

# Colobomatous cyst: Histopathological characterization

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## ABSTRACT

**Introduction:** Colobomatous cyst is one of the rare orbital cystic lesions that have wide range of differential diagnosis. It is a congenital lesion that can be easily misdiagnosed as malignant tumor, leading to exposing the patient to unnecessarily overtreatment. **Case Report:** This is a rare case of congenital colobomatous cyst in an infant girl. The cyst was associated with a microphthalmic globe. Radiologically, the cyst was located in the inferior half of the orbital cavity. Surgical excision was performed and the histopathological examination demonstrated a collapsed cyst with smooth tan lining. The wall of the cyst had an inner neuroretinal layer and an outer fibrovascular layer. **Conclusion:** Any orbital cystic lesion should not be diagnosed without the clinicopathological and radiopathological correlations, to avoid any histopathological over diagnosis of some benign cysts as a malignant one. The pathologic features of colobomatous cysts are rarely described in literature with only one article in the PubMed search discussing these features in some details.

**Keywords:** Childhood, Colobomatous cyst, Histopathology, Infant, Microphthalmic globe, Orbital cystic lesions

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## INTRODUCTION

Orbital cystic lesions in childhood differ in their pathology and management. It is crucial to differentiate these lesions from each other because their treatment varies from observation to excision. Although the pathologist is the main player in this differentiation, correlation with the clinical data and radiology is mandatory to reach the accurate diagnosis. Colobomatous cyst is one of these lesions. It is “a neuroectodermal-lined cyst formed by an ocular developmental anomaly that occur due to a failure in the closure of the optic fissure” [1–2]. It is a rare lesion that had been firstly described by Thomas Bartholin. Usually, it is appear since birth without any sex perdition. It can affect any structure in the eye. Without correlation with clinical data and imaging, colobomatous cyst can be very easily misdiagnosed as malignancy because of its rarity and unusual microscopic features [1].

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## CASE REPORT

One-year-old girl was brought by her parents to the outpatient ophthalmic clinic because of cystic lesion arising from the lateral side of the right orbital cavity since birth. The cyst was increasing in size with the time. On ophthalmic examination, the right eye showed a microphthalmic globe with an attached cyst protruding from the lateral side of the globe. The left eye had a large lower eyelid coloboma with underdeveloped upper eyelid that led to severe exposure keratopathy and resulted in corneal ulcer. The rest of the systemic examination shows cleft lip and cleft palate. The blood tests including complete blood count (CBC), hemoglobin, liver function tests (LFT), and renal function tests (RFT) were all within normal limits.

On Magnetic resonance imaging scan, there was a homogenous cystic lesion associated with microphthalmic globe, occupying the inferonasal quadrant of the right orbit (Figure 1). It measured around 14x12x11 mm in the anteroposterior, transverse and craniocaudal dimensions. There was no solid component within the cyst. No areas of hemorrhage, calcification or any post-contrast enhancement were evident. No obvious communication was present between the cyst and intracranial structures.

The cyst had been surgically resected and submitted to the pathology department in 10% neutral buffered formalin. Macroscopically, the specimen consisted of a partially collapsed cyst that measured 1.3 cm in maximum diameter. It had a smooth gray-bluish outer surface and smooth gray-tan lining wall. It contained a clear watery fluid. The entire specimen was submitted for histopathological examination. On microscopy, the cyst was formed by two layers (Figure 2A). The inner layer was comprised of primitive neuroretinal tissue showing neuropil, granular neurons and rosette formation reminiscent of the retina (Figures 2B and 2C). Glial tissue was also seen with fibrillary astrocytes likely representing optic nerve tissue (Figure 2B). Focal melanin pigments similar to the choroid layer were identified (Figures 2D). The tortuous and branching epithelial structures formed by tall to columnar simple epithelial layers could represent either the anterior epithelial layer of the lens or the ciliary processes (Figure 2E). The outermost layer of the cyst consisted of fibrovascular connective tissue, probably representing the sclera (Figure 2A). Areas of dystrophic calcification were noted in both layers (Figure 2F). There was no evidence of mitosis, nuclear atypia, or necrosis.

By immunohistochemical staining, glial fibrillary acidic protein (GFAP) highlighted the glial tissue (Figure 3A) whereas synaptophysin demonstrated the neuronal component (Figure 3B). S100 was positive in both glial and neuronal tissues (Figure 3C). Cytokeratin stained the epithelial foci whereas EMA was negative (Figures 3D and 3E). Ki67 was negative in all of the tissue types (Figure 3F).

