ophthal Focus

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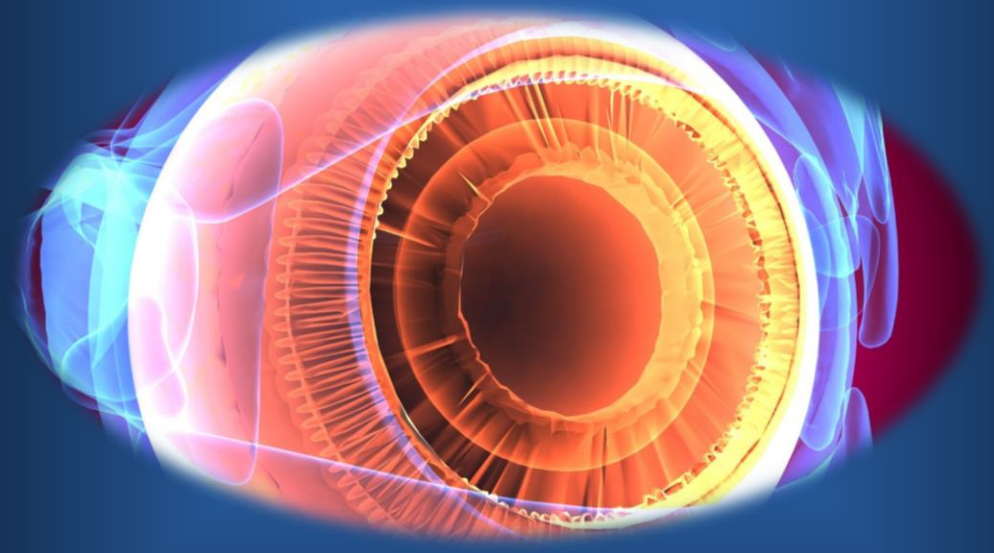


Dear Doctor,

Greetings from Micro Labs Limited. We are happy to bring you 'Ophthal Focus' which contains latest and interesting news in the field of Ophthalmology.

This issue contains

- Ocular surface biopsies of patients with xeroderma pigmentosum: a retrospective observational case series
- Conjunctival melanoma treatment outcomes in 288 patients: a multicentre international data-sharing study
- Bilateral hazy vitreous in a patient with convulsions

Should you require any specific article or medical information, please feel free to contact us at medicalservices@microlabs.in
Looking forward to your valuable feedback

Best Regards,
Medical Team, Micro Labs Limited

Ocular surface biopsies of patients with xeroderma pigmentosum: a retrospective observational case series

