

Rare orbital malignancies in xeroderma pigmentosum – a case series and review of literature*

Syed Ali Raza Rizvi,¹ Faraz Yusuf,¹ A.K. Amitava,¹
S.H. Arif,² Shaista M. Vasenwala,² Ghazala Mehdi²

¹Institute of Ophthalmology, Jawaharlal Nehru Medical College, AMU, Aligarh, UP, India;

²Department of Pathology, Jawaharlal Nehru Medical College, AMU, Aligarh, UP, India.

*Prior publication: Case 1 of this case series was published in IJO as brief communication (Rizvi SAR, et al. Orbital Amelanotic Melanoma in Xeroderma Pigmentosum: A rare association. IJO 2008;56:421-423); Presentation at a meeting: A part was presented as poster at the Annual meeting of the Oculoplastic Association of India, Hyderabad, 14th-16th December, 2007. A part was presented as free paper in 63rd Annual Conference of Delhi Ophthalmological Society, 2012.

Abstract: Xeroderma pigmentosum (XP) is a rare genodermatosis, with a defect affecting recovery of ultraviolet-induced damages and characterized by a high rate of malignancies of the exposed skin areas. Inheritance is autosomal recessive and consanguinity of parents is common. We report two siblings with a history of consanguinity having XP with rare orbital malignancies. The first case had orbital amelanotic melanoma and the second case had sebaceous gland carcinoma (SGC) with orbital extension. In this case series, we have discussed and reviewed orbital malignancies in XP with respect to this report and other cases in the literature. Although early detection and treatment of these malignancies will reduce morbidity and mortality, genetic counselling remains the most important protective measures for XP.

Key words: Xeroderma pigmentosum, orbital malignancy, amelanotic melanoma, sebaceous gland carcinoma

Introduction

Xeroderma pigmentosum (XP) is a rare autosomal recessive condition characterized by mutations in genes involved in repairing defective DNA. Hence unregulated cell growth leads to the development of cancerous tumours. The condition appears in the first years of life characteristically with pigmented naevi on exposed parts of the skin.^{1,2} Ophthalmologic abnormalities are usually limited to the anterior, UV-exposed portion of the eyes: conjunctiva, cornea, and lids.³ Ocular abnormalities are almost as common as the cutaneous abnormalities.^{1,2} Epibulbar neoplasms are found in 11% of XP patients and in order of frequency are predominantly squamous cell carcinoma, basal cell carcinoma and melanomas.¹ Consanguinity of the parents is an important factor and the condition appears to be sex-linked.⁴ We report two siblings with a history of consanguinity having XP with rare orbital

Correspondence: Syed Ali Raza Rizvi, 7, Alig Apartment, Shamshad Market, Aligarh, UP.202002, India
E-mail: draliraza2@hotmail.com

malignancies. The first case had orbital amelanotic melanoma and second case had sebaceous gland carcinoma (SGC) with orbital extension. In this case series, we have discussed and reviewed ocular manifestations and orbital malignancies in XP with respect to this report and other cases in the literature.

Case reports

Case 1: An eight-year-old male who presented with diminution of vision, photophobia, blepharospasm and lacrimation with entropion of the lower lid and macular corneal opacity involving the entire cornea in the right eye. In the left eye, the patient had loss of vision with insidious onset large reddish yellow orbital mass having an irregular outer surface measuring 5 cm x 6 cm since last year. No other ocular structures could be identified in this eye (Fig. 1a).

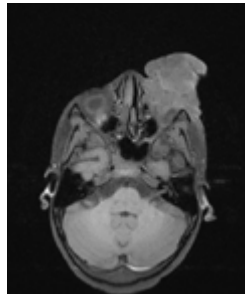


Fig. 1a. Showing large reddish-yellow mass of the left orbit.
Fig. 1b. showing MRI (axial section) of orbit with tumour extension

Cutaneous examination of the patient revealed multiple hyperpigmented freckle-like spots and hypopigmented macules all over the body. MRI of the left orbit revealed a heterogeneous mass involving and replacing the globe with loss of its contour. (Fig. 1b)

