



Intraoperative use of indocyanine green and trypan blue mixed with fibrin glue in the excision of periocular cystic lesions

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ABSTRACT

Purpose: This case series describes the use of tissue fibrin glue mixed with dye to facilitate the excision of eight orbital and periorbital cystic lesions of various complexity.

Observations: The fibrin glue was colored with indocyanine green dye (ICG) or trypan blue and injected intraoperatively into the lesions. The glue was then allowed to harden, and the lesions were excised. The dyed glue outlined the wall of the cysts, kept them formed and allowed for complete excision with ease. None of the cases had recurrence. As an observation, ICG showed superior delineation than trypan blue.

Conclusions and importance: The use of colored fibrin glue is a helpful technique in the delineation and excision of cystic lesions. Delineating the wall of the cyst with the dyed glue simplified the surgery and prevented complications such as injury to surrounding vital structures and reduced the likelihood of recurrence. ICG may be superior to trypan blue but a comparative controlled study is needed to assess the difference.

1. Introduction

Cystic lesions in the orbital and periocular areas are often a challenge during surgical excision. Incomplete excision and injury to the surrounding structures are major concerns for recurrence and complications.¹ Delineating the wall of the cyst and keeping its integrity facilitate visualization, and complete excision, thereby eliminating the need for revision surgery.

The use of fibrin glue has been reported in the excision of periorbital cystic lymphangiomas, used as adhesive and hemostatic.^{2,3} However, the use of dye mixed with fibrin glue is under reported. We describe a case series of eight patients. The series includes cystic lesions of various complexity including orbital dermoid, orbital mucocele, scleroconjunctival cyst and orbital teratoma that have been treated with fibrin sealant mixed with dye between 2009 and 2019. Six of the eight cases had imaging with computerized tomography (CT) and/or magnetic resonance imaging (MRI) prior to surgery to verify the cystic nature of the lesion. In each case the lesion was surgically accessed and identified. Before proceeding with excision, the lesion was slightly aspirated and injected with tissue fibrin sealant mixed with dye. Indocyanine green, Akron Inc, was reconstituted in sterile water at a concentration of 25 mg per 10 ml. One milliliter of the ICG mixture

(2.5mg/ml) was mixed in each syringe of the components of the fibrin glue. Trypan blue, Vision blue® 0.06% in 0.5 ml Syringe, was equally divided between the two components of tissue fibrin glue. The dye colored the cyst wall and made visualization and distinction from adjacent tissue more evident. After solidification of the fibrin glue, which kept the cyst formed and prevented leakage of the cyst content, excision of the lesion was completed. The dyes mixed with fibrin glue were indocyanine green (ICG) or trypan blue. The selection of dye was random and was based on availability. Clinical features, radiologic findings, dye used and outcome are summarized (Table 1).

Consent for surgery was obtained in all cases. The study was HIPAA compliant and adhered to the tenets of the Declaration of Helsinki as amended in 2008.

The case series was done in accordance with Institutional Review Board Guidelines at SUNY, Stony Brook.

2. Findings

2.1. Case 1

A 55-year-old woman presented with a two-year history of right proptosis and worsening vertical diplopia (Fig. 1A). She denied history

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of trauma. CT scan revealed a large right superior orbital cystic lesion extending into the frontal sinus (Fig. 1B). The roof of the frontal sinus was thinned and displayed a bony defect. MRI revealed the lesion to be contiguous with the dura with no brain tissue herniation (Fig. 1C). Right orbitotomy was performed through an eyelid crease approach. The lesion was identified and filled with tissue fibrin glue mixed with trypan blue. As the dyed tissue fibrin glue hardened, there was a clear delineation of the cyst wall which maintained its shape and prevented leakage of the cyst content. The cyst was excised in total with no CSF leak (Fig. 1D). The site of the bony defect was visualized during surgery and sealed with a Duragen (Integra LifeSciences Corporation) patch. Histopathology was consistent with dermoid cyst. The patient had unchanged visual acuity of 20/20 and a smooth postoperative course with no recurrence after 2 years of postoperative follow-up.