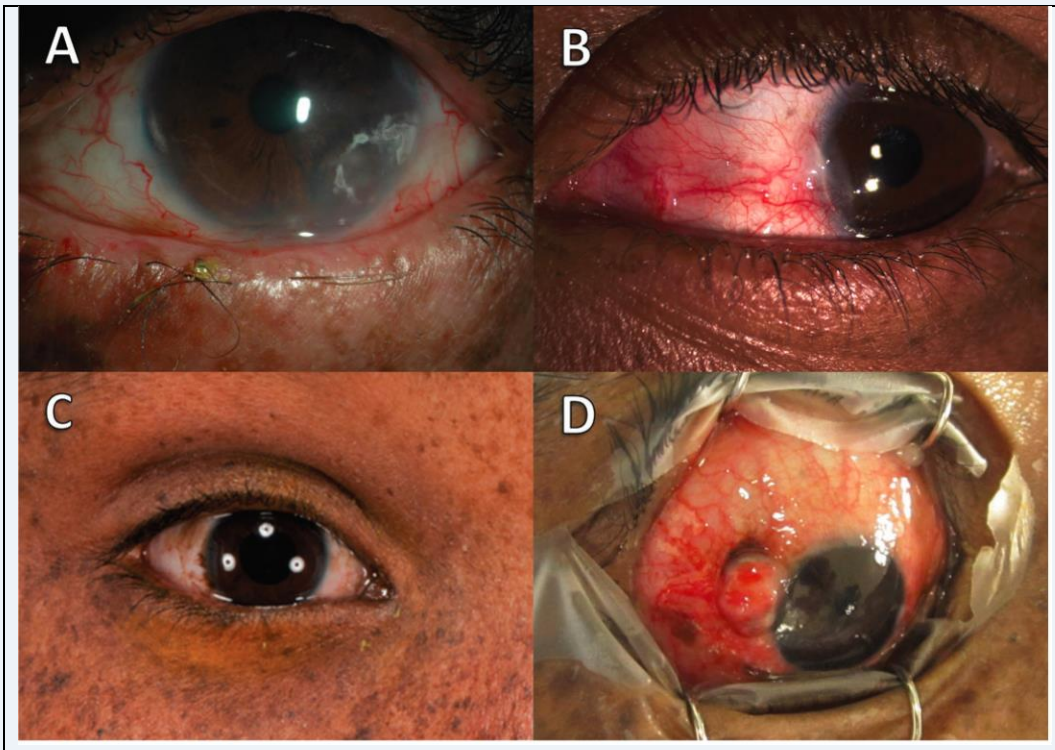
Xeroderma pigmentosum (XP) is a rare autosomal recessive disorder caused by defective DNA repair systems in response to sun exposure and is characterised by dermatological, ophthalmological and neurological consequences.1 In approximately 60% of cases, XP presents in early childhood with an exaggerated and prolonged skin reaction to sunlight which is often misdiagnosed as impetigo, neglect or cellulitis. In later life, frequent skin cancers develop and approximately 25% of patients with XP will develop neurological degeneration which can affect hearing, visual processing and motor function. Ophthalmic involvement is high, affecting up to 90% of patients with XP, and primarily occurs through sun exposure to the ocular surface. Ocular neoplasms are rare in the general population but risk of these neoplasms is increased >1000- fold in those with XP.5 10 Conjunctival intraepithelial neoplasia (CIN), squamous cell carcinomas (SCC) and melanomas have all been documented on the ocular surface of patients with XP. Where present, suspicious lesions are biopsied11; however, the rarity of XPand the paucity of reports describing the histopathology of the ocular surface of these patients make screening the ocular surface and interpreting these biopsies a challenge.

This is the largest reported series of ocular surface biopsies in patients with XP. It identifies a background of ocular surface melanocytic, degenerative and inflammatory changes, with patients with XP-C.

The study was done to describe the results of all ocular surface biopsies performed on patients with xeroderma pigmentosum (XP) under the care of

the UK Nationally Commissioned XP Service as well as the treatment of any subsequent ocular surface conditions diagnosed.

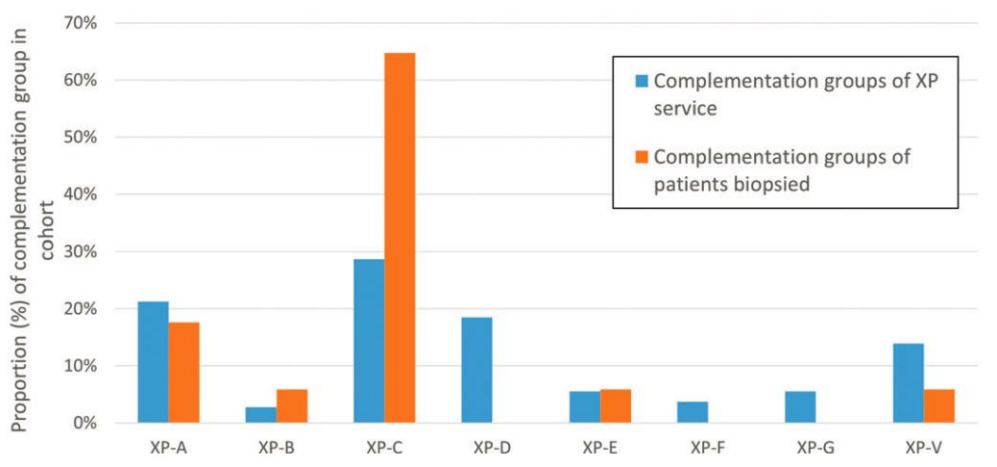
Retrospective analysis of medical records. All patients with XP seen by the service from 2010 to 2019 were included and those with ocular surface biopsies were identified. Data was collected on demographics, complementation subgroup (A–G and V), biopsy details, histopathological analysis and subsequent management.



