Management of congenital microphthalmos and anophthalmos with orbital cyst

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PURPOSE To study the effects of an individualized treatment approach to children with congenital microphthalmos and anophthalmos.

METHODS Patients with congenital microphthalmos or anopthalmos with orbital cysts who were referred to Beijing Tongren Hospital between July 2009 and July 2017 were included in this retrospective case series study. For patients ≤6 years of age, the cyst was retained to promote orbital development unless a prosthesis could not be fitted at all or disproportionate orbital growth was detected. Hydrogel orbit expanders were implanted initially if orbital volume was poor. For patients >6 years of age, the cyst was removed if it caused cosmetic problems or unsatisfactory prosthesis fitting. Eyelid procedures were performed after puberty to improve appearance.

RESULTS The study included 26 orbits of 24 patients. Of the 14 patients ≤6 years, 3 underwent cyst excision, 8 were treated with conformers only, and 3 had hydrogel orbit expander implantation initially. Of the 10 patients >6 years, 1 had the cyst removed, 5 had eyelid surgeries without removing the cyst, 3 wore an artificial eye without any surgery, and 1 used no prosthesis. During the follow-up period (range, 6 months to 8 years), 23 patients had a good cosmetic outcome and were eventually able to retain an ocular prosthesis; 1 patient could not wear prostheses but refused further treatment. No procedure-related complications were noted.

CONCLUSIONS The individualized treatment of congenital microphthalmos and anophthalmos with orbital cysts depends on the patient's age at presentation, the growth pattern of the cyst, and the volume of the affected orbit. (J AAPOS 2019;23:92.e1-6)

Microphthalmos with orbital cyst is a rare congenital malformation. Untreated microphthalmic and anophthalmic patients typically suffer from bony hypoplasia of the affected orbit.[1] However, orbital cysts in microphthalmic eyes may reduce the asymmetry between the affected and unaffected orbits, indicating a possible role of the cyst in orbital expansion.[2] Studies of normal children have shown that orbital volume increases in a linear fashion from birth to 5 or 6 years of age, with a marked decrease in rate thereafter.[1,3] Based on these findings, we propose that the indication for removing an orbital cyst in micropthalmic or anophthalmic patients should be carefully considered, especially in children ≤6 years of age. Currently there is no consensus on the management of microphthalmos or anophthalmos with orbital cysts.[4,5] Individualized interventions are necessary to improve aesthetic outcomes in these patients. We describe our experience in the management of these congenital deformities at a single institution over an 8-year period.

Subjects and Methods

The study was approved by the Ethics Committee of Beijing Tongren Hospital and adhered to the provisions of the Declaration of Helsinki for research involving human subjects. Written informed consent was obtained from all adult participants and from the parents of participating children. The medical records of patients with microphthalmos or anopthalmos with orbital cysts who were referred to Beijing Tongren Hospital between July 2009 and July 2017 were reviewed retrospectively. All the patients were examined and treated by the same surgeon (DL), and each newly diagnosed patient was referred for systemic evaluation by the pediatric service. Data collected included age at presentation, sex, laterality, ocular and systemic abnormalities, management, and outcomes.

Computed tomographic (CT) imaging of the orbital region was obtained for each patient. Radiation exposure in children was

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This work was supported by the Beijing Municipal Science and Technology Commission (Z131107002213002).

Submitted July 28, 2018.

Revision accepted October 24, 2018.

Published online March 27, 2019.

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1091-8531/$36.00

https://doi.org/10.1016/j.jaapos.2018.10.015

minimized using the as-low-as-reasonably-achievable principle[6] by adjusting parameters such as peak kilovoltage and tube current to a lower level (100kV, 93.8mAs) and limiting the scans to the orbital region. Two senior radiologists (QC, JX) read the CT images. No connection with the central nervous system or cerebrospinal fluid was detected. CT images were imported to the iPlan Cranial software (version 2.5; BrainLAB, Munich, Germany), which generated 3-dimensional reconstructions of the orbit and enabled digital measurements of orbital volume, globe volume, cyst volume, and displacement of orbital rims using techniques previously described.[1,2]

For patients ≤6 years of age, we elected to keep the cyst intact to promote orbital expansion. The cyst was removed if 1 of the following circumstances arose: (1) the prosthesis could not be fitted without removing the cyst; (2) the cyst was enlarging and caused asymmetrical development of the orbital walls; (3) the cyst prolapsed from the palpebral fissure. An artificial eye was fitted in the patient as young as possible and was regularly expanded as the child grew. The development of the orbit was monitored. If disproportionate growth of the orbit was detected, the cyst was removed. In cases where orbital volume was poor (<85% of the volume of the contralateral orbit), hydrogel orbit expanders were implanted initially.

