Case report

Retrobulbar chlorpromazine injection in a child with gliosarcoma invasion into the orbits

Franklin Jeng,[1] Andrew Reynolds [2]

[1]Ophthalmology, University at Buffalo Jacobs School of Medicine and Biomedical Sciences, Buffalo, New York, USA
[2]Ophthalmology, Ross Eye Institute, University at Buffalo Jacobs School of Medicine and Biomedical Sciences, Buffalo, New York, USA

Correspondence to
Dr Andrew Reynolds;
alr23@buffalo.edu

Accepted 12 May 2020

To cite: Jeng F, Reynolds A. *BMJ Case Rep* 2020;**13**:e233394. doi:10.1136/bcr-2019-233394

SUMMARY

This paper has two main purposes: (1) to report a rare case of paediatric gliosarcoma that invaded the surrounding orbit and (2) to demonstrate chlorpromazine injection as a potential treatment option for blind, painful eye caused by tumour invasion. A 12-year-old man who presented with headaches was found to have glioblastoma multiforme and it was excised and treated with radiation and chemotherapy. Seven months later, the tumour recurred as gliosarcoma, a rare variant of glioblastoma multiforme containing distinct gliomatous and sarcomatous components. In spite of treatment, the tumour progressed and eventually invaded into the right orbit. He subsequently developed a proptotic, blind, painful eye and was treated with retrobulbar chlorpromazine injection, which provided immediate symptomatic relief.

BACKGROUND

Managing pain in painful blind eyes continues to be a challenge in ophthalmology.[1] Enucleation remains the definitive treatment, however patients may not be medically or psychologically prepared for enucleation, particularly if the patient is a child.[2] One alternative to enucleation is retrobulbar chlorpromazine injections.[3] Chlorpromazine is a phenothiazine derivative initially used to diminish arousal in agitated patients in 1951.[3] It was first suggested as a treatment option for blind painful eyes in the 1980s by Fiore and then Bastrikov.[2] These investigators noted reduction of pain in 83% and 84% of patients.[2] Since then, many more cases of retrobulbar chlorpromazine injections have been reported to successfully achieve pain relief in painful blind eyes. However, the etiologies for painful blind eyes in these cases were primarily limited to glaucoma or trauma. Some other causes included retinal detachment, intraocular inflammation, corneal decompensation, phthisis, choroidal haemorrhage, endogenous fungal endophthalmitis, proliferative diabetic retinopathy and choroidal melanoma. Interestingly, the use of retrobulbar chlorpromazine injections in patients with orbital tumour invasion has not yet been reported. Herein, this report describes a patient who developed a gliosarcoma, a very atypical brain tumour that in and of itself warrants reporting, that subsequently invaded the surrounding orbit causing a blind painful eye. The eye was treated with retrobulbar chlorpromazine injection and provided the patient significant pain relief.

CASE PRESENTATION

A 12-year-old man with a history of glioblastoma multiforme status post resection and secondary gliosarcoma was referred to the ophthalmology service with concern for significant right eye proptosis and worsening extraocular movements. He was in good health until a year ago when he started noticing persistent worsening headaches. Imaging at the time showed a right frontal enhancing brain lesion, which was resected shortly after its discovery. Pathology of the lesion showed a high-grade glioma consistent with glioblastoma multiforme, WHO grade IV. He completed chemoradiation 2 months after its resection and began maintenance chemotherapy.

Eight months later, the patient presented again with recurrent headaches. An MRI scan was done that showed thickening of dural enhancement in the right basifrontal region concerning for recurrence versus radiation effect. Biopsy was performed and interpreted as sarcomatous component or transformation of the glioblastoma. He was re-irradiated for 2 months.

One month after radiation was completed, the patient had a ventriculoperitoneal shunt placed for worsening headaches and hydrocephalus. A CT scan at the time was concerning for lung lesions; the biopsy obtained shortly afterwards confirmed metastasis with spindle cell pathology. The patient was started on chemotherapy. Around the same time, patient started having swelling of the right cheek and eye with worsening extraocular movements and ophthalmology was consulted.

Visual acuity at the time of examination was 20/30 in the right eye and 20/20 in the left eye. There was 0% supraduction and infraduction of the right eye and restricted adduction with mild limitation of abduction. Pupils were round and reactive to light. Upper lids of the right eye were swollen and red with a 5–6 mm ptosis. The rest of the anterior eye examination was unremarkable.

An orbital CT scan was ordered and demonstrated tumour invasion into the right orbit and superior rectus muscle, with erosion of the adjacent right orbital bones. Mild right proptosis was also noted to be stable to minimally increased (figure 1).

