CASE REPORT

Xeroderma Pigmentosum: Variable Expressions among Three Siblings

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Abstract

Xeroderma pigmentosum is a rare disorder transmitted in an autosomal recessive manner. It is characterized by photosensitivity, pigmentary changes, premature skin aging, and malignant tumor development. The frequency of this disorder is approximately 1 case per 250,000 population. Two important causes of mortality are metastatic malignant melanoma and squamous cell carcinoma. Here xeroderma pigmentosum in three siblings presenting with variable expressions is reported. The severity of the condition was more in one of the more sun exposed sibling and had more signs of malignant lesions. Intraoral pigmentation was also present in all the three siblings.

Keywords: XP, photosensitivity, pigmentary changes, premature skin aging, malignant tumors, defective nucleotide excision repair, siblings.

INTRODUCTION

Xeroderma pigmentosum (XP) was first described in 1874 by Hebra and Kaposi. In 1882 Kaposi coined the term xeroderma pigmentosum for the condition, referring to its characteristic dry, pigmented skin.1 This disorder according to literature1-3 is characterized by pigmentary changes, photophobia, premature skin aging and malignant tumor development usually due to a cellular hypersensitivity to ultraviolet (UV) radiation resulting from a defect in DNA repair. The basic defect in XP is in nucleotide excision repair (NER), leading to deficient repair of DNA damaged by UV radiation. In addition to the defects in the repair genes, UV-B radiation also has immunosuppressive effects that may be involved in the pathogenesis of XP.2,3

The disease typically passes through 3 stages. The skin is healthy at birth. Typically, the first stage makes its appearance after the age of 6 months. This stage is characterized by diffuse erythema, scaling, and freckle like areas of increased pigmentation present on the sun exposed areas beginning on the face and progressing to the lower limbs, the neck, and even the trunk in extreme cases. While these features tend to diminish during the winter months with decreased sun exposure initially, as time passes, these findings become permanent. The second stage is characterized by poikiloderma consisting of skin atrophy, telangiectasias, and mottled hyperpigmentation and hypopigmentation. The third stage is heralded by the appearance of numerous malignancies including squamous cell carcinomas, malignant melanoma, basal cell carcinoma, and fibrosarcoma. These malignancies may occur as early as age 4 to 5 years and are more prevalent in sun-exposed areas.2-4

Here xeroderma pigmentosum in three siblings with variable expressions is reported.

CASE REPORT

A 12-year-old female patient (Figs 1 and 2) came to our hospital with the chief complaint of decayed teeth. She also had dark brown pigmentation all over her face. A positive family history with similar condition in two of her siblings (16-year-old elder sister and 8-year-old younger brother) was elicited. They were born to normal parents with consanguineous marriage.

On examination, multiple, small, dark brown colored lentigines appearing as tanned macules, ranging from 1 to 5 mm in diameter, were distributed mainly on the sun exposed areas with maximum on face, neck and phalanges (Figs 1 and 2). Photophobia was also present. A tender, ulcerated, rapidly growing papule of one year duration was present on her left lower eyelid which bled on slightest manipulation and was suspicious of malignancy (Fig. 3). Both of her siblings were also called and examined. Both of them had similar abnormalities including photophobia. The eldest girl (16-year-old, Figs 1 and 4) had features of poikiloderma including skin atrophy and mottled appearance of hypopigmentation and hyperpigmentation. The youngest boy (8-year-old, Fig. 1) had lentigines diffusely spread all over his face without any crusting or mottling. Intraorally, few lentigines were present on the tip of the tongue in both of her siblings (Fig. 5).
On the basis of history and clinical examination, patients were diagnosed as case of xeroderma pigmentosum for which differential diagnosis included Touraine centrofacial lentigogenesis, LEOPARD syndrome, LAMB syndrome, Nageli syndrome, Peutz jeghers syndrome, Tuberous sclerosis and Neurofibromatosis.

Biopsy of the lentigines was performed (Fig. 6) and the histological examination showed increased melanin synthesis in the basal layer of epithelium (Fig. 7).

Patients were motivated to avoid exposure to sunlight. Sun screens were prescribed to the patients along with bleaching creams and lubricating eye drops. All the decayed teeth of middle girl were restored. Patients were advised to maintain proper oral hygiene by use of various chemical and mechanical plaque control agents. Ophthalmic examination was done for the patients which showed presence of photophobia and corneal opacities. Neurological consultation was also done which showed no abnormalities. The middle...
girl was also advised for biopsy and surgical excision of suspicious malignancy which she refused. Topical antiseptic creams were then prescribed after which her lesion reduced in size. Genetic counseling was done for the family. Patients are under regular follow-up and care.