For patients >6 years of age, the cyst was excised if it caused aesthetic problems or unsatisfactory prosthesis fitting. Eyelid operations were performed after puberty to improve appearance. In cases with phimotic palpebral fissures and increased intercanthal distance, Z lateral canthoplasty was chosen to expand the palpebral fissure, and Y-V medial canthoplasty was performed simultaneously to shorten the intercanthal distance. If the intercanthal distance was normal, only Z lateral canthoplasty was performed. Ptosis repair and conjunctivoplasty were performed if necessary.

To remove a cyst, a transcutaneous or transconjunctival incision was made overlying the cyst. Careful dissection was made to expose the anterior wall of the cyst, which was then carefully isolated to preserve the cyst wall. The connection to the microphthalmic globe was separated and the cyst was removed intact. For patients with anophthalmos and cyst, if the optic nerve was connected to the cyst, it was severed. The incision was closed with 7-0 polyglactin 910 running sutures (Figure 1).

The horizontal palpebral length was measured before treatment and at 1 year after surgery. For unilateral cases, success was defined as an increased microphthalmic-to-contralateral ratio of the horizontal palpebral length. Patient appearance was also evaluated subjectively by parents, patients, and the treating surgeon. The satisfaction was measured using the following 4-level scale: "not satisfied," "slightly satisfied," "satisfied," and "very satisfied." The results were dichotomized as satisfied and unsatisfied, the former including those who responded "satisfied" or "very satisfied"; all others were classified as "unsatisfied."[7]

Results

We identified 24 patients (16 males) who were treated for microphthalmos or anophthalmos with orbital cysts during the study period (Table 1). Two patients were affected bilaterally (1 case of microphthalmos and 1 case of anophthalmos). The median age at presentation was 6 years (range, 4 months to 32 years). Thirteen of the unilateral cysts were on the right side, and 9 were on the left (Table 1).

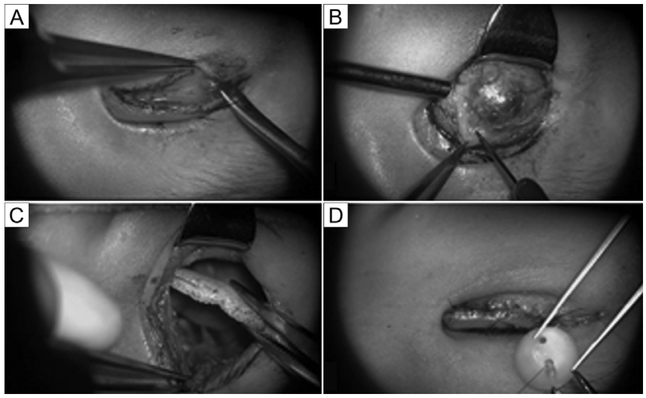

FIG 1. Excision of the orbital cyst and reconstruction of the orbital floor. A, An infraciliary incision is made. B, Careful dissection and isolation of the cyst is performed. C, A Medpor floor implant is placed to reconstruct the orbital floor after cyst excision. D, A hemisphere hydrogel expander is inserted into the socket.

Two patients had iris coloboma in the contralateral eye. Two patients had systemic conditions, including congenital megacolon and cleft lip/palate in 1 patient and atrial septal defect in another patient. Three patients had maternal exposure to hair dye (2 patients) and upper respiratory tract infection (1 patient) during early pregnancy. One mother was >40 years of age when she was pregnant.

Of the 14 patients ≤6 years of age, 3 were treated by cyst excision (2 bilateral; see Figure 2), 8 were treated conservatively with conformers only, and 3 required use of hydrogel orbit expanders (Figure 3; Table 2).

In 1 patient with abnormal orbital expansion due to rapid cyst growth, the orbital floor was reconstructed with a Medpor floor implant (Stryker, MI) after cyst excision. Hemisphere hydrogel socket expanders (Osmed GmbH, Ilmenau, Germany) were placed into the socket at the end of the procedure (Figure 1).