Examples of the ocular surface pathology in patients with xeroderma pigmentosum (XP). (A), Right eye of a patient in their early 30s with XP-C (complementation subgroup C) showing prominent corneal vascularity and corneal scarring. (B) Right eye of 18-year-old patient with XP-C showing atypical pterygium, biopsy of which confirmed squamous cell carcinoma. (C) Right eye of 8-year-old patient with XP-C showing increased conjunctival pigmentation. Also note increased cutaneous pigmentation with widespread freckling (lentigines). (D) Right eye of same patient 2 years later with prominent right lateral limbal mass, vascularity and pigmentation. Biopsy showed a prominent inflammatory cell infiltrate, conspicuous vascular proliferation and melanocytic hyperplasia.

Of 108 patients seen in our service, 17 underwent at least one ocular surface biopsy. 45 biopsy samples were available from 13 patients of which 65% were performed on patients from complementation subgroup C (XP-C).

Biopsies were categorised as either non-mapping (clinically abnormal ocular surface tissue) or mapping (multiple sites including clinically normal tissue). 67 percent of non-mapping biopsies had a mass as their indication and 46% showed ocular surface squamous neoplasia. General non-dysplastic damage was seen in 67% of non-mapping biopsies and melanocytic changes were seen in 25% of non-mapping and 81% of mapping biopsies. 47 percent of biopsy outcomes required no additional treatment but, of those that did, 50% received mitomycin C.



Xeroderma pigmentosum (XP) complementation groups of patients biopsied versus total XP service population.

XP-A, xeroderma pigmentosum (complementation subgroup A); XP-B, Xeroderma pigmentosum (complementation subgroup B); XP-C, xeroderma pigmentosum (complementation subgroup C); XP-D, xeroderma pigmentosum (complementation subgroup D); XP-E xeroderma pigmentosum (complementation subgroup E); XP-F xeroderma pigmentosum (complementation subgroup F); XP-G xeroderma pigmentosum (complementation subgroup G); XP-V, xeroderma pigmentosum (variant).

This is the largest reported series of ocular surface biopsies in patients with XP. It identifies a background of ocular surface melanocytic, degenerative and inflammatory changes, with patients with XP-C showing the most severe effects. This study highlight challenges faced in interpreting their histopathology and in planning subsequent treatments.

Source: Vekinis J et al. Br J Ophthalmol Epub ahead of print: doi:10.1136/bjophthalmol 2020-316125.

Conjunctival melanoma treatment outcomes in 288 patients: a multicentre international data-sharing study

Conjunctival melanoma is rare, comprising <1% of all (whole body) melanomas. The incidence is less than 1 case per million population, but it is on the rise. Tumour staging is widely performed according to the eighth edition of the American Joint Committee on Cancer (AJCC) staging systemTo relate conjunctival melanoma characteristics to local control.

The most common treatment is wide excision with cryotherapy. Over the last several decades, topical chemotherapy and/or radiotherapy have been applied both as primary therapy and adjuvant therapy. Despite close surveillance and intensive therapy at subspeciality centres, the 10-year tumour recurrence rates are reported to be as high as 9%. Reported risk factors for local recurrence include non-bulbar tumour location, higher AJCC stage, increased tumour thickness and ulceration.

This multicentre international study showed that eighth edition of AJCC tumour staging was related to the risk of local recurrence of conjunctival melanoma after treatment.

This is the the first multicentre, international, registry-based study of tumour characteristics and control as well as the cumulative 5-year and 10-year local recurrence rates in patients with conjunctival melanoma. This database has been used to validate/assess the eighth edition of the AJCC staging manual for conjunctival melanoma.