2.2. Case 2

A 25-year-old male presented with one-year history of intermittent periorbital pain, swelling and discharge. He described recurrent skin breakdown outside the lateral orbital rim with recurrent discharge at the site of a previous incision and drainage of an abscess (Fig. 2A). CT scan with contrast revealed a cystic mass in the temporal fossa with a small component in the lateral orbit (Fig. 2B). He underwent left orbitotomy through an eyelid crease approach. Intraoperatively, a soft mass with associated scarring was identified in the lateral orbit (Fig. 2C). The lesion was injected with tissue fibrin glue mixed with Indocyanine green (ICG) dye (Fig. 2D). A skin incision was then performed around the external scar in the temporal fossa, the site of recurrent discharge. A tract filled with ICG dyed fibrin glue was visualized coming through as the orbital mass was being injected (Fig. 2D and 2E). The fistula tract exit was superior and temporal to the eyebrow corresponding to the temporal fossa lesion on CT. The tract was cored out and excised along with the orbital lesion both of which were containing ICG stained tissue fibrin glue. The bone surrounding the fistula tract at lateral orbital rim was burred using 2mm diamond bone burr (Stryker). Histopathology was consistent with dermoid cyst. The patient had unchanged visual acuity of 20/30 and remained recurrence free at 2-year period of postoperative follow up.

2.3. Case 3

A 56-year-old male presented with a 5-year history of progressive left proptosis (Fig. 3A). He had a history of a motor vehicle accident 10 years prior with head injury for which he underwent a craniotomy. CT scan revealed a large cystic lesion occupying the superior orbit and frontal sinus (Fig. 3B). MRI with contrast showed the cystic lesion to be possibly



Fig. 1A. Preoperative photograph in case 1 demonstrates right proptosis and inferior displacement of the right globe.

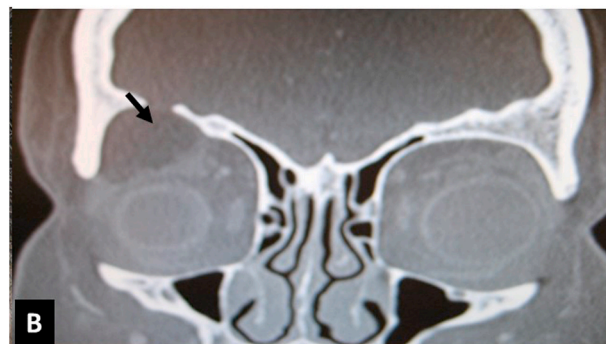


Fig. 1B. Coronal CT scan in case 1 with large orbital cystic lesion in the right superior orbit extending into the frontal sinus through a bony defect in the orbital roof. The lesion is marked with black arrow.

communicating with the dura (Fig. 3C). Dynamic imaging studies ruled out cerebrospinal fluid (CSF) leak into the lesion. Orbitotomy was performed through an eyelid crease approach. The lesion was identified and filled with tissue fibrin glue mixed with ICG dye (Fig. 3D). As the fibrin glue with dye hardened, there was a sharp delineation of the cyst wall from the surrounding structures. The cyst was excised in total with no CSF leak (Fig. 3E). Histopathology was consistent with mucocele. Proptosis resolved after surgery and visual acuity was stable at 20/20. The patient remained recurrence free with a postoperative follow up period of two and a half years.

Table 1

Summary of cases with the dye used with fibrin glue.

Case	Age	Signs and symptoms	Imaging	Diagnosis	Dye	Postoperative follow-up
1	55yrs	Right Proptosis	MRI and CT: Right orbit cystic lesion invading the frontal sinus with bony defect of the sinus roof	Right orbit dermoid cyst	Trypan blue	24 months
2	25yrs	Temporal fossa scar lateral to the left eyebrow with recurrent discharge	CT: Temporal fossa mass with an orbital component	Left orbit dermoid cyst with fistula tract	ICG	24 months
3	56yrs	Left Proptosis and hypoglobus	MRI and CT: Large cystic lesion in the superior orbit and frontal sinus with possible communication with dura	Left orbit mucocele	ICG	30 months
4	33yrs	Right Bleb like cyst with thinning of sclera around the cyst	none	Right episcleral epithelial cyst	ICG	12 months
5	74yrs	Left Cystic mass in lateral fornix	CT: Cyst in lateral fornix adherent to lacrimal gland	Left lacrimal gland cyst	Trypan blue	24 months
6	7yrs	Right lateral orbital rim mass	none	Right lateral orbital rim dermoid cyst	Trypan blue	12 months
7	57yrs	Left proptosis	MRI and CT: Deep orbital dermoid cyst adjacent to the optic nerve	Left orbit dermoid cyst	ICG	24 months
8	23yrs	Right upper eyelid abscess with hair elements through skin fistula	MRI and CT: Orbital cystic lesion communicating with the eyelid abscess	Right orbit benign teratoma	ICG	9 months

MRI: Magnetic resonance imaging. CT: computerized tomography. ICG: Indocyanine green.

