface epithelium and basal cells represented peripheral palisades (H&E, ×10).

those clinical variability of the patient could be explained by variable expressivity that might be prone to this novel mutation.

In conclusion, GGS is a rare hereditary disease. Confirmation of GGS diagnosis with molecular and genetic analyses ensures that patients receive better clinical follow up, and make it possible to provide genetic counseling to families of affected patients.

CONFLICTS OF INTEREST

The authors have nothing to disclose.

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