CASE REPORT

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.[5,6] Although spontaneous hyphema is a common presenting sign in JXG,[6] buphthalmos, and corneal opacity in the neonatal period were reported only in one case, which has high IOP values.[7] 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.[9,10] 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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Conflict of interest: None

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.

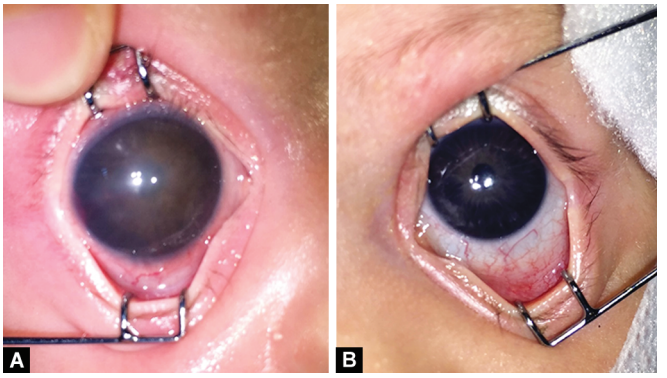
The aqueous sampling was performed to screen for infectious causes, including cytomegalovirus, and the results were negative. Gonioscopy was normal, which was performed in the same session. Laboratory tests revealed that the level of cholesterol, triglyceride, and white blood cell count was normal, and 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 determined around the side port entrance. The ingrowth did not respond to cryotherapy and resulted in phthisis bulbi.

After a 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).



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

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]

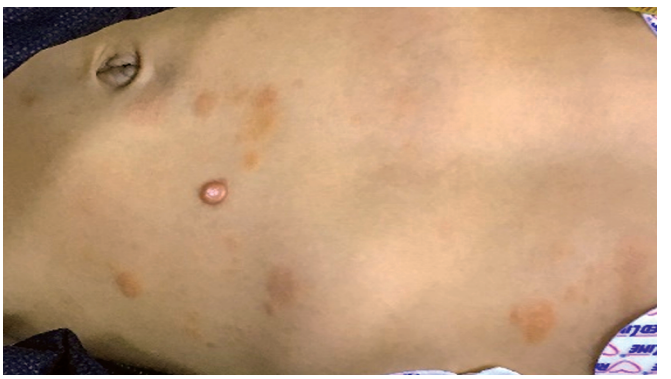
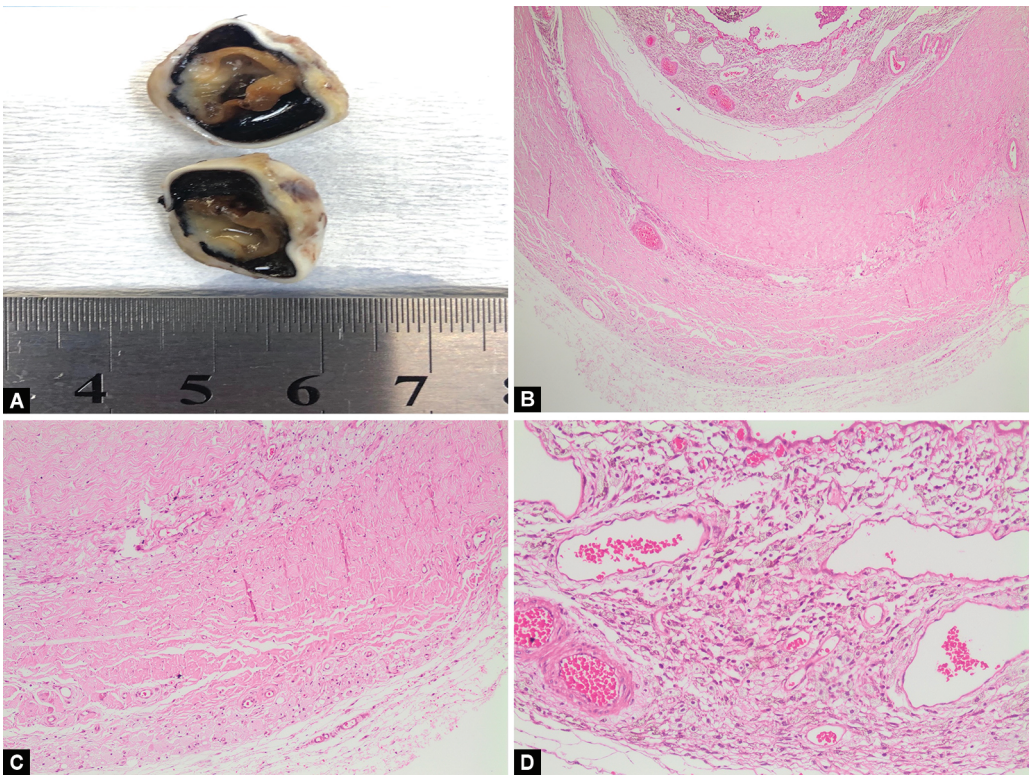


Fig. 2: The appearance of firm yellowish nodules on the skin of the patient



Figs 3A to D: Macroscopic appearance and histopathology of enucleation material (hematoxylin and eosin staining). (A) Gross section of enucleation material with retinal detachment, retinal thickening due to gliosis, subretinal hemorrhage, and thickened sclera in the phthisic eye; (B) 4x magnification of sclera and episclera; (C) 10x magnification of sclera and episclera; (D) 20x magnification of choroid

For the first time in the literature, Ramos Suarez et al. reported a 22-day-old neonatal case presented with buphthalmos and corneal opacity.[7] They started topical corticoids after seeing the yellowish infiltration invading the angle. However, because the iris lesions did not respond to medical treatment, AGV implantation was performed within 3.5 months of the patient. They were able to confirm the diagnosis by the skin lesions 10 months after birth. Similarly, in our case, the hyphema and the high IOP could not be controlled with the antiglaucomatous medical treatment, including topical corticosteroids. For this reason, we had to perform AGV implantation at the patient's age of 1.5 months. To our knowledge, it was the second AGV implantation surgery in neonatal JXG in the literature.

Although there is presently no standard care for the ophthalmic manifestations of JXG, usually nonsurgical approaches are preferred because they pose less risk of intraocular bleeding.[6] Initial medical management often consists of topical, local, or systemic corticosteroid therapy reported to all have a high success rate.[6] However, considering these two cases, it can be speculated that the neonatal presentation of ocular JXG may have a more aggressive course and be more resistant to medical treatment. Future case reports or case series are needed to learn more about this rare issue.

The literature shows that epithelial ingrowth resulted in a 50% rate of phthisis bulbi despite the treatment.[13] Unfortunately, in our case, epithelial ingrowth developed 3 months after the pars plana lensectomy, which did not respond to cryotherapy and had progressed to phthisis bulbi. Enucleation was performed at the 3 years of life to support orbital and facial growth and 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,[6,8] and among them, posterior involvement could be shown pathologically only in two enucleated eyes.[9,10] 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; thus, 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.

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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