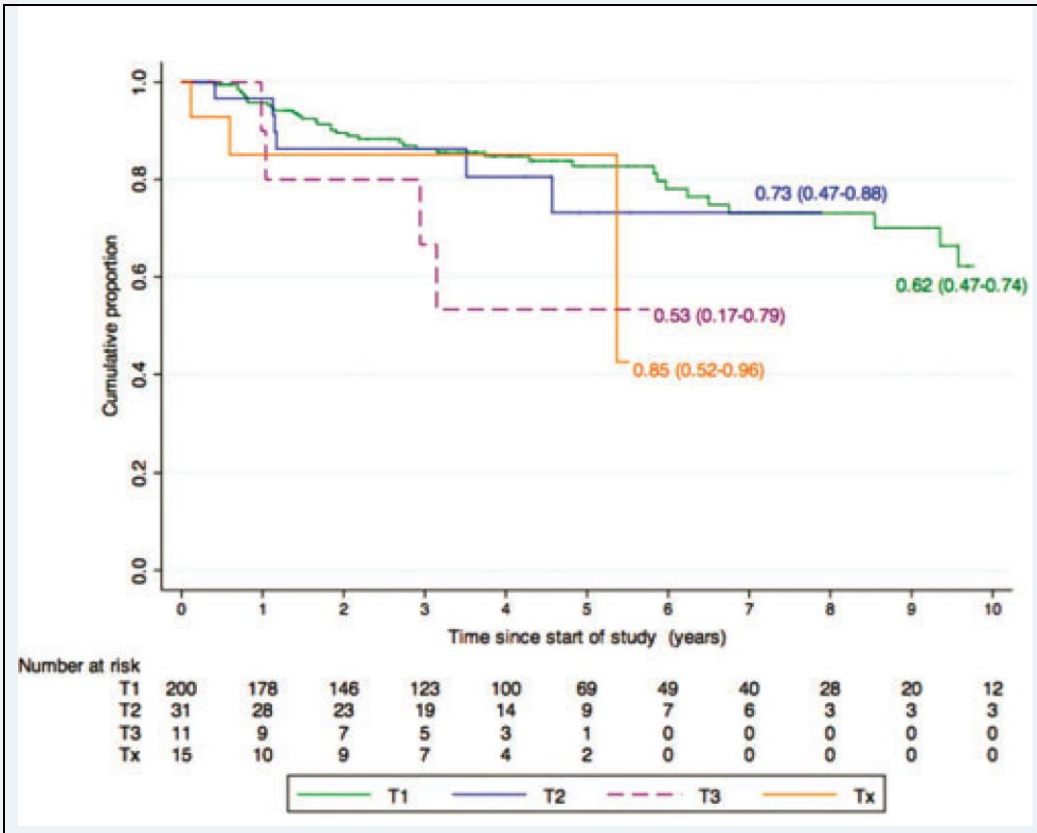
Retrospective, registry-based interventional study with data gathered from 10 ophthalmic oncology centres from 9 countries on 4 continents. Conjunctival melanoma patients diagnosed between January 2001 and December 2013 were enrolled in the study. Primary treatments included local excision, excision with cryotherapy and exenteration. Adjuvant

treatments included topical chemotherapy, brachytherapy, proton and external beam radiotherapy (EBRT). Cumulative 5-year and 10-year Kaplan-Meier local recurrence rates were related to clinical and pathological T-categories of the eighth edition of the American Joint Committee on Cancer (AJCC) staging system.

288 patients had a mean initial age of 59.7±16.8 years. Clinical T-categories (cT) were cT1 (n=218,75.7%), cT2 (n=34, 11.8%), cT3 (n=15, 5.2%), cTx (n=21,7.3%) with no cT4. Primary treatment included local excision (n=161/288, 55.9%) followed by excision biopsy with cryotherapy (n=108/288, 37.5%) and exenteration (n=5/288, 1.7%). Adjuvant therapies included topical mitomycin (n=107/288, 37.1%), plaque-brachytherapy (n=55/288, 19.1%), proton-beam (n=36/288, 13.5%), topical interferon (n=20/288, 6.9%) and EBRT (n=15/288, 5.2%). Secondary exenteration was performed (n=11/283, 3.9%). Local recurrence was noted in 19.1% (median=3.6 years). Cumulative local recurrence was 5.4% (3.2–8.9%), 19.3% (14.4–25.5%) and 36.9% (26.5–49.9%) at 1, 5 and 10 years, respectively. cT3 and cT2 tumors were twice as likely to recur than cT1 tumours, but only cT3 had statistically significantly greater risk of local recurrence than T1 (p=0.013). Factors such as tumour ulceration, plica or caruncle involvement and tumour thickness were not significantly associated with an increased risk of local recurrence.

