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Letter to the editor

A case of dyskeratosis congenita associated with hypothyroidism and hypogonadism

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Dear Sir,

Dyskeratosis congenita is a very rare multisystemic disorder and it can be accompanied by different endocrinological pathologies. We would like to draw attention to this rare disease by reporting a case diagnosed as dyskeratosis congenita. More specifically, a 30-year-old male patient was referred with the findings of micropenis and atrophic testicles. His parents had cousin marriage. His elder brother had similar symptoms. There were hypopigmented skin lesions over his entire body. The skin was dry and the nails were dystrophic (Figure 1A). His axillary hair and pubic hair were normal but his facial hair was sparse. He had alopecia in the outer third of his eyebrows (Omnibus sign) and a saddle nose (Figure 1B, C). Micropenis was present and the testicles were found to be hypoplastic (left testicle: 11x5mm, right testicle: 10x5mm). Laboratory findings: WBC: 3140/mm^3, neutrophil: 1740/mm^3, Hb: 12.5gr/dL, plt: 187000/mm^3, free testosterone: 1.4pg/mL (8.69-54.69), total testosterone: 0.70ng/mL (1.75-7.81), FSH: 77.28mIU (1.7-19.2), LH: 15.38mIU (1.24-8.62), free T3: 3.35pg/ml (2.3-4.2), free T4: 0.98ng/dl (0.74-1.52), TSH: 10.88µIU/ml (0.35-5.50). Hypergonadotropic hypogonadism was suspected. Hyperkeratosis keratoderma

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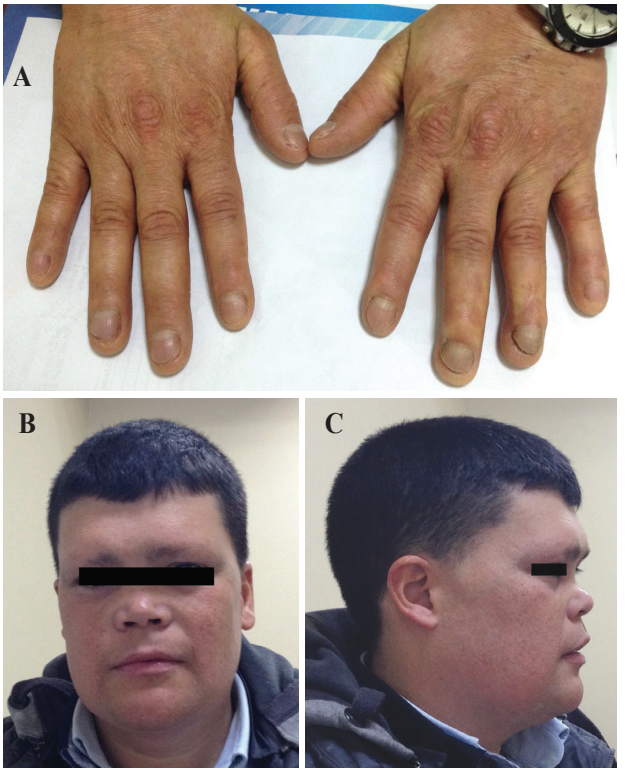

Figure 1. (a) Dystrophic nail image of our case with dyskeratosis congenita; (b) Anterior view of omnibus sign and saddle nose; (c) lateral view of omnibus sign and saddle nose.

was found in his skin biopsy while the biopsy of the lymph node from the right cervical area revealed a granulomatous lymphadenitis. (Figure 2A, B, C). The final diagnosis of dyskeratosis congenita (DC) was based on the clinical and histopathological findings. His family history was negative for DC.

Dyskeratosis congenita is an uncommon multisystemic genetic disorder. It was first described by Zinsser in 1906 and is also known as Zinsser-Cole-Engman syndrome.[1] It usually shows an X-linked recessive inheritance; however, autosomal dominant and recessive forms have also been identified. Ten different genes (DKC1, TERC, TERT, TINF2, WRAP53, NOP10, NHP2, CTC1, RTEL1 and ACD) are associated with DC. Mutations in these genes lead to telomere shortening.[2] DC is characterized by the presence of two of four major clinical features (skin pigmentation, nail dystrophy, leukoplakia and bone marrow failure) or the coexistence of two or more other findings with one major clinical feature (lung diseases, tooth abnormalities, sparse hair, omnibus sign, malignancy, intrauterine growth restriction, liver diseases, peptic ulcus, enteropathy, ataxia, hypogonadism, microcephaly, urethral stricture, osteoporosis, aseptic necrosis, scoliosis, deafness).[3] Bone marrow failure, lung involvement and tendency to develop malignancy are the main complications leading to mortality. Bone marrow failure often presents in the 2nd or 3rd decades; however, it may also be observed in the newborn period or the 6th and 7th decades. There may be a reduction in the number of red and white blood cells or platelets or a reduction in all blood cell types (pancytopenia).[4] Our patient's main complaints were micropenis and atrophic testicles. He was diagnosed with hypergonadotropic hypogonadism. Presence or absence of other coexisting syndromes was investigated. Typical features of Klinefelter syndrome such as tall stature and gynecomastia were not present in our case. The karyotype analysis showed 46XY, thus excluding Klinefelter syndrome. Similarly, our case did not have the features of Noonan syndrome, such as triangular face shape, mental retardation and congenital heart defect. Our patient had hypogonadism, hypothyroidism, dry skin, dystrophic nails (Figure 1A), skin pigmentations, tooth abnormality, scoliosis, omnibus sign and saddle nose (Figure 1B, C), lung disease and bicytopenia. Syphilis was investigated due to the patient's saddle nose but was not found. Likewise, leprosy was excluded after our investigation owing to the presence of omnibus sign and granulomatous lymphadenitis. Mycological evaluation did not show any positive result as regards nail dystrophies. Tendency to develop malignancy is one of the known characteristics of DC. Since our patient had anemia and leucopenia, bone marrow biopsy was performed but