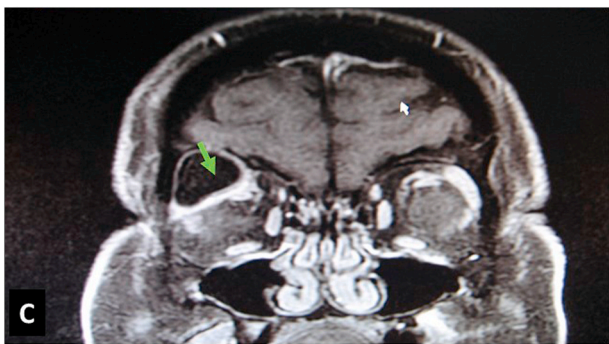


Fig. 1C. MRI of brain and orbit with contrast showing the cystic lesion is contiguous with the dura without herniation of brain tissue. The lesion is marked with green arrow. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)



Fig. 2B. Coronal CT scan of orbit with contrast showing a large temporal fossa mass with a small mass in the lateral orbit. The lesion is marked with black arrow.



Fig. 1D. The cystic lesion cast inclusive of fibrous capsule displays hardened fibrin glue and trypan blue marked with black arrows (case1). (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)



Fig. 2C. Exposure of the orbital component of the cyst through left orbitotomy and eyelid-crease approach.



Fig. 2A. Preoperative lateral view of case 2 showing a scar at the site of recurrent fistula marked with black arrow. The surgical marker indicates the lid crease approach for planned orbitotomy.

2.4. Case 4

A 33-year-old female was referred for evaluation of a “bleb versus conjunctival cyst” with a 1-year history of progressive enlargement. The patient reported that she had undergone orbital reconstructive surgery in addition to strabismus surgery 12 years prior after traumatic injury. The patient denied visual changes, or restriction of ocular motility. Clinical examination revealed a 2-cm conjunctival cyst which was well circumscribed, non-movable and contained serous fluid adjacent to an area of scleral thinning (Fig. 4A). Preoperative imaging was not done prior to surgery since the lesion was episcleral. Transconjunctival excision of the lesion was performed. The lesion was partially aspirated to

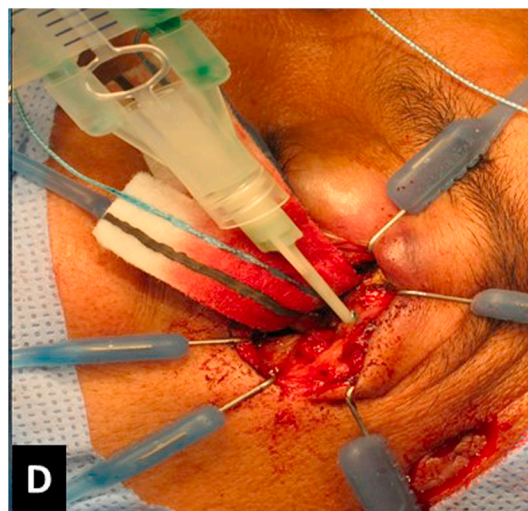


Fig. 2D. Fibrin glue-ICG mixture as it is being injected into the orbit part of the lesion.

allow for injecting the dyed glue without rupturing the cyst. Through the same port of entry and by exchanging the syringe, the lesion was injected with fibrin glue mixed with ICG dye (Fig. 4B). As the tissue fibrin glue hardened, the conjunctiva was opened and retracted. The