			Univariate analysis		Multivariable analysis	
Variable	No. patients (%)	Interval	HR	95% CI	HR	95% CI
Age	288 (100)	1-year increment	1.02	1.00 to 1.04	1.02	0.99 to 1.06
Male	147 (51)	Versus female	0.97	0.53 to 1.63	–	–
Ulceration (n=143)	14(10)	Versus no ulceration	1.46	0.30 to 6.21	0.53	0.06 to 4.46
Plica involved (n=287)	31(11)	Versus no involvement	0.84	0.59 to 1.20	0.33	0.03 to 3.13
Caruncle involved (n=288)	32(11)	Versus no involvement	0.81	0.57 to 1.16	1.18	0.15 to 9.25
Tumour stage (cT2)	34	Versus T1	0.99	0.41 to 2.38	2.92	0.66 to 12.84
Tumour Stage (cT3)	15	Versus T1	**3.06***	1.07 to 8.70	**8.06****	1.55 to 41.67
Tumour stage (Tx)	21	Versus T1	1.89	0.57 to 6.19	2.15	0.70 to 7.21
Invasive melanoma (n=288)	219(76)	Versus no invasion	1.01	0.68 to 1.49	0.82	0.59 to 1.14
Tumour thickness (n=201)	201 (70)	1 mm increment	0.99	0.83 to 1.17	0.82	0.59 to 1.14

Cox proportional hazards model for predicting local recurrence



Kaplan-Meier survival curves showing cumulative local recurrence rates for patients with different clinical T-staging.

This multicentre international study showed that eighth edition of AJCC tumour staging was related to the risk of local recurrence of conjunctival melanoma after treatment. The 10-year cumulative local recurrence remains high despite current management.

Source: Jain P, Finger PT, Fili M, et al. Br J Ophthalmol Epub ahead of print: doi:10.1136/bjophthalmol2020-316293

Bilateral hazy vitreous in a patient with convulsions

A 41-year-old gentleman presented with complaints of decreased vision and floaters in both eyes (OU) since six months with a history of convulsions for six years. Best-corrected visual acuity (BCVA) was 20/200 OU, with normal intraocular pressures. The slit-lamp examination showed quiet anterior segment OU [Figure 1]a and [Figure 1]b. Fundus examination after pupillary dilatation revealed dense vitreous opacities that prevented a clear fundus view [Figure 1]c. The anterior vitreous showed strands of opacities with numerous focal attachments to the posterior lens capsule. Ultrasound B-scan revealed plenty of low reflective dot echoes with an attached retina and a normal choroid [Figure 1]d.

The slit-lamp examination showed the presence of vitreous opacities that attach to the posterior lens capsule by “foot plates” or “pseudopodia-lentis” suggestive of vitreous amyloidosis [Figure 1]a and [Figure 1]b. The history of convulsions further supports the diagnosis of familial amyloidotic polyneuropathy (FAP). The patient underwent pars plana vitrectomy in the right eye. The histopathology of the vitreous sample demonstrated acellular eosinophilic material on hematoxylin and eosin stain [Figure 1]e with strongly positive Congo-red staining [Figure 1]f. Vision improved to 20/20 in OD at 6 weeks of follow up after vitrectomy. MRI of the brain and orbit was advised at the discretion of his neurologist. The patient was advised for vitrectomy in the left eye. The Diagnosis was Vitreous amyloidosis.