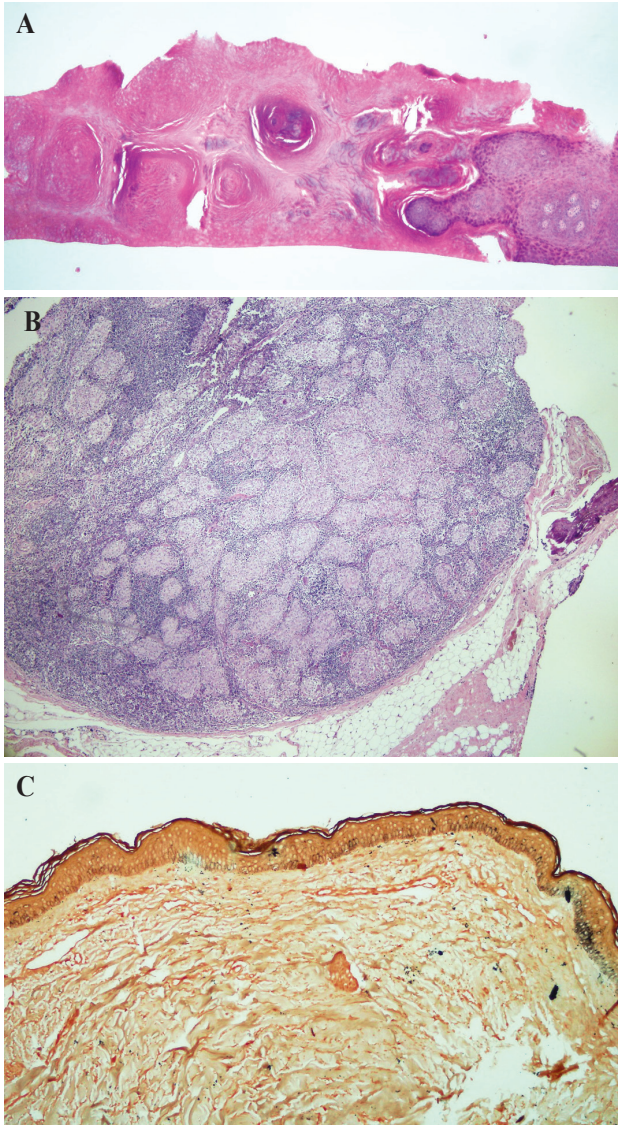

Figure 2. (a) Thick hyperkeratosis appearance of the skin (H&E ×20); (b) disseminated histiocytic proliferation that changes the normal appearance of lymph node and granulomas that are characterized by rare giant cell formation (H&E ×40); (c) appearance of melanin pigmentation on the skin (Fontana-Masson ×40).

no malignancy was detected. Nevertheless, the patient will be followed up because of bone marrow failure. As numerous swollen lymph nodes were detected with full-body CT scan, cervical lympadenopathy biopsy was performed and granulomatous lymphadenitis was reported. Sarcoidosis was excluded.

In conclusion, the diagnosis of DC was established in our patient on the basis of all clinical and laboratory findings. Unfortunately, no molecular genetic testing was performed. DC is an uncommon multisystemic genetic disorder of which skin pigmentation, nail dystrophy, leukoplakia and bone marrow failure are the major clinical features. Bone marrow failure, lung involvement and tendency to develop malignancy are the main complications leading to mortality. Hypergonadotropic hypogonadism is one of the minor criteria for DC. Based on the above, the endocrinological evaluation should be performed with particular care. To the best of our knowledge, there has been no case report showing DC associated with hypogonadism and hypothyroidism, and our aim has been to bring this association to clinicians' attention.

CONFLICT OF INTEREST

The authors do not have any conflict of interest.

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