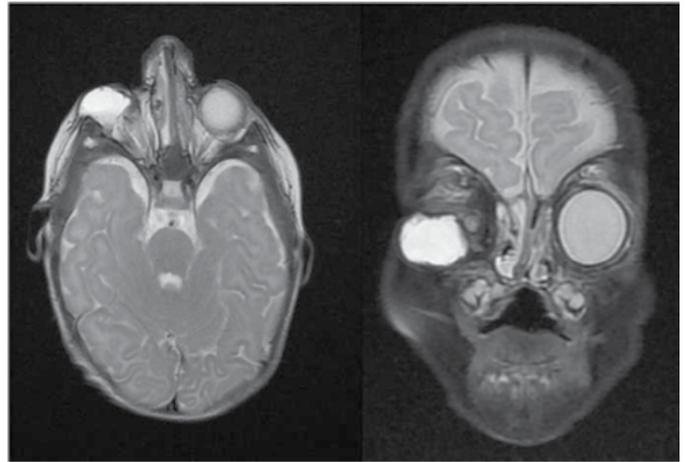


Figure 1: Radiological pictures showing cyst arising in the inferior half of the orbital cavity in association with microphthalmic globe.

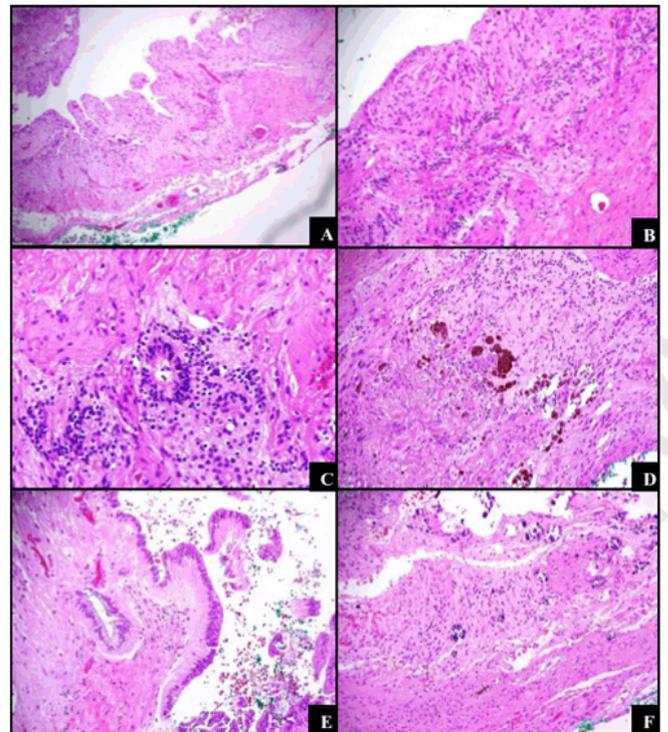


Figure 2: (A) The inner neuroglial layer and outer fibrovascular layer, (B) The inner layer is formed by glial tissue with an underlying layer of neuroretinal tissue, (C) Rosettes formations, (D) Areas of melanin pigmentation, (E) Tortuous epithelial foci, and (F) Dystrophic calcification. (A–F: H&E stain, x200).

## DISCUSSION

Based on the histopathological features alone, the differential diagnosis included: meningocele/meningoencephalocele, ectopic/heterotopic brain tissue, cystic teratoma (dermoid cyst), small round blue cell tumors (SRBCTs) such as neuroblastoma and retinoblastoma, congenital cystic eye and microphthalmos/anophthalmos with cyst (colobomatous cyst). With the exception of the

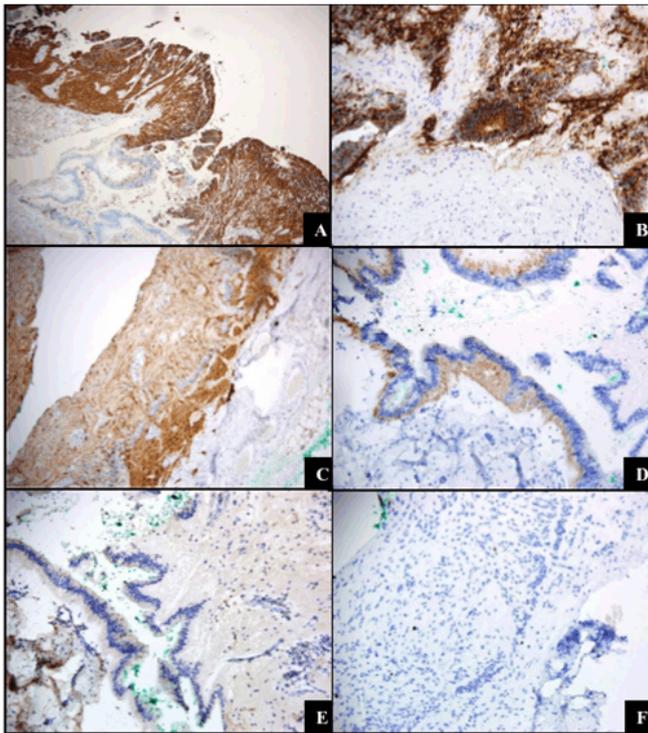


Figure 3: (A) glial fibrillary acidic protein (GFAP) stain highlighting the glial component in the inner wall of the cyst, (B) Synaptophysin stains the neuroretinal tissue beneath it. (C) S100 is positive in both glial and neuroretinal tissues. Epithelial foci are (D) positive for CK-pan but (E) negative for EMA. (F) Ki67 is negative in all the components. (A–F: Immunohistochemical stains, x100).