Total exenteration of the orbital mass was carried out. On histopathological examination, section showed mixed spindle cells and epitheloid cell melanoma. The predominant tumor cells were epitheloid and were largely amelanotic, thus confirming XP with orbital amelanotic melanoma. (Fig. 1c)

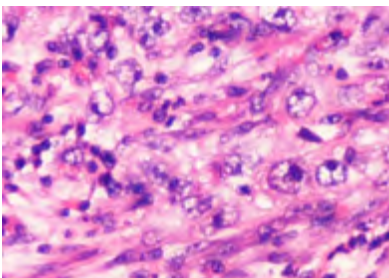


Fig. 1c. Photomicrograph showing sheet of plump epitheloid tumor cells with large nuclei and prominent nucleoli. Melanin is absent in tumor cells. (H&E, x400)

Case 2: The second patient was a six-year-old child, the younger sibling of the above-mentioned case, presenting with a large orbital mass in the left eye. The mass was approximately 4.0 cm x 6.0 cm in size with an irregular surface, multi-nodular

and cystic, having multiple points of haemorrhages and superadded infection extending to the left maxilla. The right eye of the patient revealed lower-lid ectropion, conjunctival scarring and corneal xerosis. The mass had started as a small nodule in the left upper lid rapidly increasing to the present size in three months (Fig. 2a). MRI of the left orbit showed a heterogeneous mass filling the orbit, not extending beyond it and with no intracranial spread. (Fig. 2b)

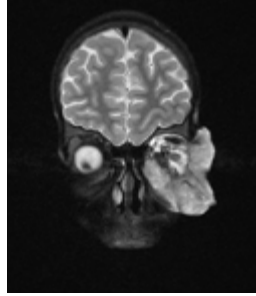


Fig. 2a. Showing large irregular mass of left orbit extending up to maxilla

Fig. 2b. showing MRI (coronal section) with involvement of orbit and maxilla

Radiologically, both the tumours appear similar, heterogeneous in nature involving the orbit. However the mass in second patient has involved the ipsilateral maxilla. This sibling also showed similar hyper/hypopigmented lesions all over the body, being prominent on the exposed areas. Exenteration of the tumor was carried out and on gross examination a single mass of 4.0 cm x 5.0 cm x 3.0 cm was noted. Histopathological examination of the tumor mass revealed sebaceous gland carcinoma with squamoid differentiation (Fig. 2c).

No regional lymphadenopathy or distant metastasis was seen in both the cases at the time of presentation. Skin biopsy in both cases confirmed the diagnosis of XP. The first patient died after two years of presentation due to intracranial metastasis while second case has lost to follow up.

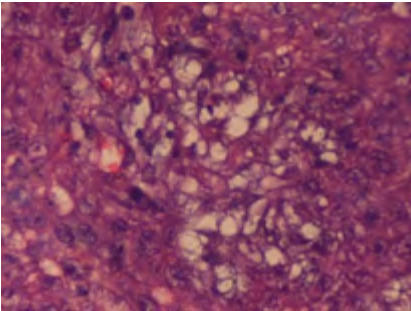


Fig. 2c. Photomicrograph showing sebaceous gland carcinoma with squamoid differentiation (H&E, x40)

Discussion

XP is an inherited condition characterized by extreme sensitivity to ultraviolet (UV) rays from sunlight mostly affecting the eyes and areas of skin exposed to the sun.¹ XP is characterized by sun sensitivity (severe sunburn with blistering, persistent

erythema on minimal sun exposure, marked freckle-like pigmentation of the face before age two years), ocular involvement (photophobia, keratitis, atrophy of the skin of the lids), and a greatly increased risk of cutaneous neoplasms (squamous cell carcinoma, basal cell carcinoma, melanoma).