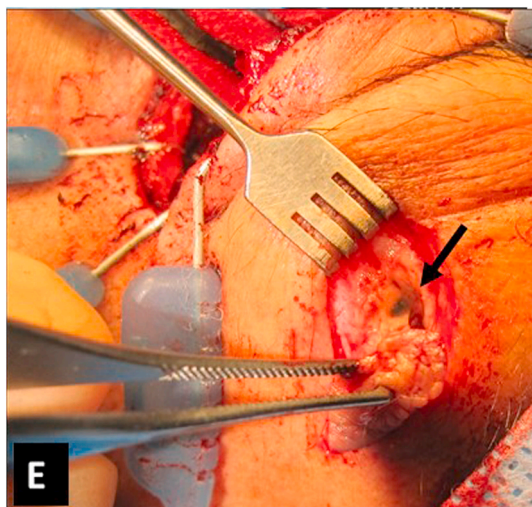


Fig. 2E. The ICG dye as it exits along the distal aspect of the fistula tract marked with black arrow in the temporal scar showing connection with the orbital mass.



Fig. 3A. Preoperative photograph of case 3 demonstrating left proptosis and inferior displacement of the globe.

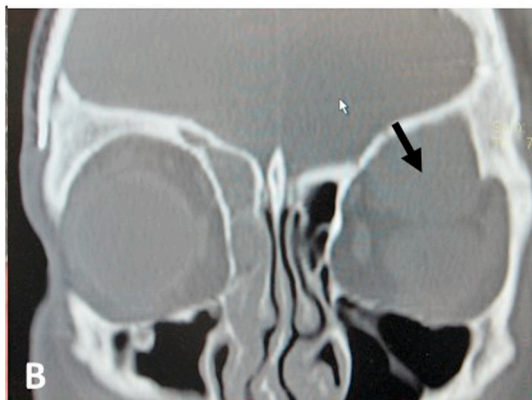


Fig. 3B. Coronal CT scan showing large orbital cystic lesion in the left superior orbit and the frontal sinus. The lesion is marked with black arrow.

lesion was exposed. It was well highlighted with ICG and distinct from the sclera. Blunt and sharp dissection around the capsule completed the excision of the cyst in total (Fig. 4C and 4D). The superior rectus insertion was reinforced using partial thickness scleral passes. The cyst



Fig. 3C. Coronal MRI with contrast showing the cystic lesion to be in possible communication with the adjacent dura. The lesion is marked with black arrow.

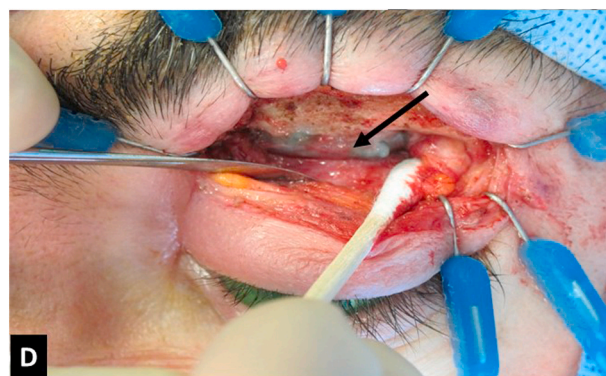


Fig. 3D. Orbitotomy through eyelid crease approach showing the lesion in case 3 after it has been filled with a fibrin glue-ICG mixture. The lesion is marked with black arrow.



Fig. 3E. The cystic lesion, which has a greenish tint from ICG, measuring approximately 2 cm in longest dimension, excised in total (case 3).

was adherent to the muscle insertion and had compromised its integrity but the use of dyed glue prevented transection of the tendon and disinsertion of the muscle. Histopathology was consistent with epithelial inclusion cyst (Fig. 4E and 4F) The preoperative visual acuity of 20/30 remained stable. The eyelid edema and chemosis resolved after 3 weeks and no recurrence was observed at one year of follow up.

2.5. Case 5

A 74-year-old female presented with a slowly expanding left conjunctival cystic swelling over a period of 1 year. Clinical examination

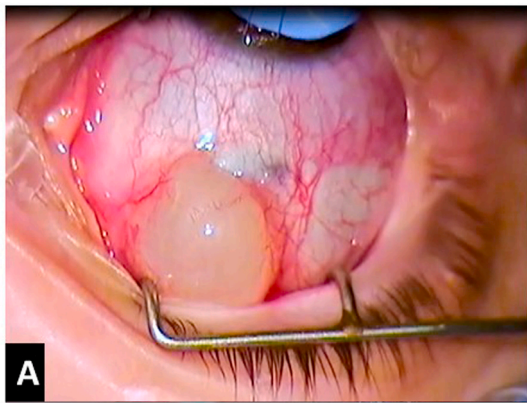


Fig. 4A. A well-circumscribed scleral-conjunctival cyst containing serous fluid (case 4).