Of patients >6 years of age, 1 had a cyst excision (Figure 4), 5 underwent lid procedures without removing the cyst, 3 wore an ocular prosthetic without any surgery, and 1 did not wear a prosthesis because the mildly microphthalmic eye had little effect on appearance (Table 2).

Histopathology examination of the cysts revealed that the lining was composed of neuroglial tissue resembling the primitive retina, whereas the outer layer consisted of collagenous connective tissue (Figure 2E).

The median follow-up time was 4 years (range, 6 months to 8 years). Based on the subjective assessments of patients, parents, and the surgeon, excellent cosmesis was achieved in 23 of the 24 patients (Figures 2-4). One patient (case 23) had a fair cosmetic result after cyst excision, because the extremely narrow conjunctival sacs prevented a satisfactory prosthesis fitting, but the family did not want further treatment. Other patients were eventually able to wear a prosthesis. The prosthesis was gradually changed for larger ones, depending on the expansion of the socket and

Table 1. Clinical findings and management of patients with microphthalmos or anophthalmos with orbital cysts

Case	Age at presentation/ cyst excision	Sex	Diagnosis (with orbital cyst)	Laterality	Systemic abnormalities	Ocular abnormalities	MCR of orbital volume, %	Treatment	Cosmetic outcome	Follow-up, years
1	8 mos/2 yrs	M	Microphth	R	Nil	Nil	88	Exc	Good	4
2	24 yrs/24 yrs	M	Microphth	R	Nil	Nil	105	Exc	Good	4
3	4 yrs	F	Microphth	R	Nil	Nil	102	Conf	Good	8
4	23 yrs	M	Microphth	L	Nil	Nil	79	Lid	Good	8
5	17 yrs	F	Microphth	R	Nil	Nil	80	Lid	Good	8
6	6 yrs	M	Microphth	R	Nil	Nil	83	Exp	Good	7
7	3 yrs	M	Microphth	L	Nil	Nil	80	Exp	Good	6
8	27 yrs	M	Microphth	R	Nil	Nil	90	Lid	Good	8
9	27 yrs	F	Microphth	L	Nil	Right iris coloboma	93	Nil	Good	5
10	5 yrs	M	Microphth	R	Nil	Nil	96	Conf	Good	3
11	22 yrs	M	Microphth	L	Nil	Nil	79	Lid	Good	4
12	4 yrs	F	Microphth	L	Nil	Nil	91	Conf	Good	3
13	3 yrs	M	Microphth	R	Nil	Nil	74	Exp	Good	3
14	12 yrs	M	Microphth	R	Nil	Nil	97	Conf	Good	2
15	9 yrs	M	Microphth	R	Nil	Nil	81	Conf	Good	2
16	16 mos	F	Microphth	L	Nil	Nil	96	Conf	Good	7
17	32 yrs	M	Microphth	L	Nil	Nil	99	Lid	Good	3
18	2 yrs	M	Microphth	R	Nil	Left iris coloboma	98	Conf	Good	8
19	19 yrs	F	Microphth	L	Nil	Nil	101	Conf	Good	8
20	12 mos	F	Microphth	R	Nil	Nil	89	Conf	Good	8
21	6 mos/12 mos	M	Microphth	Bilat	Congenital megacolon, cleft lip/palate	Nil	—	Exc	Good	12
22	4 mos	F	Microphth	R	Nil	Nil	104	Conf	Good	6
23	11 mos/11 mos	M	Anophth	Bilat	atrial septal defect	Nil	—	Exc	Fair	Lost
24	6 yrs	M	Microphth	L	Nil	Nil	98	Conf	Good	2

Anophth, anophthalmos; *Bilat*, bilateral; *Conf*, conformer only; *Exp*, initial orbit expander implantation; *Lid*, lid surgeries; *MCR*, microphthalmic to contralateral ratio; *Microphth*, microphthalmos; *Exc*, cyst excision.