later, none of these differential diagnoses is associated with microphthalmos, clinically. Meningocele/meningoencephalocele represents an invagination of the meninges. Histologically, it is a cyst lined by meningeal and astrocytic tissue without retinal components. Radiologically, this cyst must have a communication with the intracranial structures. Ectopic/heterotopic brain tissue is usually located in the nose or rarely in the occipital region. Similar to meningocele/meningoencephalocele, the lesion is formed by meningeal and astrocytic tissues without retinal components. Unlike meningocele/meningoencephalocele, the lesion will not have any communication with the intracranial structures on imaging. Dermoid cyst usually has different architectural arrangement of the tissues (inner skin and skin appendages) and it is not associated with microphthalmic eye. Small round blue cell tumors (such as neuroblastoma and retinoblastoma) are formed by sheets of malignant small round blue cells showing high nuclear/cytoplasmic ratio, nuclear pleomorphism and increased mitotic activity without any glial differentiation. These tumors never stain for GFAP, which was positive in our case. In congenital cystic eye, no globe is identified on clinical or radiological grounds.

Our case presented clinically at birth with microphthalmic eye and an orbital cyst that was

confirmed radiologically. The microscopic and immunohistochemical features are indicative of ocular and neuroretinal differentiation. The constellation of clinical features, imaging and histopathological characteristics is diagnostic of microphthalmos/anophthalmos with cyst (colobomatous cyst).

According to Shields classification of orbital cysts of childhood, colobomatous cyst was classified as “a cyst of neural tissue related to ocular maldevelopment” [1]. It was defined as “a neuroectodermal-lined cyst formed by an ocular developmental anomaly that occur due to a failure in the closure of the optic fissure” [1–2]. It was first described in 1673 by Thomas Bartholin who is a Danish physician and anatomist [2]. Since that time, less than 150 cases have been reported in literature [3]. Out of these, only one article discussed the pathological features of colobomatous cyst. The etiology of the failure of closure of the optic fissure is largely unknown. Genetics such as PAX2 and PAX6, and teratogenic agents may play a role in the causation [4]. This disease can affect any structure in the eye [2, 5].

The clinical presentation of this cyst ranges from undetectable cyst to a large protruding one, but the typical presentation is a protruding cyst in the inferonasal quadrant of the eye associated with a microphthalmic globe [1–3, 5–10]. It usually presents at birth [1, 6, 7, 11] but can be detected even antenatally by ultrasound [12]. The vast majority are sporadic cases, but rare familial cases have been reported also [1]. Most of the colobomatous cysts are unilateral with bilateral cysts accounting for 27% of the cases. If bilateral, they are often associated with systemic anomalies, but no specific convincing syndrome or genetic/chromosomal abnormality is identified [1, 3, 5–8, 11, 13]. There is no sex or laterality preference [1, 8].

Radiologically, there is a microphthalmic globe associated with a cyst arising from its inferonasal quadrant. The cyst has homogenous contents with no post-contrast enhancement [9–10]. There may be a connection between the cyst and the vitreous cavity [1, 5–7, 9–11]. Grossly, the cyst had smooth gray-bluish outer surface and smooth gray-tan lining wall. It contained clear-yellowish serous fluid [11]. Microscopically, the cyst was formed by two layers: inner and outer layers [1, 3, 5–8, 16]. The inner layer was formed by a primitive neuroretinal tissue showing neuropil, retinal neurons, resetting formation, glial tissue (mostly astrocytes), and some melanin pigments (from the choroid). Foci of epithelial cells (from ciliary body) may be present. The outer layer was a fibrovascular connective tissue that continuous with the sclera [1, 3, 5–8, 14, 15]. It may contain foci of cartilage or dystrophic calcification. Lieb et al. ran some immunohistochemical stains and they found that the glial tissue was positive for GFAP whereas the NF highlighted the axons of the optic nerve in the background [8]. Chan et al. examined the aspirated fluid cytologically and they found that the fluid contained RBCs and some hemosiderin-laden macrophages [11].

Under the electron microscope, the glial cells showed some microvilli at their surface [8].

