Corneal Involvement in Xeroderma Pigmentosum; a Histopathologic Report

Mozhgan Rezaei Kanavi, MD; Mohammad-Ali Javadi, MD; Hamid-Reza Zabihi Yeganeh, MD

Shaheed Beheshti Medical University, Tehran, Iran

Purpose: To report the histopathologic features of corneal involvement in a patient with xeroderma pigmentosum (XP).

Case Report: A 19-year-old man with XP presented with bilateral corneal leukoma and decreased visual acuity predominatly in his right eye. Penetrating keratoplasty was performed in the right eye due to severe corneal opacity, vascularization and lipid deposition. The corneal button underwent histopathologic evaluation which disclosed chronic interstitial lipogranulomatous keratitis.

Conclusion: To our knowledge, this is the first report of corneal involvement in xeroderma pigmentosum from Iran describing the histopathologic features in this rare condition.

J Ophthalmic Vis Res 2008; 3 (1): 66-69.

Correspondence to: Mohammad-Ali Javadi, MD. Professor of Ophthalmology; Ophthalmic Research Center, No. 5, Boostan 9 St., Amir Ebrahimi Ave., Pasdaran, Tehran 16666, Iran; Tel: +98 21 22585952, Fax: +98 21 22590607; e-mail: ma_ javadi@yahoo.com

INTRODUCTION

Xeroderma pigmentosum (XP) is a rare precancerous autosomal recessive skin disorder which is exacerbated by exposure to ultraviolet radiation. The underlying abnormality is defective DNA repair leading to benign lesions and malignant transformations.[1] Its prevalence is as low as one case per 250,000 worldwide with no racial predilection. XP presents in the first decade of life with hypersensitivity to ultraviolet radiation resulting in dryness, unusual erythema and pigmentary changes in sun-exposed areas of the skin. Additionally, dermal telangiectasia and several benign, precancerous and malignant neoplasms may emerge.[2]

Ocular complications include severe involvement of the eyelids, sclera and cornea. Corneal involvement presents as dryness, superficial inflammation, angiogenesis, ulceration, opacification, development of pterygium-like growths and epithelial neoplasms.[2] Pathological corneal changes in these patients range from disorganized epithelium and Bowman's layer destruction to neovascularization and perivascular infiltration of inflammatory cells in the stroma.[3] There are few reports describing corneal involvement in XP patients; herein we present the clinical presentation and histopathologic features of the cornea in such a patient.

CASE REPORT

A 19-year-old male subject and a known case of XP was referred to our clinic with bilateral corneal opacification and loss of vision, more severe in the right eye, from childhood. There was no document regarding cutaneous tumor or malignancy. Gross examination revealed widespread hyperpigmentation of the eyelids

and slitlamp examination disclosed severe corneal opacification accompanied by stromal neovascularization and lipid deposits. Due to severity of the condition, the right eye underwent penetrating keratoplasty.

The corneal button was sent to the pathology laboratory of the Eye Bank of I.R. of Iran. The specimen was approximately 7 mm in diameter, yellowish-white in color and completely opacified. The corneal disc was cut into two halves and fine tissue sections were made after histological preparation which then underwent hematoxylin and eosin (H&E), Congo red, periodic acid Schiff (PAS) and Gram staining. Light microscopy of H&E stained sections revealed corneal thickness to about 2 mm (Fig. 1), irregular and somehow thinned epithelium with basal and subepithelial bullous changes (Fig. 2-A). Extensive foci of stromal neovascularization accompanied by chronic granulomatous inflammation (Fig. 2-B) with giant multinuclear cells (Fig. 3-A) surrounding intrastromal cholesterol clefts (Fig. 3-B) were seen. The Descemet membrane had apparently normal thickness, however endothelial cell count was severely reduced (Fig. 1). There was patchy destruction of Bowman's layer replaced by fibrous tissue. Congo red staining was negative for amyloid deposits and no microorganisms were detected on Gram and PAS staining. The observed histopathological changes were compatible with chronic interstitial lipogranulomatous keratitis.

