Juvenile Xanthogranuloma Presented with Buphthalmos and Corneal Clouding in Neonatal Period: A Case Report

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Abstract

Aim: To report an ocular juvenile xanthogranuloma (JXG) case presented with buphthalmos, corneal cloudiness, and normal intraocular pressure (IOP) in the neonatal period and treated with Ahmed glaucoma valve (AGV) implantation.

Background: JXG is a rare disorder predominantly seen in infants, but the neonatal presentation is extraordinary. Although spontaneous hyphema is a common presenting sign in JXG, buphthalmos and corneal opacity in the neonatal period were reported only in one case, which had high IOP values at presentation.

Case presentation: Sixteen-day-old male patient presented with buphthalmos, diffuse corneal clouding, and 11 mm Hg of IOP value in the right eye. IOP increased to 28 mm Hg three weeks later, and spontaneous hyphema developed, which did not respond to antiglaucomatous medications and topical corticosteroids. AGV was implanted, and the IOP decreased to 13 mm Hg postoperatively. In the follow-ups, numerous firm yellowish nodules were noticed on the patient’s skin during the examination under general anesthesia. Histopathological examination of the skin nodules was compatible with the diagnosis of JXG. Lens subluxation and phacodonesis were developed during the follow-up and were managed with pars plana lensectomy. After a silent period of 3 months, epithelial ingrowth was determined around the side port entrance. Unfortunately, the ingrowth did not respond to cryotherapy and resulted in phthisis bulbi. Pathological evaluation of the enucleated phthisic eye revealed posterior segment involvement.

Conclusion: Ocular JXG can be present with buphthalmos, corneal opacity, and normal IOP values without any skin lesions in the neonatal period. Neonatal presentation of JXG may be associated with limited medical therapy response and aggressive disease course.

Clinical significance: This case report introduces the second ocular JXG case, which presented with buphthalmos and corneal cloudiness, and the third pathologically proven posterior segment involvement of JXG in the literature.

Keywords: Ahmed glaucoma valve, Buphthalmos, Case report, Histopathology, Juvenile xanthogranuloma, Neonatal, Posterior segment involvement, Secondary glaucoma.

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Background

Juvenile xanthogranuloma (JXG), the most common form of non-Langerhans’ cell histiocytosis, is a rare disorder predominantly seen in infants.1 In immunohistochemical (IHC) studies, JXG lesions stain with macrophage markers (CD68), but unlike Langerhans cells, they do not stain with S-100 protein and CD1a, proving the non-Langerhans origin.2 The skin disorder is mainly characterized by a typically raised, yellowish-orange cutaneous lesion, regressing spontaneously over 1–5 years.3

Extracutaneous involvement most commonly occurs in the eye and has been reported to accompany approximately 0.3–10% of patients with the cutaneous disease.3 Most of the cases are seen during the first year of life, but the neonatal presentation is extraordinary.4,5 The skin lesions in JXG can precede, follow, or co-occur with the ocular involvement.

The most common ocular finding is diffuse or discrete iris nodules, which could be quite vascular and may bleed spontaneously, resulting in hyphema.3,6 Although spontaneous hyphema is a common presenting sign in JXG,3 buphthalmos, and corneal opacity in the neonatal period were reported only in one case, which has high IOP values.1 Occasionally, the lesions may rarely present in other ocular areas such as eyelids, conjunctiva, cornea, ciliary body, choroid, optic nerve, and orbit.6 Posterior segment involvement is also infrequent.8 There are only two pathologically proven cases in the literature that have posterior involvement.5,10 Both were painful and blind eyes enucleated due to the suspicion of malignancy.

This case report aims to present a challenging diagnosis of an unusual case of ocular JXG in the neonatal period who presented with buphthalmos and corneal clouding despite normal IOP. Written consent was obtained from the legal guardians of the patient.

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**Case Description**

A 16-day-old male neonatal presented with corneal clouding in the right eye ever-increasing since birth. The patient’s medical and family history was unremarkable. An ocular examination of his right eye revealed buphthalmos with diffuse corneal clouding, conjunctival hyperemia, and iris heterochromia with yellowish superficial dots and membranes (Fig. 1A). Fundus details of the right eye could not be seen due to corneal cloudiness. The ocular examination of the anterior and the posterior segment of the left eye was normal (Fig. 1B). IOPs were 11 mm Hg and 10 mm Hg with Tono-Pen (Reichert, NY, USA), and the corneal diameters were 13 mm and 11 mm in the right eye and left eye, respectively.

