Dyskeratosis congenita (DC), otherwise known as Zinsser-Engman Cole Syndrome is associated with the mucocutaneous triad of nail dystrophy, oral leukoplakia and abnormal reticulate skin pigmentation. Ninety percent present with nail dystrophy initially affecting the fingernails followed by the toenails. It may begin with nail ridging and longitudinal splitting resulting in small or absent nails. Eighty percent of affected individuals present with mucosal leukoplakia which is a pathognomonic feature involving the buccal mucosa, tongue, and oropharynx. Noncutaneous abnormalities may also be observed in the gastrointestinal, genitourinary, neurological, ophthalmic and skeletal systems.

In 1995, a dyskeratosis congenita registry was done wherein majority of affected individuals were male which suggested an X-linked inheritance. However, further studies show that it may also be autosomal dominant or autosomal recessive. For the X-linked type, the gene abnormality has been identified as DKC1 which maps to Xq28 leading to the encoding of dyskerin which plays a vital role in telomere maintenance and ribosomal biogenesis. It has an overall incidence of less than 1 in 1 million presenting with a variety of clinical manifestations. According to the Philippine Dermatologic Society Health Information System (PDS-HIS) central data from 2011 and 2017, there have only been 2 reported cases of DC with both cases in the pediatric age range.

We report a 28-year-old male who was referred to our department due to generalized reticulated pigmentation of the skin. Twenty-two years prior to consult (PTC), he was noted to present with hyperpigmented macules admixed with hypopigmented macules initially noted on the upper extremities which later on spread onto the face, trunk and lower extremities. Ten years PTC, the patient noted longitudinal ridging and nail splitting initially on the fingernails followed by the toenails. Five years PTC, he noted loss of ridging on the palmar aspect with hyperhidrosis.

Due to the persistence of symptoms he was referred to our institution for evaluation and management. Review of systems show epiphora and history of back pain.

Birth history revealed that the patient was born full-term via normal spontaneous delivery at a lying-in clinic to a then 25-year-old G2P2(2002) mother who had no illnesses or complications. The mother had regular prenatal check-ups.

He had no developmental delay or any learning difficulties which was later confirmed by his mother. No similar lesions noted in the family nor any familial history of delayed gross motor, fine motor, language and social skills. Family history was unremarkable and no other relatives were reported with the similar lesions nor any history of immunodeficiency diseases, pulmonary fibrosis, liver disease, bone marrow failure or leukemia or malignancy (Figure 2). There is no history of consanguinity in the

Figure 1. (A) Oral Leukoplakia (B) Reticulate Skin Pigmentation (C) Nail dystrophy
Pertinent findings in the physical examination revealed generalized reticulated skin pigmentation, palmoplantar keratoderma and oral leukoplakia (Figure 1). Dermoscopy showed irregularly-shaped and unevenly distributed pigmented lines and dots with hypopigmented holes (Figure 3B). This is similar to a previously reported case wherein dermoscopy revealed “a net-like distribution of pigmented skin consisting of pigmented ‘‘lines,’’ hypopigmented ‘‘holes,’’ and diffuse reddish pigmentation in the pigmented lines.” Dermoscopy also confirmed findings of adermatoglyphia on all fingers (Figure 3A). Ophthalmologic findings showed lacrimal duct stenosis on both eyes. Nail findings show longitudinal ridging and nail splitting (Figure 1C).

Ancillary tests like complete blood count (CBC) revealed thrombocytopenia. Renal and liver function tests, serum electrolytes, and reticulocyte count were unremarkable. Chest radiograph showed hazy densities on both upper lung fields. Lumbosacral x-ray revealed mild compression fracture at L1. Skin punch biopsy was done on his back revealing orthokeratotic basket-woven stratum corneum overlying an atrophic epidermis with focal basal vacuolar changes. The dermis reveals a mild perivascular predominantly lymphocytic inflammatory infiltrate with scattered melanophages (Figure 4). This is similar to the histopathologic findings found in diagnosed DC cases showing epidermal atrophy, melanocytes in the dermis and conspicuous inflammatory cells.

Genetic study for a rare type of Autosomal Recessive Ectodermal dysplasia was done due to the similarities in clinical findings and the rarity of the case. The result showed no potentially pathogenetic mutations found after entire coding region as well as the intron/exon boundaries of GRHL2 has been sequenced.

Ideally, telomere length testing should be done to confirm the diagnosis wherein a finding of short telomere length across all cell types (i.e, granulocytes, naïve T-cells, memory T-cells, memory B-cells, and NK/NKT cells) at length less than the first percentile for age. Another ideal test for confirmation would be genetic sequencing for DKC1, TINF2, TERT, TERC, WRAP53 (TCAB1), NOP10, NPH2, RTE1L1, CTC1, ACD and PARN. However, these were not available in the Philippines. The diagnosis was based on the clinical features of the case.

The diagnosis of DC is based on presentation of the mucocutaneous triad. The patient presents with nail dystrophy, oral leukoplakia and reticulate skin pigmentation. Other features include: 1) bone marrow failure, 2) growth delay, 3) developmental delay, 4) neurologic manifestations (e.g. cerebellar hypoplasia), 5) ophthalmologic manifestations (e.g. epiphora due to lacrimal duct stenosis, blepharitis, retinal hemorrhages), 6) hearing loss, 7) dental involvement (e.g. extensive caries, taurodontism or enlarged pulp chambers), 8) lung involvement (e.g. pulmonary fibrosis), 9) gastrointestinal tract and liver involvement (e.g. dysphagia, upper abdominal pain, jaundice, biliary atresia, congenital hepatic fibrosis).

Figure 2. Diagram showing the patient’s genogram.

Figure 3. Dermoscopy findings (A) Adermatoglyphia on second finger (B) Hypopigmented holes and pigmented lines on skin
gastrointestinal bleeding), 10) genitourinary involvement (e.g. urethral stricture, phimosis), 11) musculoskeletal and endocrine disease (e.g. hip or back pain due to osteoporosis or avascular necrosis), 12) other mucocutaneous findings (e.g. adermatoglyphia, atrophy of dermal papillae, patchy alopecia).

The principal cause of early mortality is bone marrow failure which is noted to affect 80% of affected individuals. This is due to the deficient renewing capability of hematopoietic stem cells. Additionally, individuals have an increased predisposition to malignancy and pulmonary fibrosis which may also lead to mortality.

DC is a multisystem disorder requiring the partnership of various subspecialties. The principal cause of premature mortality is bone marrow failure or mortality. However, DC patients may also present with malignancy by the third decade or with lung disease more specifically pulmonary fibrosis. For this patient, further testing is required to evaluate current hematologic, immune and pulmonary status. To monitor for bone marrow failure, the patient is scheduled for bone marrow aspiration and biopsy as well as complete blood count done bi-yearly depending on the findings. To monitor for pulmonary status specifically for pulmonary fibrosis, the patient has also been scheduled for pulmonary function test and has been recommended for high resolution non-contrast computed tomography. To monitor for malignancies, therein plays the multidisciplinary approach wherein annual exams are done by dermatology, ophthalmology, and otorhinolaryngology to monitor for any malignant changes.

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Figure 4. Orthokeratotic basket-woven stratum corneum overlying an atrophic epidermis with focal basal vacuolar changes. The dermis reveals a mild perivascular predominantly lymphocytic inflammatory infiltrate with scattered melanophages. (A) (H & E x40); (B) (H & E x100)