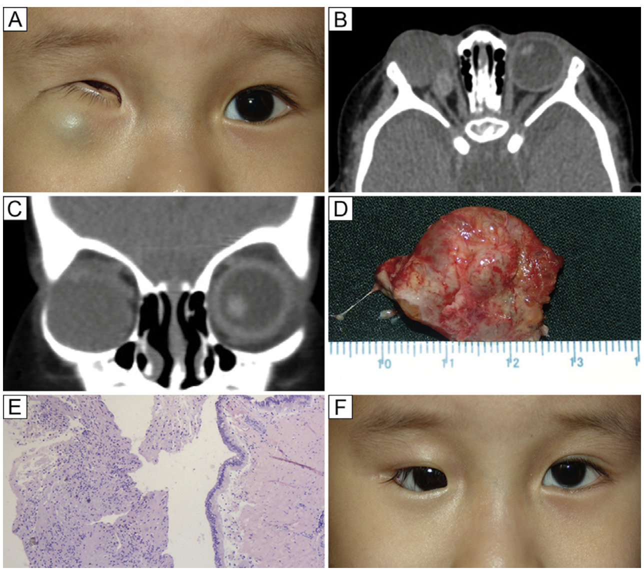

FIG 2. Right microphthalmos with orbital cyst in a 2-year-old boy. The patient underwent cyst excision and orbital floor reconstruction at 2 years. A, Preoperative photograph showing a bluish bulge in the right lower eyelid. B, Axial computed tomography (CT) scan showing a large cyst displacing the microphthalmic globe posteriorly. C, Coronal CT scan showing the cyst along the orbital floor, displacing it inferiorly. D, Gross appearance of the excised cyst. E, Hematoxylin and eosin staining of the cyst showing neuroepithelial cells resembling the primitive retina. F, Postoperative appearance of the same patient.

the growth of the eyelids. Among the 22 unilateral cases, by the 1-year follow-up, the horizontal palpebral length increased by an average of 2.0 mm, from 91.0% of the contralateral unaffected eye to 95.7%. For the bilateral case (case 21), the average palpebral length increased from 13.25 to 17 mm. No procedure-related complications were noted.

Discussion

Microphthalmos with cyst is the result of failed closure of fetal fissure with further distension of the retinal layers at the margins of the cleft.[8] The cyst is usually located in the inferior portion of the globe and appears as a bluish bulge in the lower eyelid. Whether a simple coloboma or a cyst forms is determined by the extent of separation between the 2 layers of the optic cup.[9] In our series, 2 patients (case 9 and 18) with a colobomatous cyst had iris coloboma in the fellow eye. Anophthlamos with cyst is also referred to as congenital cystic eye, caused by failed invagination of the optic vesicle during the period of 2–7 mm stage of embryo.[10]

Colobomatous cysts are histopathologically similar to congenital cystic eyes, but the latter lack globe structures. In some cases, clinical differentiation may be difficult. Imaging is invaluable in diagnosis and differential diagnosis. In our study, careful examination of CT images by 2 senior radiologists (QC and JX) revealed that all cases but one (case 23) had globe structures.

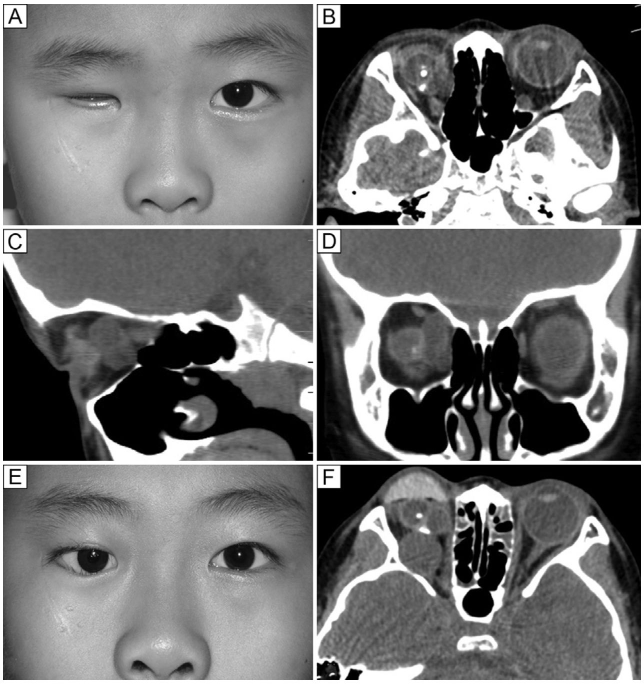

FIG 3. Right microphthalmos with orbital cyst in a 6-year-old boy. The cyst was retained and a hydrogel orbit expander was implanted. A, Before treatment. B, Axial CT scan showing the microphthalmic globe with calcification. C, Sagittal CT scan showing the cyst located behind the microphthalmic globe. D, Coronal CT scan showing the cyst medial to the globe. E, Postoperative appearance of the patient at 9 years of age. F, Axial CT scan showing the hydrogel orbit expander behind the globe.