The aqueous sampling was performed to screen for infectious causes, including cytomegalovirus, and the results were negative. Gonioscopy was normal, which was performed in the same session. Laboratory tests revealed that the level of cholesterol, triglyceride, and white blood cell count was normal, and the serology for TORCH infections and *Toxocara spp.* were negative. Third weeks after weekly follow-ups, IOP increased up to 28 mm Hg, and spontaneous hyphema was seen in the right eye, which did not respond to antiglaucoma medications and topical corticosteroids for three days. Therefore, an AGV implantation was performed uneventfully. Intraoperatively, the yellowish membrane-like formations were peeled off from the iris. The IOP decreased to 13 mm Hg postoperatively. Corneal cloudiness persists in the center despite clearing in the peripheral areas.

Two months later, the patient was prepared for an examination under general anesthesia, and numerous firm yellowish nodules between 2 and 20 mm in diameter were noticed at the abdomen skin around the umbilicus and under the left nipple (Fig. 2).

A biopsy taken from his skin lesions revealed infiltration of histiocytes, foamy cells, and Touton giant cells in the dermis with variable lymphocytes, eosinophils, and neutrophils. Further pathological examination with IHC staining revealed positive staining with CD68 and no staining with S-100 protein and CD1a, confirming the diagnosis of JXG.

The patient was diagnosed with secondary glaucoma due to ocular JXG. During the patient’s subsequent visits, corneal cloudiness regressed, and the tube position was stable in the anterior chamber. The fundus examination revealed widely spread pigment clumps around the atrophic retina, and optic atrophy was noted. Under topical prednisolone acetate and cyclopentolate therapy, the IOP maintained around 13 mm Hg. However, lens subluxation and phacodonesis were observed at the last examination, and pars plana lensectomy was performed. After a silent period of 3 months, an epithelial ingrowth was noted. Under topical prednisolone acetate and cyclopentolate therapy, the IOP maintained around 13 mm Hg. However, lens subluxation and phacodonesis were observed at the last examination, and pars plana lensectomy was performed. After a silent period of 3 months, an epithelial ingrowth was determined around the side port entrance. The ingrowth did not respond to cryotherapy and resulted in phthisis bulbi.

After 2 years follow-up, the patient’s parents decided to have enucleation surgery because of persistent pain in the eye and cosmetic concerns. Pathological examination of the enucleation material revealed retinal detachment with gliosis areas, osseous metaplasia of the retina pigment epithelium, subretinal melanin pigment accumulation, and hemorrhage. Besides, choroidal, scleral, and episcleral infiltration of histiocytosis was observed in the microscopic examination, which was compatible with JXG (Fig. 3).

**Discussion**

Juvenile xanthogranuloma (JXG) is a benign, self-limiting, non-Langerhans’ cell histiocytosis characterized by cutaneous lesions. Some cases may develop ocular involvement, most commonly presented as an iris granuloma and spontaneous hyphema due to uveal involvement causing neovascularization, resulting in vision-threatening complications such as glaucoma.5

Although JXG is most commonly seen in the first year of life, the ocular presentation of the JXG is exceptional in the neonatal period. A literature review of three publications with large case series revealed that only two out of 82 reported patients were 4-week-old or less.5,6,11 In our case, the fact that the patient was born with buphthalmos and had increasing corneal cloudiness suggests that the patient may have had episodes of increased IOP during the prenatal period. Although ocular JXG is listed among secondary congenital glaucoma,12 it is a challenging diagnosis due to its rarity in the neonatal period. The absence of skin lesions at the presentation and the increased IOP unresponsiveness to topical corticosteroids made the diagnosis even more difficult in our case. The diagnosis could not be made since the pathology result of the material peeled over the iris was insufficient. The diagnosis could only be made with the skin lesions seen during the examination under general anesthesia in the patient’s 5th month. Sixty percent of the ocular JXG patients may not have skin lesions; moreover, the development of skin lesions may delay up to 10 months after ocular involvement.3

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**Figs 1A and B:** Clinical appearance of the patients’ eyes at the presentation. (A) Right eye with buphthalmic appearance, corneal clouding, conjunctival hyperemia, and iris heterochromia due to yellowish superficial dots and membranes; (B) Left eye with normal appearance

**Fig. 2:** The appearance of firm yellowish nodules on the skin of the patient
relieve parents’ cosmetic concerns. The microscopic pathological examination of the enucleation material revealed choroidal, scleral, and episcleral infiltration of histiocytosis, which was compatible with the diagnosis of JXG. Cases with posterior segment involvement are uncommon in the literature, and among them, posterior involvement could be shown pathologically only in two enucleated eyes. To our knowledge, our case is the third case of JXG with pathologically proven posterior segment involvement.