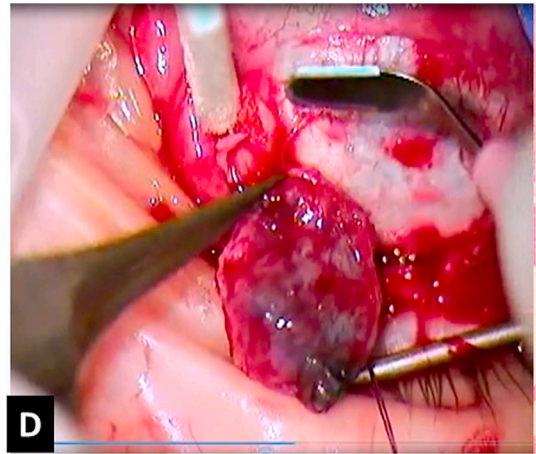


Fig. 4D. The cystic lesion being removed in total with capsule intact.

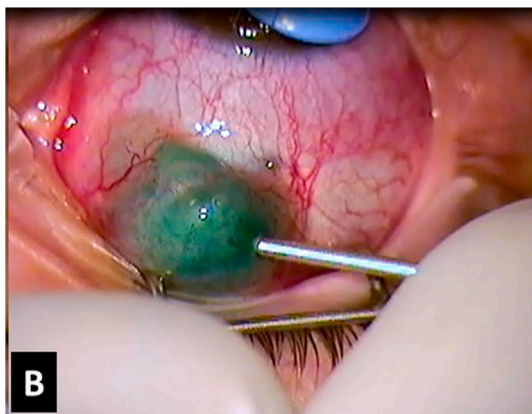


Fig. 4B. The cystic lesion in case 4 injected with fibrin glue mixed with ICG.

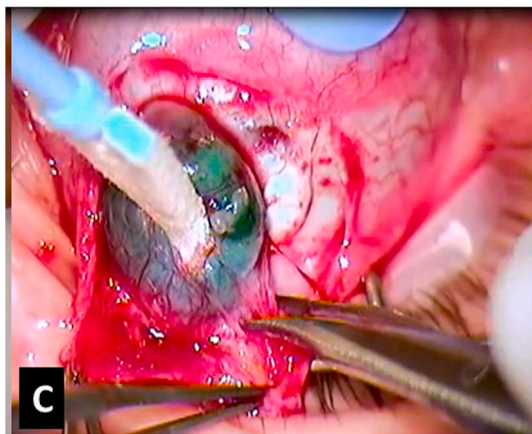


Fig. 4C. The cystic lesion being excised from the surrounding Tenon's capsule and conjunctiva.

demonstrated an anterior orbital cystic mass in the lateral fornix. CT scan revealed a 1 cm cystic lesion contiguous with the lacrimal gland. The anterior orbital space containing the lesion was accessed through an inferolateral fornix approach. The conjunctiva was gently incised and retracted with blunt dissection to expose the lesion which was identified and injected with tissue fibrin glue mixed with trypan blue dye. The solidified tissue fibrin glue with dye maintained the lesion integrity and highlighted its capsule from the surrounding soft tissue. The lesion was excised in total with no perforation. It was consistent with a lacrimal

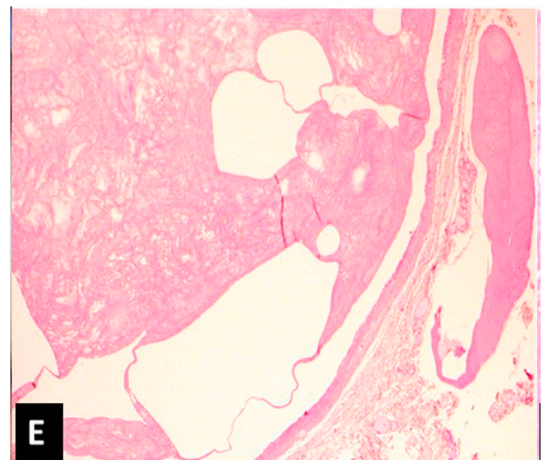


Fig. 4E. PAS stain (2.5X) of cyst in case 4 showing eosinophilic hyaline material filling epithelial-lined cavity.