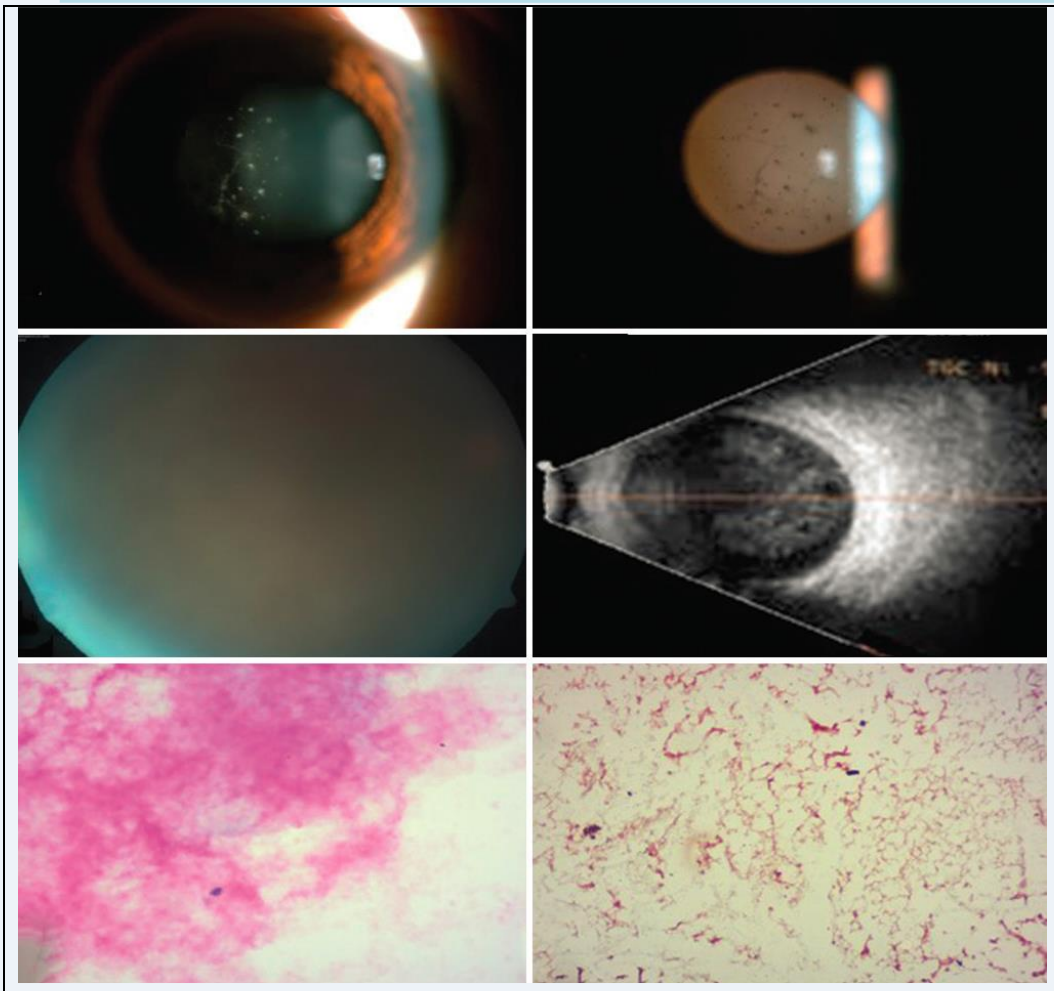


Figure 1: (a) Slit-lamp photo of the right eye showing vitreous opacities attached to the posterior surface of the lens capsule. (b) Retroillumination photograph showing the vitreous fibrils attached to the posterior lens surface. (c) Dense vitreous haze obscuring the fundus view. (d) USG B scan showing plenty of low reflective dot echoes in the vitreous with an attached retina and a normal choroid. (e) H and E staining of the vitreous sample post vitrectomy demonstrating eosinophilic material. (f) Positive Congo red staining

Vitreous amyloidosis occurs in familial amyloidotic polyneuropathy (FAP), caused by mutations in the transthyretin (TTR) gene. TTR is a tetrameric plasma protein (prealbumin) which polymerizes into a beta-pleated structure of amyloid fibril and deposits in the peripheral nerves (80-90%), cardiac muscle (80%), kidneys (6%), and eye (10%). Leptomeningeal involvement in FAP often manifested as convulsions and was reported in 5%

of cases. Ocular findings include abnormal conjunctival vessels, keratoconjunctivitis sicca, pupillary abnormalities, vitreous opacities, and secondary glaucoma. The incidence of vitreous opacities varies from 5.4% to 35% and the density of the opacities determines the visual acuity and symptoms. Clinical features of vitreous amyloidosis include pseudopodia lentis, glass wool vitreous, and retinal perivascular deposits. Pseudopodia lentis are whitish opacities or the foot plates, present on the posterior surface of the lens capsule which extend into the opacified vitreous. Treatment includes partial vitrectomy, with residual vitreous acting as a filter that prevents the amyloid material from reaching the angles and causing or exacerbating an existing component of glaucoma.

Source: Trivedi M et al. Indian J Ophthalmol 2020;68:1736