**Conclusion**

In conclusion, this report presented an ocular JXG case associated with buphthalmos and glaucoma unresponsive to antiglaucoma medications and corticosteroids in the neonatal period. Unilateral buphthalmos with fluctuating IOP and spontaneous hyphema in a neonatal child should alert the clinician toward this rare diagnosis of JXG. Delayed skin lesions could make the diagnosis more challenging; therefore, ophthalmologists should be aware of the various ophthalmic manifestations in JXG. This study showed neonatal JXG could be a more aggressive course, and more aggressive medical treatments, such as oral or systemic corticoids, may be considered for the unresponsive high IOP in the early period.

**Clinical Significance**

This case report introduces the second ocular JXG case, which presented with buphthalmos and corneal cloudiness and the third pathologically proven posterior segment involvement of JXG in the literature.
Ocular Juvenile Xanthogranuloma in a Neonate

Authors Contribution
All authors conceived and designed the study. BD, MOS, ME, and VD acquired the data. DY and LC analyzed and interpreted the data. VD and MOS wrote the manuscript. ME revised the final manuscript.

Consent to Participate
Consent and approval were obtained from Institutional Ethics Committee of Marmara University (Istanbul, Turkey) for processing the data of patients’ records in this retrospective study.

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REFERENCES
1. Chaudhry IA, Al-Jishi Z, Shamsi FA, et al. Juvenile xanthogranuloma of the corneoscleral limbus: case report and review of the literature. Surv Ophthalmol 2004;49(6):608–614. DOI: 10.1016/j.survophthal.2004.08.004
2. Dehner LP. Juvenile xanthogranulomas in the first two decades of life: a clinicopathologic study of 174 cases with cutaneous and extracutaneous manifestations. Am J Surg Pathol 2003;27(5):579–593. DOI: 10.1097/00000478-200305000-00003
3. Chang MW, Frieden IJ, Good W. The risk intraocular juvenile xanthogranuloma: survey of current practices and assessment of risk. J Am Acad Dermatol 1996;34(3):445–449. DOI: 10.1016/s0190-9622(96)90437-5
4. Sonoda T, Hashimoto H, Enjoji M. Juvenile xanthogranuloma. Clinicopathologic analysis and immunohistochemical study of 57 patients. Cancer 1985;56(9):2280–2286. DOI: 10.1002/1097-0142(19851101)56:9<2280::aid-cncr2820560923>3.0.co;2-l
5. Zimmerman LE. Ocular lesions of juvenile xanthogranuloma. Nevoxanthoedothelioma. Am J Ophthalmol 1965;60(6):1011–1035. DOI: 10.1016/0002-9394(65)92808-4
6. Samara WA, Khoo CT, Say EA, et al. Juvenile xanthogranuloma involving the eye and ocular adnexa: tumor control, visual outcomes, and globe salvage in 30 patients. Ophthalmology 2015;122(10):2130–2138. DOI: 10.1016/j.jophtha.2015.06.009
7. Ramos SA, Ayet RI, Serra CA. Neonatal glaucoma associated with juvenile xanthogranuloma: case report. Arch Soc Esp Oftalmol 2017;92(8):394–397. DOI: 10.1016/j.joftal.2017.02.012
8. Gohari AR, Reith J, Scarborough M, et al. Multifocal juvenile xanthogranuloma presenting with a hand mass and bilateral vitreous hemorrhage in a neonate. Retin Cases Brief Rep 2010;4(4):346–351. DOI: 10.1097/icb.0b013e3181aff4f3
9. Wertz FD, Zimmerman LE, McKeown CA, et al. Juvenile xanthogranuloma of the optic nerve, disc, retina, and choroid. Ophthalmology 1982;89(12):1331–1335. DOI: 10.1016/s0161-6420(82)34637-0
10. Zamir E, Wang RC, Krishnakumar S, et al. Juvenile xanthogranuloma masquerading as pediatric chronic uveitis: a clinicopathologic study. Surv Ophthalmol 2001;46(2):164–171. DOI: 10.1016/s0039-6257(01)00253-3
11. Sanders TE. Intraocular juvenile xanthogranuloma (nevoxanthogranuloma); a survey of 20 cases. Trans Am Ophthalmol Soc 1960;58:59–74; PMID: 13746162.
12. Abdolrahimzadeh S, Fameli V, Mollo R, et al. Rare diseases leading to childhood glaucoma: epidemiology, pathophysiology, and management. Biomed Res Int 2015;2015:781294. DOI: 10.1155/2015/781294
13. Weiner MJ, Trentacoste J, Pon DM, et al. Epithelial downgrowth: a 30-year clinicopathological review. Br J Ophthalmol 1989;73(1):6–11. DOI: 10.1136/bjo.73.1.6