DISCUSSION

Xeroderma pigmentosum is an inherited precancerous dermatosis due to defective DNA repair after injury induced by ultraviolet exposure. Its clinical course is characterized by progressively increasing skin pigmentation and atrophy followed by development of dermal tumors. Ocular complications include eyelid, scleral and corneal involvement in up to 80% of cases which may be due to greater exposure to sunlight.[4,5]

Corneal involvement in XP may manifest as dryness, exposure keratitis, opacification, angiogenesis, band-like nodular keratopathy, ulceration and even perforation.[5] These manifesttations have been reported in 40% of cases.[6] Ley and Applegate[7] believed that DNA destruction due to ultraviolet radiation is responsible for the corneal opacification and neovascularization. In our patient, corneal involvement comprised of severe opacification, stromal neovascularization and lipid keratopathy but no sign of ulceration or acute infection. Haller et al[1] described the histopathological manifestations of XP in corneas of a patient which included degeneration of basal corneal epithelial cells, destruction of Bowman's layer and development of a degenerative pannus extending onto the underlying stroma. Freedman[3] reported irregularity and bullous changes in the epithelium and neovascularization of the stroma as well as perivascular infiltration of inflammatory cells and shedding of corneal endothelial cells in addition to the above-mentioned changes in Bowman's layer and superficial stroma. Histopathological features in our patient, likewise, included irregular epithelium with bullous alterations, focal destruction of Bowman's layer replaced by fibrous tissue and extensive foci of neovascularization in the stroma together with moderate to severe decrease in endothelial cells. The outstanding findings in our patient included cholesterol clefts throughout the stroma in addition to chronic lipogranulomatous inflammation and giant multinuclear cells, which were not observed in previous reports.

Previously defined ultrastructural features of XP-involved corneas on transmission electron microscopy have included subepithelial canals located at the basal epithelium, varying amounts of lattice collagen in Descemet membrane and the presence of multiple melanin granules in residual endothelial cells.[1]

To our knowledge, this is the first report describing the histopathological features of the cornea in a patient with XP from Iran. The prominent feature was presence of extensive lipogranulomatous inflammatory reaction surrounding severe lipoid infiltration in the corneal stroma.

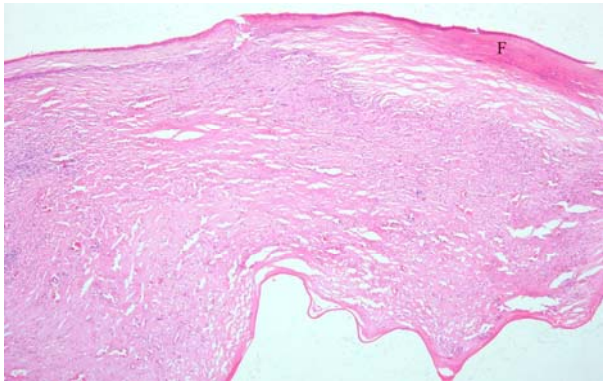

Figure 1 Notably increased corneal thickness accompanied by severe subepithelial and anterior stromal fibrosis (F), foci of neovascularization with intra-stromal inflammation and severe loss of corneal endothelial cells (hematoxylin & eosin staining, ×40).