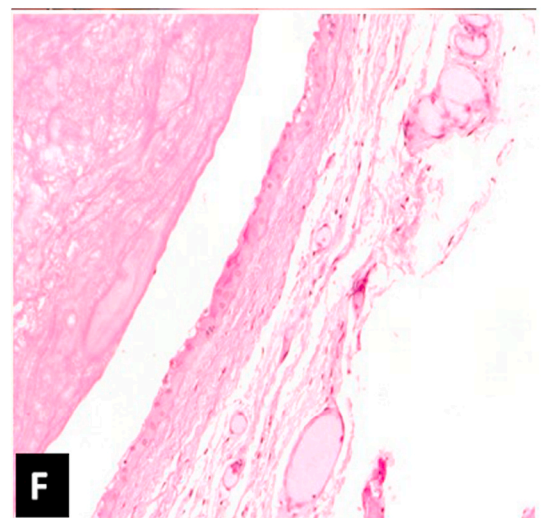


Fig. 4F. PAS stain (210X) highlighting lamellar hyaline material to the left and cyst wall to right.

gland cyst. The patient had stable visual acuity of 20/20 with no recurrence at 2 years of follow up.

2.6. Case 6

A 7-year-old girl presented with a history of right lateral orbital rim mass since infancy. The lesion was progressively increasing in size. It was clinically consistent with a dermoid cyst. Preoperative imaging was not done prior to surgery since the lesion was movable along the rim. A lateral lid crease incision was performed to access the lesion along the lateral orbital rim. The dermoid was found to be larger than anticipated with extension toward the temporal fossa. The content was injected with fibrin glue mixed with trypan blue. Since the lesion was fully highlighted with dye, the posterior wall was outlined and a dumbbell-shaped dermoid was ruled out. Excision of the lesion was completed in total without perforation or leakage. Histopathology confirmed the diagnosis of dermoid cyst. The patient had an uneventful postoperative course with unchanged visual acuity of 20/20 and no recurrence after one year of follow up.

2.7. Case 7

A 57-year-old male presented with an incidental finding of a large left orbital cyst on brain MRI following a motor vehicle accident. External evaluation revealed medial distortion of left upper lid that was considered by the patient as part of his normal appearance since childhood (Fig. 5A). He had normal visual function and normal visual field evaluation. Hertel ex-ophthalmometry revealed 2 mm of left proptosis with resistance to retropulsion. CT scan of the orbit revealed a 2.7 cm cystic lesion consistent with chronic orbital dermoid cyst with remodeling of the medial and superior orbital walls (Fig. 5B and 5C). On axial and sagittal views, the lesion was in close proximity to the medial rectus and optic nerve (Fig. 5C and 5D). Orbitotomy was performed through a medial eyelid crease approach. The lesion was identified and filled with tissue fibrin glue mixed with ICG (Fig. 5E). This prevented leakage of the cyst content and outlined the wall of the cyst. It was separated from vital structures and extirpated in total. An endoscope was used in the medial orbit to aid with visualization. Patient had an uneventful post-operative course with preserved vision of 20/20 and a normal visual field. Histopathology was consistent with orbital dermoid cyst. He had no recurrence after two years of postoperative follow up.

2.8. Case 8

A 23-year-old female presented from a community hospital with right upper eyelid abscess with pre-septal cellulitis following excision of an eyelid lesion. She was admitted for intravenous antibiotics and had partial resolution of the cellulitis with multiple recurrences. Follow up imaging revealed a right superolateral orbital cystic lesion

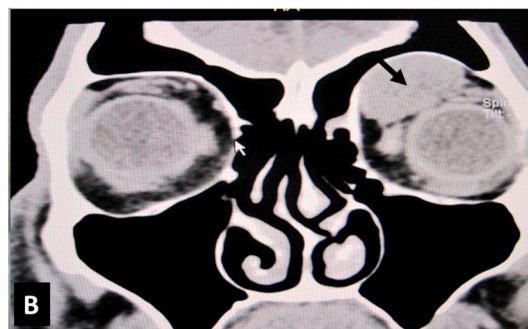


Fig. 5B. Coronal CT scan with large orbital cystic lesion, marked with black arrow, in the left supero-medial orbit adjacent to the globe with remodeling of the orbital roof.