While some of these cysts spontaneously regress, others continue to grow causing some complications [6, 8, 16, 17]. Some believe that their growth is due to the accumulation of the fluids within the cyst. Others think that the proliferation of the glial tissue may be a factor in their enlargement [8, 11, 16, 17]. Observation is the management of choice for colobomatous cysts. The aim is to give the orbital cavity the needed time for its growth and development. Repeated aspiration of the cyst is performed when fluids accumulate. Surgical excision with prosthetic implantation is reserved for patients with complications (such as proptosis, dehydration, infection and ulceration) [1, 5–7, 11, 17].

## CONCLUSION

We presented a rare case of colobomatous cyst (microphthalmos with cyst) with detailed histopathological characterization. These complex and diverse features are unusual to the practicing pathologist and pose a diagnostic challenge and can result in misdiagnosis of malignancy. Correlation with the clinical presentation and imaging is imperative to reach the accurate diagnosis.

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## Author Contributions

Abdullah Al-Khamiss – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published

Ayman Ayoubi – Analysis and interpretation of data, Revising it critically for important intellectual content, Final approval of the version to be published

Muhammad Manzoor – Analysis and interpretation of data, Revising it critically for important intellectual content, Final approval of the version to be published

Sadeq Al-Dandan – Analysis and interpretation of data, Revising it critically for important intellectual content, Final approval of the version to be published

## Guarantor

The corresponding author is the guarantor of submission.

## Conflict of Interest

Authors declare no conflict of interest.

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## REFERENCES

- Shields JA, Shields CL. Orbital cysts of childhood—classification, clinical features, and management. *Surv Ophthalmol* 2004 May-Jun;49(3):281–99.
- Onwochei BC, Simon JW, Bateman JB, Couture KC, Mir E. Ocular colobomata. *Surv Ophthalmol* 2000 Nov-Dec;45(3):175–94.
- Chapter 1, The eye. Heegaard S, Grossniklaus H (eds.). *Eye Pathology: An Illustrated Guide*. 1st ed. Berlin: Springer-Verlag Berlin Heidelberg; 2015. p. 1–37.
- Chapter 20, Eye. Sadler TW (eds.). *Langman's medical embryology*. 12th ed. Philadelphia: Lippincott Williams & Wilkins; 2012. p. 329–38.
- Doglietto F, Massimi L, Dickmann A, Tamburrini G, Caldarelli M, Di Rocco C. Microphthalmia and colobomatous cyst of the orbit. *Acta Neurochir (Wien)* 2006 Oct;148(10):1123–5.
- Demirci H, Peksayar G, Demirci FY, Buyukbabani N, Demiryont M. Bilateral microphthalmos with colobomatous orbital cyst. *J Pediatr Ophthalmol Strabismus* 2002 Mar-Apr;39(2):110–3.
- Kim UR, Arora V, Shah AD, Srinivasan KG. Case report: Ocular malformation with a 'double globe' appearance. *Indian J Radiol Imaging* 2009 Oct-Dec;19(4):298–300.
- Lieb W, Rochels R, Gronemeyer U. Microphthalmos with colobomatous orbital cyst: clinical, histological, immunohistological, and electronmicroscopic findings. *Br J Ophthalmol* 1990 Jan;74(1):59–62.
- Simmons JD, Masters DL, Char D. Computed tomography of ocular colobomas. *AJNR* 1983;4(5):1049–52.
- Kaufman LM, Villablanca JP, Mafee MF. Diagnostic imaging of cystic lesions in the child's orbit. *Radiol Clin North Am* 1998 Nov;36(6):1149–63, xi.
- Chan W, Ho C. Case report bilateral microphthalmos and unilateral colobomatous orbital cyst: successful management by repeated aspiration. *HKJ Ophthalmol* 2005;9(1):37–9.
- Singh AD, Traboulsi EI, Reid J, et al. Orbital cyst: prenatal diagnosis. *Ophthalmology* 2009 Oct;116(10):2042–42.e2.
- Foxman S, Cameron JD. The clinical implications of bilateral microphthalmos with cyst. *Am J Ophthalmol* 1984 May;97(5):632–8.
- Singh U, Subramanian A, Bal A. Congenital orbital teratoma presenting as microphthalmos with cyst. *Indian J Ophthalmol* 2009 Nov-Dec;57(6):474–5.
- Weiss A, Martinez C, Greenwald M. Microphthalmos with cyst: clinical presentations and computed tomographic findings. *J Pediatr Ophthalmol Strabismus* 1985 Jan-Feb;22(1):6–12.
- Chapter 8, The malformed eye. Roberts F, Thum CK (eds.). *Lee's Ophthalmic Histopathology*. 3rd ed. London: Springer-Verlag; 2014. p. 237–40.
- Raynor M, Hodgkins P. Microphthalmos with cyst: preservation of the eye by repeated aspiration. *J Pediatr Ophthalmol Strabismus* 2001 Jul-Aug;38(4):245–6.

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