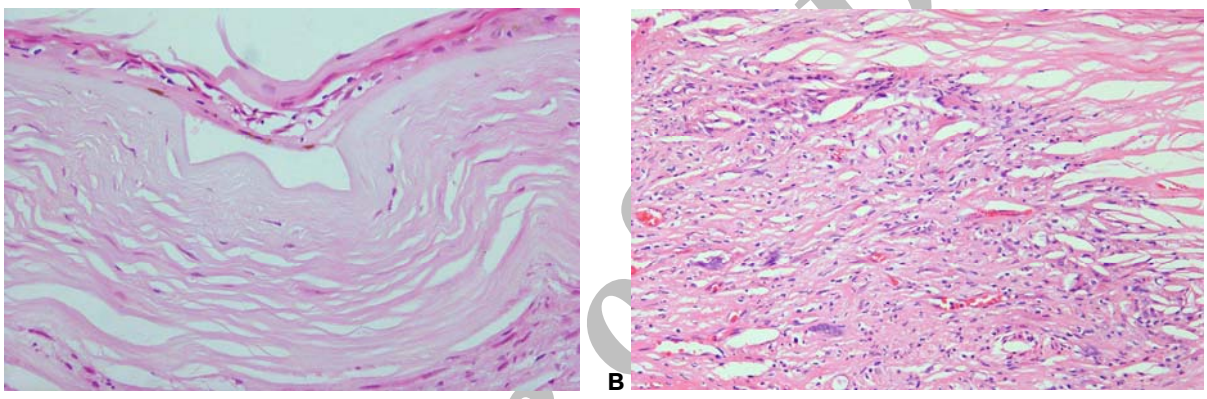

Figure 2 (A) Bullous changes in the basal epithelial cells (hematoxylin & eosin staining, ×400); (B) Neovascularization foci with chronic granulomatous inflammation and intra-stromal cholesterol clefts (hematoxylin & eosin staining, ×200).

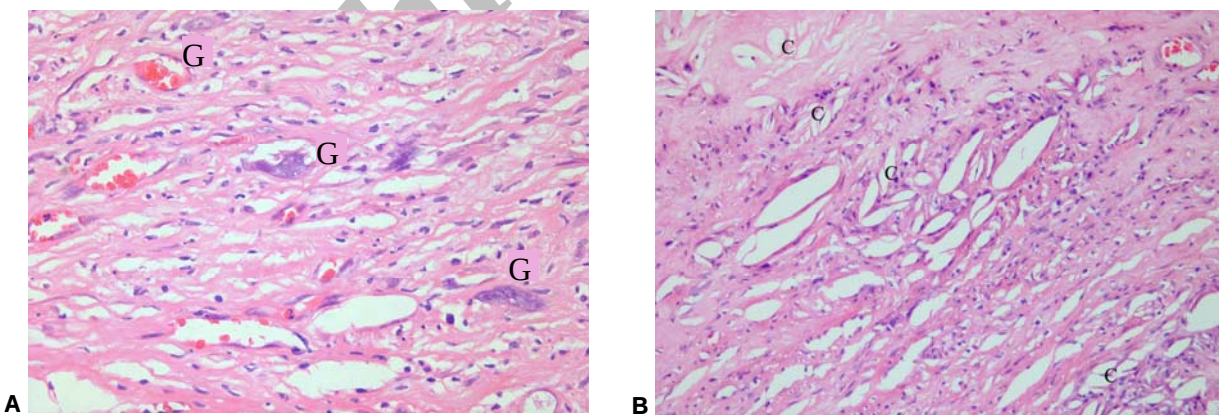

Figure 3 (A) Multinuclear giant cells (G) in lipogranulomatous reaction of the stroma and foci of neovascularization (hematoxylin & eosin staining, ×400); (B) Intra-stromal cholesterol clefts (C) and lipogranulomatous reactions (hematoxylin & eosin staining, ×200).

REFERENCES

1. Haller EM, Langmann G, Schwab C. Histology and transmission electron microscopy of the cornea in xeroderma pigmentosum type C. *Graefes Arch Clin Exp Ophthalmol* 1991;229:395-400.

2. Spencer WH. Conjunctival manifestations of dermatologic and metabolic disease. In: Spencer WH. Ophthalmic pathology, an atlas and textbook. 4th ed. on CD Rom, Chapter 2.
3. Freedman J. Corneal transplantation with associated histopathologic description in xeroderma pigmentosum occuring in a black family. *Ann Ophthalmol* 1979;11:445-448.
4. Stenson S. Ocular findings in xeroderma pigmentosum: report of two cases. *Ann Ophthalmol* 1982;14:580-585.
5. Kraemer KH, Lee MM, Scott J. Xeroderma pigmentosum-cutaneous, ocular and neurologic abnormalities in 830 published cases. *Arch Dermatol* 1987;123:241-250.
6. Goyal JL, Anand Rao V, Srinivasan R, Agrawal K. Oculocutaneous manifestations in xeroderma pigmentosa. *Br J Ophthalmol* 1994;78:295-297.
7. Applegate LA, Ley RD. DNA damages involved in the induction of opacification and neovascularization of the cornea by ultrraviolet light. *Exp Eye Res* 1991;52:493-497.