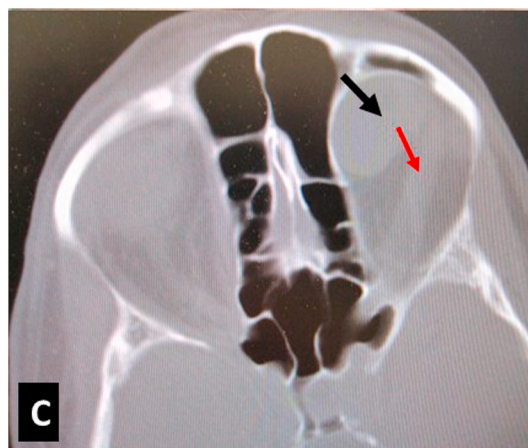


Fig. 5C. Axial view of orbital CT scan with remodeling of the medial wall. The lesion is marked with black arrow and the optic nerve in red. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

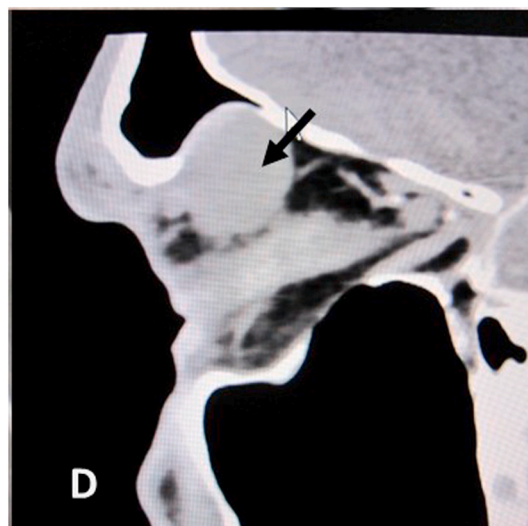


Fig. 5D. Sagittal view of orbital CT scan. The lesion is marked with black arrow.



Fig. 5A. Preoperative photograph of case 7 demonstrates left upper lid distortion and medial ptosis with mild proptosis.

communicating with the eyelid abscess anteriorly. On examination she had a fistula tract with clumps of eyelash like hair extruding through the drainage site of the lesion. She underwent anterior orbitotomy through an eyelid crease approach. The fistula tract was injected with tissue

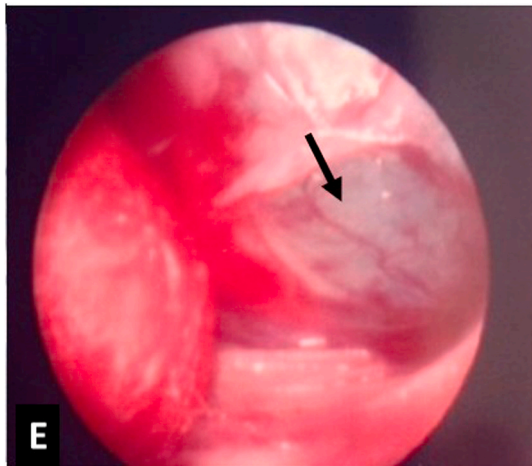


Fig. 5E. Orbitotomy through eyelid crease approach showing the lesion in case 7 after it has been filled with a fibrin glue-ICG mixture. The lesion is marked with black arrow.

fibrin glue with ICG dye. The cyst was well delineated and excised in total with no leakage of content. Histopathology was consistent with benign orbital teratoma. The cellulitis, secondary to the inflammation induced by the cyst content, resolved after surgery with stable visual acuity of 20/20 and no recurrence at nine months of follow up.

3. Discussion

The use of tissue fibrin glue has been reported in the excision of cystic lymphangiomas.^{2,3} Boulos et al. described three cases where a combination of cyst content aspiration, intra-lesion injection of fibrin glue followed by surgical excision allowed for complete resection of the lesions. In addition, it prevented intra-operative and postoperative bleeding.² Hayasaki et al. reported a case of progressive exophthalmos secondary to cystic lymphangioma that recurred after partial excision. The cyst was completely sealed with no recurrence after the use of intra-lesion fibrin glue.³ Intralesional fibrin glue without surgical excision was previously described by Castanon et al. in nineteen cases of cystic lymphangiomas in the head and neck region.⁴ They used puncture and aspiration followed by intra-lesion fibrin glue. Multiple injections were needed for complete remission in seventeen cases.

