An adolescent with dyskeratosis congenita

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Introduction

Dyskeratosis congenita is a genetically and clinically heterogeneous rare disorder with a mean age of survival of approximately 30 years. The muco-cutaneous features usually manifest at the age of 5-15 years. The clinical triad is reticulated hyperpigmentation, nail dystrophy and mucosal leukoplakia[1]. Awareness of the mucocutaneous features which could be a mimic of common disorders as lichen planus or a serious disorder like graft versus host disease is important to detect these cases. Specially in a set up like Sri Lanka where the clinical diagnosis could not be supported by mutational analysis a clinical suspicion of this rare disorder is important as they need frequent follow up to detect complications.

Case report

A 17-year old male presented with progressive abnormality of nail plates for the last 5 years and a persistent ulceration on the tongue for last 3 years. He was having no other systemic symptoms and had no affected family member with similar symptoms, and no history of blood transfusions.

On examination there was mucosal ulceration on lateral sides of tongue with whitish hyperkeratosis on the dorsum (Figure 1). The buccal mucosa was normal. Both toe and finger nails were affected with nail plate thinning, longitudinal splitting and pterigyium formation in some (Figure 2). Additionally he was noted to have a rippled hyperpigmentation on neck, upper chest and palms (Figure 3). There was no atrophy or telengiectasia. There was no alopecia, greying of hair, hyperhidrosis or palomoplantar keratoderma. He had no mental retardation and the systemic examination was normal.

A skin biopsy of a hyperpigmented lesion on neck revealed epidermal atrophy, focal basal cell vacuolation, pigmentory incontinence and mild lymphocytic infiltrate in the dermis. A short course of oral steroids was given to rule out the possibility of lichen planus.

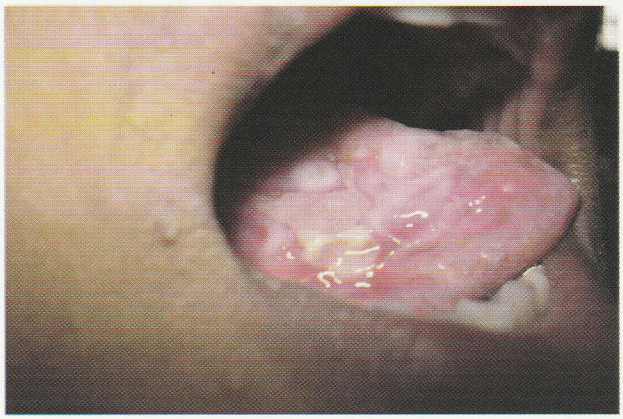

Figure 1.

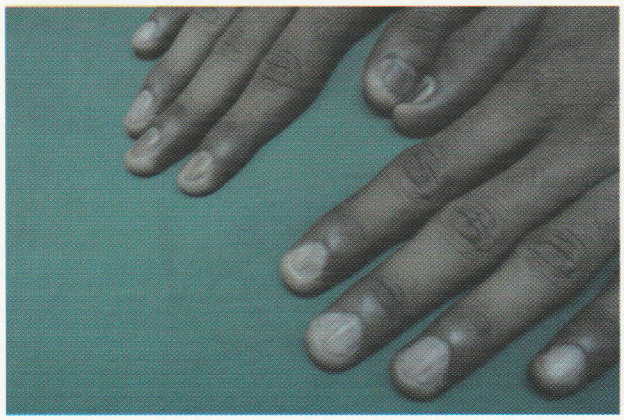

Figure 2.

Figure 3.

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Re-examination after 2 months revealed no change of the cutaneous features. The provisional diagnosis of dyskeratosis congenita was made and further investigations were started. His full blood count revealed cytopenia affecting one cell line, with repeatedly low platelet counts. His stool for occult blood, urine full report and chest X ray were normal. Genetic studies were not done due to unavailability of facilities. A biopsy from the oral lesion was performed to rule out squamous cell carcinoma.

Discussion

Dyskeratosis congenita is a rare genodermatosis with a clinical triad of rippled hyperpigmentation, nail dystrophy and mucosal leukoplakia. The genetic transmission is mostly X linked recessive, which is the severe phenotype but autosomal dominant and recessive forms are also reported[2]. It is believed to be a disorder of mutations in the genes DKC1, TERT, TERC, NOP10, all of which encodes for the proteins in telomerase complex[3]. Telomerase is responsible to add telomere repeats at the ends of chromosomes and prevent chromosome shortening in cell division. Telomere activity is highly prominent in cells with high cell turnover explaining the mucocutaneous and haemopoetic cell involvement in dyskeratosis congenita.

The clinical features usually manifest in the first decade of life. The rippled hyperpigmentation is seen on sun exposed areas and sometimes associated with atrophy and telengiectasia. Other associated cutaneous features can be palmoplantar keratoderma, hyperhidrosis and alopecia of scalp or eye brows[4]. The nail dystrophy is seen on 90% of the cases with nail changes as longitudinal splitting, thinning of the nails, pterygium formation and total loss of nail plates in later stage. Leukoplakia is seen in 80% with ulceration and verrucous lesions involving the buccal mucosa or tongue. Oral leukoplakia is usually evident by mid teens. It can rarely involve the other mucosal surfaces as well.

Our patient demonstrated all three cardinal mucocutaneous features of the disease. The clinical presentation and age of onset can vary greatly even within individuals of the same family[2]. Other non cutaneous feature less commonly associated can affect the neurological system, gastrointestinal tract, eye, lungs and bones.

The disease is known to have a high mortality with deaths occurring due to bone marrow failure in 70%. Bone marrow failure affecting at least one cell line is evident in 85-90% by the age of 30 years and the median age of onset of this is 10 years. Mortality is also associated with pulmonary complications due to lung fibrosis and abnormal pulmonary vasculature. Dyskeratosis is linked with increased risk of malignancies which usually manifest in the third decade. Squamous cell carcinoma occur in the oral cavity or other mucosal surfaces in GI tract, larynx or urethral mucosa mostly over the places of leukoplakia. Additionally malignancies as squamous cell carcinoma of skin, Hodgkin lymphomas, adeno-carcinoma of gastrointestinal tract, bronchial and laryngeal carcinoma are reported.

The histology of rippled hyperpigmented lesions are mostly non specific and interface dermatitis as in our patient is reported[4]. Confirmation of the diagnosis is aided by mutational analysis.

The important aspect in management is frequent follow up and investigations to detect complications. It is important to avoid drugs with pulmonary toxicity in these patients.

Therapeutic options are mostly palliative, but bone marrow and stem cell transplantation have been carried out with variable success[4].

References

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