Bradford et al. found that individuals with XP had an increased risk of non-melanoma (basal cell and squamous cell) skin cancer and cutaneous melanoma at UV-exposed sites at the median age of nine years and 22 years respectively.⁵

Parental consanguinity which is important in any autosomal recessive disorder was noted in 40% of XP patients in the Goyal⁶ series compared with 31% reported in the Kraemer's series.¹

The two cases reported by us were from the same family where a history of consanguinity was present. Our first case is an advanced orbital melanoma with amelanosis which is a rare occurrence.⁷ Faza⁸ et al. in their case series of 12 cases of melanoma with XP, also found orbital melanoma, though not amelanotic.⁸ Many researchers have reported several cases of ocular melanomas but none have discussed amelanosis in ocular melanoma.⁵

The second case reported by us is the sibling of the former case having sebaceous gland carcinoma with orbital extension an unlikely association of XP. So far, we have not yet found any article citing the association of sebaceous gland carcinoma with XP. Kraemer et al. in their largest case series of 830 cases of XP did not find a single case of sebaceous gland carcinoma.¹ Calugaru et al. reported an epibulbar squamous cell carcinoma penetrating the orbit.⁹ Gaasterland et al. in their case report also showed orbital involvement with squamous cell carcinoma.¹⁰

In XP, melanoma can arise both from ocular surface and adenexa with secondary invasion to orbit. [1] However, second case of sebaceous gland carcinoma must have primarily arisen from eyelids before extending to the orbit. It has long been recognized by both clinicians and pathologists that the vast majority of patients with this condition sooner or later develop malignant tumors of the diseased areas, appearing during adolescence or early adult life leading to eventual death from local extension or, less often, from metastases. The neoplasms may take the form of basal-cell or squamous-cell carcinoma or of malignant melanoma.

Hence not only our case series of XP with amelanotic melanoma and sebaceous gland carcinoma with orbital extension is a unique presentation occurring in the same family. We also recommend that SGC, though rare, should also be included in the differential diagnosis of ocular neoplasms in XP.

Although early detection and treatment of these malignancies will reduce morbidity and mortality, genetic counselling remains the most important protective measures for XP.

References

1. Kraemer KH, Lee MM, Scotto J. Xeroderma pigmentosum. Cutaneous, ocular, and neurologic abnormalities in 830 published cases. *Arch Dermatol* 1987;123:241-250.
2. Kraemer KH, Lee MM, Andrews AD, Lambert WC. The role of sunlight and DNA repair in melanoma and nonmelanoma skin cancer. The xeroderma pigmentosum paradigm. *Arch dermatol* 1994;130:1018-1021.

3. Dollfus H, Porto F, Caussade P, Speeg-Schatz C, Sahel J, Grosshans E, et al. Ocular manifestations in the inherited DNA repair disorders. *Surv Ophthalmol* 2003;48:107-122.
4. Francois J (ed.). *Heredity in Ophthalmology*, p. 205. St. Louis: CV Mosby Co 1961.
5. Bradford PT, Goldstein AM, Tamura D, Khan SG, Ueda T, Boyle J, et al. Cancer and neurologic degeneration in xeroderma pigmentosum: long term follow-up characterizes the role of DNA repair. *J Med Genet* 2011;48:168-176.
6. Goyal JL, Rao VA, Srinivasan R, Agarwal K, Oculocutaneous manifestations in xeroderma pigmentosum. *Br J Ophthalmol* 1994;78:295-297.
7. Rizvi S.A.R, Amitava A.K, Mehdi G, Sharma R, Shahid M. Orbital Amelanotic Melanoma in Xeroderma Pigmentosum: A rare association. *Indian Journal of Ophthalmol* 2008;56:421-423.
8. Fazaa B, Zghal M, Bailly C, Zeglouli F, Goucha S, Mokhtar I, et al. Melanoma in xeroderma pigmentosum: 12 cases. *Ann Dermatol Venereol* 2001;128(4):503-506.
9. Calugaru M, Barsu M. Exuberant epibulbar tumor penetrating into the orbit in xeroderma pigmentosum. *Graefes Arch Clin Exp Ophthalmol* 1992;230(4):352-357.
10. Gaasterland DE, Rodrigues MM, Moshell AN. Ocular involvement in xeroderma pigmentosum. *Ophthalmology* 1982; 89(8):980-986.