Our unpublished series described the combined use of tissue fibrin glue with dye in periocular lesions in a thesis report to the American Society of Ophthalmic Plastic and Reconstructive Surgery (ASOPRS) in 2015. Since then there have been two published articles in the literature describing the use of fibrin glue mixed with methylene blue to facilitate the excision of branchial cleft fistulae and cysts.^{5,6} A recent case report illustrated the excision of dacryops of the orbit with the use of fibrin glue with trypan blue.⁷ We believe this technique is still underrepresented in the ophthalmic literature. Our series includes a variety of cases with different levels of complexity and illustrates this technique with two different dyes, Indocyanine green and trypan blue. None of the published reports combined ICG with tissue fibrin glue.

The use of tissue fibrin glue mixed with dye facilitated the excision by providing clear visualization of the lesions and separation from adjacent tissues. The orbital dermoid (case 1) and orbital mucocele (case 3) were in a critical location adjacent to the dura. The use of tissue fibrin glue with dye improved visualization of the cyst boundaries and prevented complications such as violation of the dura, CSF leak and incomplete excision. The fistula tract in the recurrent dermoid (case 2) was tortuous and would have been hard to differentiate from the surrounding scar tissue. The use of fibrin glue with dye inflated the tract allowing it to be excised under direct visualization. The scleroconjunctival lesion (case 4) was concerning for scleral perforation. Delineating

the capsule of the lesion provided protection against violating the sclera and made extirpation of the cyst significantly easier. The large orbital dermoid in case 7 was adjacent to the medial rectus, superior rectus and optic nerve. The lesion was visualized with ease, separated from adjacent tissue and excised without damage to vital structures.

In our series, ICG was used in five cases and trypan blue in the remaining three. The amount of ICG or Trypan blue added can be titrated if more intense coloring is desired. Although this is not a controlled study comparing the two dyes, the ICG seemed to offer better visualization than trypan blue. ICG had a vivid green tone easier to distinguish from electrocautery marks and clotted blood on the field. Another advantage to ICG dye is the ability to demonstrate fluorescence when using a near infrared filter (NIRF). ICG-guided near infrared fluorescence (NIRF) has been described in the excision of cavernous sinus dermoid cyst and splenic pseudocyst.^{8,9} Moreover, the application of ICG-guided NIRF, supported by existing laparoscopic and robotic platforms, is expanding in various surgical procedures including colorectal and hepatobiliary surgery.¹⁰

Fibrin glue has a long track record of clinical safety and a widespread use among the subspecialties, including prevention of seroma and hematoma after abdominoplasty and breast surgery.^{11–13} Other applications include complete excision of hepatic cysts and excision of pilonidal sinus with closure and obliteration of the dead space with fibrin glue.^{14,15} CT-guided percutaneous injection of fibrin glue been reported in symptomatic sacral arachnoid cysts as a non-surgical alternative.¹⁶

Dyes such as ICG and trypan blue are of familiar usage to ophthalmologists in intraocular surgery. The combination of dye and fibrin glue is safe for application in the periocular area. Tissue fibrin glue is commonly used with amniotic membrane graft in pterygium surgery and has proven safe with extremely rare anaphylactic and allergic reactions.⁸

4. Conclusions

Our series illustrates a simple and safe technique, dye stained tissue fibrin glue, that facilitates the excision of periocular cystic lesions, and possibly decreases the recurrence rate. This technique allows greater visualization, tissue preservation and more precise excision. It is a valuable adjunct tool to surgical excision of cystic lesion in the orbit and periocular area. ICG may have an advantage over trypan blue and merits a controlled comparative investigation.

4.1. Patient consent

Surgical consent, obtained in all cases, included the consent to be photographed or videotaped and photographs may be used for teaching purposes. The series does not contain personal information that can lead to identification of patients.

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Declaration of competing interest

The authors have no financial disclosures.

Authorship

All listed authors meet the ICMJE criteria.

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