**DISCUSSION**

Xeroderma pigmentosum is a rare disorder transmitted in an autosomal recessive manner. The frequency is approximately 1 case per 250,000 population. An equal incidence has been reported in males and females. A history of consanguinity may be elicited as in our case.2,3

Individuals with XP are at an increased risk of developing skin cancer due to mutations in XP genes, which cause defective DNA repair resulting in inability to fix UV-damaged DNA. Normally, DNA repair is achieved through NER or post-replication repair (PRR). One XP gene is linked to PRR and its complementation group is XPV. A spectrum of clinical disease exists for XP and its severity depends on the amount of sun exposure combined with the total residual amount of DNA repair.5 This holds true in our case as the middle girl had maximum number of lentigines compared to her other siblings as she spent most of her time in the sunlight.

The disease is usually detected at age 1 or 2 years. Photosensitivity in XP is variable, but it generally occurs in the range of 290 to 320 nm. Ocular problems occur in nearly 80% of individuals with XP which include photophobia, conjunctivitis, eyelid solar lentigines, ectropion, symblepharon, vascular pterygia and epitheliomas of the lid. Finally, the propensity for malignancies, such as squamous cell carcinoma, basal cell carcinoma, sebaceous cell carcinoma, and fibrosarcoma, can also involve the eyes of patients with XP.2,5,6,7 In our case, photophobia and corneal opacities was present in all the three siblings. The middle girl also presented with epithelioma of the lid.

Oral manifestations of this disorder are rare. Malignancies like squamous cell carcinoma can develop on various parts of oral mucosa.9 Although occurrence of intraoral lentigines is not reported but their occurrence is a possibility as seen in our cases. The dentists should avoid using UV light in these patients, irrespective of intraoral lesions, because UV induced epithelial damage may cause dysplasia when DNA repair mechanisms are dysfunctional.9

The diagnosis of XP can be established with studies like cellular hypersensitivity to UV radiation and chromosomal breakage studies, complementation studies, and gene sequencing to identify the specific gene complementation group.2,10

The histologic findings of the first stage of the disease include hyperkeratosis and increased melanin pigment (this corresponds to the clinical freckling) in the basal cell layer (not necessarily accompanied by an increase in the numbers of melanocytes). In the second stage, atrophy ensues, and the hyperkeratosis and the hyperpigmentation are more marked. Telangiectasia may be prominent. These findings correspond to poikiloderma. The histologic appearances of the various tumors that complicate XP are seen in the third stage of XP.1-3 In our case, the youngest boy had histologic findings consistent with the first stage of disease whereas the eldest and the middle girl showed findings consistent with the second stage of disease.

The goal of treatment is to protect the patient from sunlight. Regular visits to the dermatologists and oral physicians is necessary for the purposes of patient education as well as early detection and treatment of any malignancies. Sunscreens (physical and chemical) should be applied to all exposed surfaces. Oral retinoids have been shown to decrease the incidence of skin cancer in patients with XP.11 Chemical therapy with 5-fluorouracil may be useful for actinic keratoses. Three case reports illustrate the efficacy of topical imiquimod 5% cream in clearing small basal cell carcinomas in sun exposed areas of individuals with XP and slowing the rate of new tumor development.12 A new approach to photoprotection is to repair DNA damage after UV exposure. Surgical care includes complete excision of malignancies when diagnosed.10
Follow-up care should be geared to educate the patient and the patient’s parents about effective sun protection and early recognition of skin cancer. Genetic counseling should be offered for families at risk. Complications of this disorder includes development of multiple cutaneous neoplasms at a young age. Fewer than 40% of patients survive beyond age 20 years.1,3

CONCLUSION

Xeroderma pigmentosum is a rare disorder which not only cause physical abnormalities but also social and psychological problems because of its diffuse unesthetic presentation. The extent of damage is proportional to exposure to ultraviolet radiation as seen in our cases. Intraoral lentigines can occur. Dentists should carefully use ultraviolet lights. Constant education of the patient is the most important objective in the management of XP. Research for the optimal treatment of XP is ongoing and hope lies in the promise of protein and gene therapy.

REFERENCES

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