Table 2. Management of patients with microphthalmos or anophthalmos with orbital cysts

Age group	Management	No.
≤6 years	Cyst excision	3
	Conformer therapy	8
	Orbital expander implantation	3
>6 years	Cyst excision	1
	Prosthesis (with/without lid surgeries)	8
	Observation	1

Other differential diagnoses include dermoid cysts, teratomas, encephaloceles, and meningoceles. Dermoid cysts usually locate at the superotemporal part of the orbit in association with the frontozygomatic suture. Teratomas contain tissues of more than 1 germ layer and are usually very large. The cystic portions should appear very bright on the T2-weighted imaging. Encephaloceles or meningoceles communicate with the intracranial cavity. The characteristic clinical manifestations and imaging helped us to differentiate colobomatous cysts from these diseases.

Microphthalmos or anophthalmos with orbital cysts may be unilateral or bilateral, and they may exist independently of or in conjunction with other ocular or systemic abnormalities. In our series, there were 2 bilateral cases, both of which had associated systemic deformities. Rates of

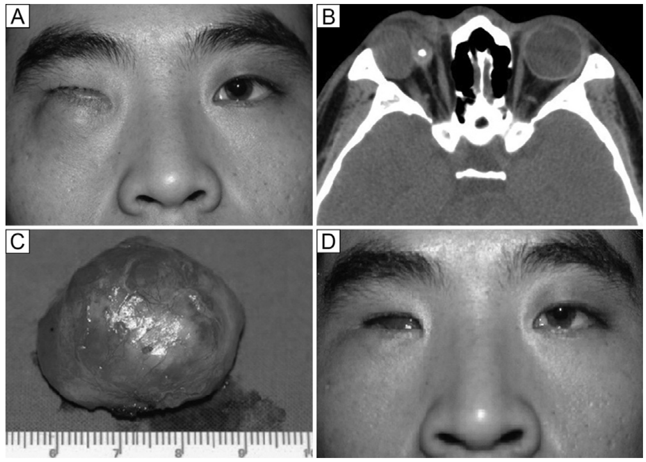

FIG 4. Right microphthalmos with orbital cyst in a 24-year-old man. A, Severe lower eyelid swelling before treatment. B, Axial CT scan showing a large cyst and the microphthalmic globe. C, Gross examination of the excised cyst. D, Postoperative appearance of the patient.

bilateral cysts and systemic involvement are higher in other studies.[4,5]

The exact cause of microphthalmos or anophthalmos with orbital cysts remains unclear: both exogenous and genetic factors may contribute to the etiology. In our series, 2 mothers had a history of virus infection, 1 mother had exposure to hair dye during early pregnancy, and 1 mother was of advanced maternal age.

In our previous study, microphthalmic eyes with large cyst-plus-globe volume showed better symmetry with the fellow eye compared with micropthalmic eyes without orbital cyst or with cases with small cysts.[2] We conclude that the presence of the orbital cysts in microphthalmic eyes play an important role in orbital development.

In patients ≤6 years of age, when the cyst is small and the microphthalmos is not severe, conformer therapy is all that is required. When the cyst shows slow growth with appropriate bony and socket expansion, the cyst should be retained to promote orbital growth. In our series, more than 50% of the patients ≤6 years of age (8/14) were in this treatment group.

