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Conradi-Hünermann-Happle Syndrome Misdiagnosed as Rud's Syndrome in Korea

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Dear Editor:

During preparing the first international symposium of mosaic disorders in pediatric dermatology in 2014, we had reviewed almost all reported articles about mosaic skin disorders in Korea. At that time, we had noticed one and only case report of Rud's syndrome[1].

In this case report, the patient was 16-year-old Korea girl who presented with lamellar ichthyosis in mosaic pattern, mental retardation, hypogonadism, short stature, alopecia, sparse eyebrows, strabismus, cataracts, and congenital dislocation of the hip. The patient was diagnosed as Rud's syndrome with clinical triad of ichthyosis, mental retardation and hypogonadism.

In 2012, Rudolf Happle revealed that Rud's syndrome does not exist[2]. In his article, he reminded the original description of two cases by Einar Rud in 1927 and 1929 and concluded that there was no nosological entity that could be called Rud's syndrome and this disorder is not memorable for dermatologists and has just literally been "lost in translation"[2].

Then, what is the correct diagnosis of only one Korean case of Rud's syndrome?

We think this patient's condition should be included in the spectrum of chodrodysplasia punctata.

The patient has left sided bony abnormality, ocular abnormalities including cataracts and strabismus and then the patient may have normal life expectancy.

In spectrum of chondrodysplasia punctata, the correct diagnosis of the patient may be Conradi-Hünermann-Happle (CHH) syndrome.

CHH syndrome is rare genodermatosis (Online Mendelian Inheritance in Man no. 302960) that primarily affects the skin, bones, and eyes[3]. Annual incidence has been estimated to be at least 1/400,000 birth with 95% of patients being female[4]. Cutaneous lesions have been observed in more than 95% of cases and usually are present at birth as erythroderma with Blaschkolinear ichthyosiform lesions that fade over time[3]. Other cutaneous findings are follicular atrophoderma and patchy-patterned alopecia. CHH syndrome typically features chondrodysplasia punctata (punctuate calcifications of the epiphyseal regions) and can be associated with asymmetric shortening of long bones, scoliosis, and congenital hip dislocation[3-5]. Cataract is the main ocular symptom and is described in about 60% of reported cases. Lyonization explains the clinical presentation with cutaneous findings following Blaschko lines, cataracts and asymmetrical bone lesions. Definite diagnosis can be made using DNA analysis, confirming the X-linked dominant mutation in the emopamil binding protein gene at Xp11.22-23[5].

Although this case was not an example of a DNA-confirmed diagnosis, her clinical manifestations were consistent with CHH syndrome. We cannot find reported cases with CHH syndrome in Korean literatures. Perhaps the case diagnosed with Rud's syndrome in 2000 may be the first reported case with CHH syndrome in Korea.

There may be more misdiagnosed orphan patients with CHH syndrome in Korea. We expect to see CHH syndrome confirmed with DNA analysis in Korea near future.

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CONFLICTS OF INTEREST

The authors have nothing to disclose.

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Increased Immunoreactivity of LGR4 in Histologically Aggressive Basal Cell Carcinoma

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Dear Editor:

Sir, Basal cell carcinoma (BCC) is the most common malignant tumor of the skin. BCC is locally invasive and highly destructive, but rarely metastasizes[1]. Identification of the pathogenic mechanisms underlying BCC could facilitate treatment and prevention of this cancer. It is generally accepted that BCC arises from keratinocyte stem cells[2], but its biological mechanisms, including those of its carcinogenesis, remain unknown. Leucine-rich repeat-containing G-protein-coupled receptor (LGR4) is expressed in proliferating tissues, including stem cells[3]. LGR4 was reported to be expressed in the epidermis and hair follicles of human skin[4]. Recently, it was reported that LGR4 promoted skin carcinogenesis by mediating the activation of MEK1/ERK1/2 and Wnt/β-catenin pathways in mouse model[5]. To our knowledge, no study has addressed LGR4 expression in BCC. In this study, we investigated the expression and localization of LGR4 in BCC via immunohistochemical analysis.

This study was approved by the ethics committee of The Catholic University of Korea (no. XC14SIMI0060K). All patients gave written informed consent. A total of 46 biopsy specimens that had been diagnosed as BCCs were collected from the three branch hospitals of The Catholic University of Korea. Paraffin sections of BCCs (total, n=47: including nodular [n=19], superficial [n=10], micro-

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