Dear Editor,

Bone marrow aspiration and trephine biopsy were sought for evaluation of pancytopenia in a 22-year-old adolescent male who presented with severe weakness, fatigue, and increasing breathlessness for last 6 months. He had a history of two units of packed whole blood transfusion for the above-mentioned symptoms within the last 6 months before coming to our hospital. Remarkably, he also had a history of peculiar skin pigmentation and scalp hair loss and graying, which started when he was 10 years of age. He also had a complaint of occasional loose motions and passing black stool twice in the last month. Physical examination revealed a thin built male with marked conjunctival pallor. There was no edema, clubbing, icterus, lymphadenopathy, hepatosplenomegaly, or sternal tenderness. Skin examination revealed reticulated (hyper- and hypopigmented) macules all over the body, including the palms, soles, and forehead. There was a uniform and marked dystrophy of finger and toe nails. He had gray scalp hairs and sparse eye lashes, predominantly noted on the lateral aspects. Oral examination revealed dental carries and leucoplaikic patches involving dorsum of the tongue and the hard palate (Figure 1a-g). His systemic examinations were within normal limits, and radiological evaluation did not show any skeletal abnormalities. He was born to non-consanguineous parents, had normal milestones of development, and had no family history of a similar complaint.

The routine hemogram showed microcytic hypochromic anemia (hemoglobin: 36 g/L, mean corpuscular volume: 70 fL, serum ferritin: 14 ng/mL [ref: 150-450 ng/mL]), total leukocyte count: 3x10^9/L with normal differential; absolute neutrophil count: 1.8x10^9/L; total platelet count: 22x10^9/L; corrected reticulocyte count: 0.6%; and no abnormal cells in the peripheral blood smear. His stool occult blood test was positive. Upper gastrointestinal endoscopy revealed an antral ulceroproliferative growth that on histopathological examination was consistent with intestinal type adenocarcinoma. The adjoining gastric mucosa showed atrophy and cystic change with loss of parietal cells, and focal pyloric-type metaplasia. The lamina propria showed pauci-cellularity, patchy hyalinization, and fibrosis. There was no evidence of Helicobacter pylori-associated inflammation, activity, or intestinal metaplasia. The proliferative index (Mib-1) in the tumorous area was 5% in contrast to total absence in the non-neoplastic mucosa, thus suggesting a replicative senescence. Bone marrow aspiration and trephine biopsy findings were consistent with a diagnosis of severe aplastic anemia (marrow cellularity=20% for age; Figure 2a-g). Thus, clinical presentation in correlation with laboratory findings was consistent with the diagnosis of a genodermatosis with bone marrow failure-dyskeratosis congenita (DKC). The patient and their parents were counseled for further management at a higher center but refused any definite therapy and then lost to follow-up. Informed consent was obtained from the parent of the patient, and the identity of the patient was kept confidential.

Dyskeratosis congenita, bone marrow failure, and gastric adenocarcinoma: an insight into telomere biology

Dyskeratosis congenita or Zinsser-Cole-Engman syndrome is a rare inherited bone marrow failure syndrome (IBMFS) characterized by diagnostic triad of reticulated skin hyperpigmentation, nail dystrophy, and oromucosal leukoplakia (1). DKC is a disease of defective telomere maintenance, and patients with DKC have premature telomere shortening and subsequent replicative senescence, leading to premature stem cell failure, aging, and cancer predisposition. To date, nearly 14 genes have been identified with DKC of which mutation involving DKC1, TERT, TERC, and NOP10 genes account for nearly 65% of all cases. While cutaneous hyperpigmentation and nail changes are the earliest manifestation in DKC, there is increased predilection for bone marrow failure, solid and hematolymphoid malignancies, and pulmonary fibrosis, which constitute
rarely reported (9). The present case demonstrated significant villous atrophy, extensive apoptosis, and anaphase telomere disease in young children (<10 years of age). Esophageal intraepithelial lymphocytosis was extremely common, whereas recurrent enteropathy and enterocolitis with gastrointestinal stenosis at the cervico-thoracic junction, gastric lamina propria fibrosis, atrophic gastritis, parietal cell dropouts, and epithelial cancers, myelodysplastic syndrome, and leukemia (4). An algorithmic approach for the diagnosis of a telomeropathy (DKC) has been suggested by Townsley et al. (10). Accordingly, all subjects with an appropriate personal or family history of aplastic anemia/myelodysplasia/acute leukemia, who present with cytopenias, macrocytosis along with dermatologic triad should undergo bone marrow evaluation (for marrow failure) and peripheral blood stress cytogenetic testing for Fanconi anemia. The diagnosis can then be confirmed by measuring the mean telomere content by flow-fluorescent in-situ hybridization (FISH) in peripheral blood lymphocytes; values less than the first percentile compared with age-matched controls accurately identifies individuals with the likely disease (10).

Dyskeratosis congenita should always be considered as a differential diagnosis for inherited bone marrow failure syndrome and evaluated with cytogenetics and/or telomere studies. To the best of our knowledge, the present case is possibly the sixth case of gastric carcinoma (and first such case with coexistent aplastic anemia) to be reported in patients with such bone marrow failure syndrome.
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Informed Consent: Written informed consent was obtained from the patient who participated in this study.

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REFERENCES


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