Contrary to prior studies,[4] however, we suggest that early cyst excision should be performed in three situations. First, excision is recommended if the cyst prevents prosthesis fitting or causes displacement of the orbital walls. When the cyst is large and located anteriorly, the eyelids and the conjunctival fornix are displaced, with the result that a prosthesis cannot be retained, as seen in cases 1, 21, and 23 in our series. Compression and atrophy of orbital soft tissues is also of concern. If conformers are not fitted properly at an early age, the fornix shortening and palpebral fissure narrowing result in unsatisfactory prosthesis fitting as the child grows. Moreover, these large, anterior cysts could cause inappropriate and undesired expansion of the orbit, as seen in case 1, where downward displacement of the orbital floor was detected, necessitating orbital floor reconstruction with an implant. The second circumstance calling for excision is spontaneous, or post-traumatic hemorrhage into the cyst cavity causing rapid enlargement of the cyst and necessitating removal, as in cases 21 and 23. Pathological examination of these cases revealed that the excised cysts were filled with dark hemorrhagic fluid instead of yellowish translucent fluid, as previously described.[11] Finally, cyst removal should be performed if the cyst prolapses out of the palpebral fissures and the bony orbit becomes too large.

Complete surgical excision is recommended for cyst removal. Polito and Leccisotti[11] have recommended decompressing the cyst by aspiration prior to removal. However, in our experience, decompression of the cyst makes dissection more difficult. If possible, the cyst should be removed intact to ensure complete removal. Although we do not advocate cyst aspiration due to high recurrence rate,[4,5] combined with ethanolamine oleate sclerotherapy, aspiration may provide a higher resolution rate.[12,13] Compared to surgical excision, sclerotherapy seems to be less complicated, but studies regarding its use in the treatment of orbital cyst associated with microphthalmos are very limited. In the only case series study in which 7 cysts received sclerotherapy, one patient required repeat treatment, and another patient showed partial response.[12] Possible complications related to the injection of a sclerosant were not clear in such patients. Another consideration is whether sclerotherapy would induce inflammatory fibrosis to render subsequent secondary implant surgery more difficult.

Hemisphere hydrogel expanders are useful to expand the socket and the palpebral fissure and can be easily placed into the fornix. Within 72 hours, the hydrogel gradually enlarges from 0.2 ml to 1.5 ml and expands the fornices and eyelids. Conformer fitting can occur in approximately 1-2 months. The use of hydrogel socket expanders makes frequent conformer fittings unnecessary in the first months of treatment. This is also convenient for patients who travel great distances and have no local care. Increasingly larger conformers are fitted after this initial phase.

The existence of orbital cysts in microphthalmic eyes potentially plays a positive role in orbital development[2] and many patients may achieve good cosmetic outcomes with increasingly larger conformers fittings only. However, in patients $\leq$6 years of age, where orbital volume is severely reduced, more aggressive orbital expansion techniques should be considered, such as hydrogel orbit expanders. In this study, based on the imaging calculations of the orbital volume, we placed in hydrogel orbit expanders in patients with a volume of <85% that of the contralateral side (cases 6, 7, and 13). The advantages of hydrogel orbit expanders have been shown in prior studies.[7,14,15] Being easy to implant and replace, the hydrogel expander enlarges gradually and promotes orbital expansion. Other tissue expanders such as inflatable expanders with a remote reservoir were also considered, but they require office filling and are more complicated than hydrogel orbit expanders.[16] In contrast to balloon expanders, the hydrogel device starts swelling immediately when inserted into the living tissue until reaching the final volume. The expansion procedure is much more comfortable for the patients. Another important advantage of the hydrogel expander is its excellent ability to promote eyelid development, which is crucial for a satisfactory cosmetic result.[17]

In our study, the proportion of patients who started treatment after puberty (9/24) was higher than that in prior studies.[4] The hypoplastic bony orbit in this age group severely compromises the cosmetic outcome. The importance of early intervention should be emphasized, and patients with microphthalmos and anophthalmos with orbital cysts should be referred for treatment as soon as possible after birth to achieve the best outcome.

Due to the small sample size, procedure-related complications were not found in this study, but orbit expander dislocation and socket expander loss occasionally occur in our treatment of other microphthalmic patients.[7] Expander dislocation can be treated successfully with a surgical relocation of the expander. When the socket expander is lost, shrinking of the socket could be prevented by immediate replacement of the expander or insertion of a prosthesis.

Because micropthalmos or anophthalmos with orbital cyst is very rare, the sample size in this study was small, and each subclass was quite small. Furthermore, cosmetic appearance is a subjective variable. Despite these limitations, our experience in the management of microphthalmos or anophthalmos with orbital cysts highlights the need for individualized intervention for each patient. Age at presentation, growth pattern of the cyst, and orbital volume are all critical factors in decision making about treatment.

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