An MRI scan that was performed a month later demonstrated rapid tumour extension into underlying soft tissue in the superior aspect of the orbit and downward displacement (figure 2). He presented to the ophthalmology clinic a few days later unable to open his right eye due to worsening swelling and new pain. Examination at that time was significant for inferior corneal thinning with

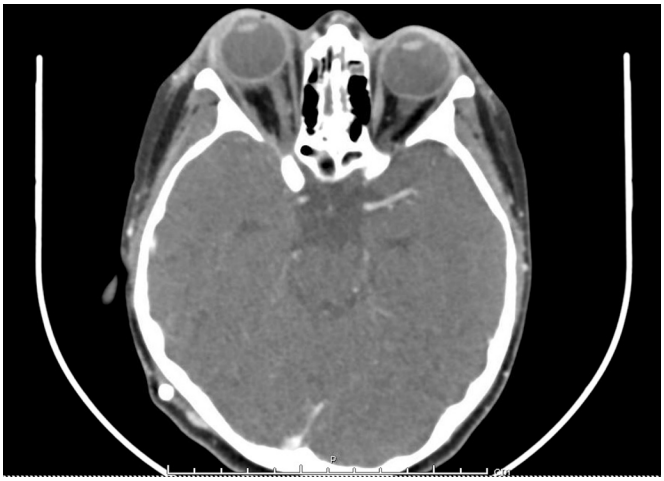

Figure 1 CT axial image of the orbits demonstrating right eye proptosis.

infiltrate. The posterior examination showed choroidial folds, obvious 'teardrop sign' with posterior tentation surrounding the nerve. Visual acuity was measured to be no light perception.

TREATMENT

Frequent use of erythromycin ointment was recommended, and the patient was scheduled for urgent tarsorrhaphy the following day in order to help relieve patient's pain and prevent further ulceration of the cornea.

At the 2-week postoperative visit, the patient reported some pain relief with tarsorrhaphy. However, due to continued expansion of the tumour and increased proptosis, the suture broke down with an incidental contact from the family dog. There was again significant lagophthalmos and corneal ulceration on examination, along with continued severe pain that was recalcitrant to opiate pain medication. The decision was made to proceed with repeated tarsorrhaphy the same week. During the second tarsorrhaphy procedure, 2cc of 25 mg/mL chlorpromazine and 2cc of bupivacaine were given retrobulbar via the right lower eyelid in an attempt to alleviate the patient's ocular pain and reduce the frequency of opiates.

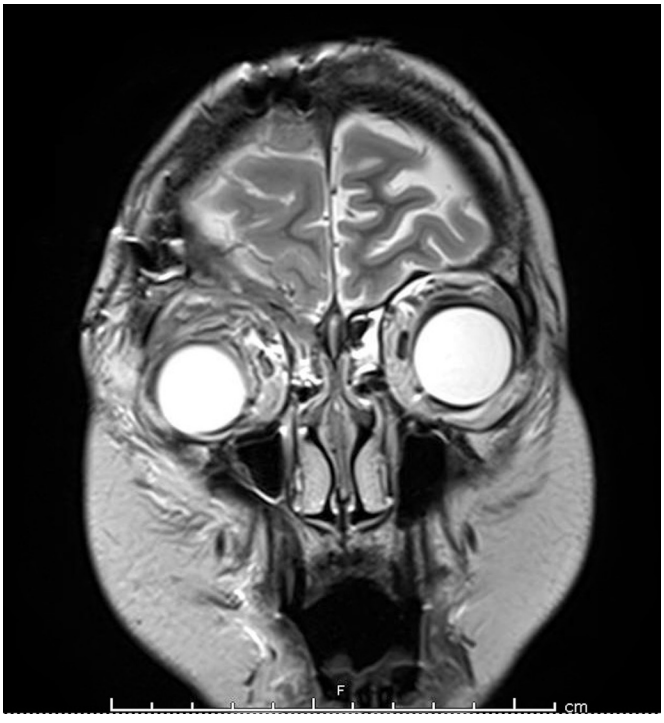

Figure 2 MRI coronal image of the orbits 1 month after CT scan demonstrating rapid tumour extension into underlying soft tissue in the superior aspect of the orbit and downward displacement.

OUTCOME AND FOLLOW-UP

The patient followed up at the ophthalmology clinic 1 week after the procedure and expressed complete pain relief after the retrobulbar chlorpromazine injection. Unfortunately, the left orbital tumour was also rapidly enlarging and causing proptosis and vision loss. The patient was referred for palliative external beam radiation, which he completed prior to succumbing to his disease 2 weeks later.

DISCUSSION

Retrobulbar chlorpromazine injections have been shown to be a safe and effective alternative in the treatment of blind painful eyes when medications prove unsatisfactory and when enucleation is not possible or wanted.[2] The exact mechanism of pain control is unknown. Some authors have hypothesised that the most likely mechanism is the membrane-stabilising effect of chlorpromazine on the ciliary ganglion.[4] Regardless of the mechanism of action, numerous studies have been done to show its high success rate in treating blind painful eyes. In one study, Chen *et al* reported that 80% of patients (16 out of 20) achieved successful pain control with one injection of retrobulbar chlorpromazine.[2] This is comparable to Fiore *et al*'s study that reported 83% pain relief out of 63 patients and Bastrikov's study that reported 83.8% pain relief out of 56 patients.[5 6] In another study, Estafanous *et al* reported that seven out of nine achieved at least partial relief of pain after chlorpromazine injection.[4]

However, the etiologies for painful blind eyes in the majority of these studies were primarily limited to glaucoma or trauma. None of the studies or case reports looked at the effectiveness of retrobulbar chlorpromazine injections on managing eye pain caused by tumour invasion.

The patient described in this case report developed a gliosarcoma, which is a rare brain tumour characterised by histomorphologic heterogeneity, with alternating areas of glial and mesenchymal differentiation.[7] According to the WHO classification of central nervous system tumours, gliosarcoma is regarded as a distinct variant of glioblastoma multiforme.[7] Gliosarcomas comprise 1.8%–2.4% of glioblastoma multiformes and primarily affect adults in the fifth to seventh decades of life, with a higher proportion found in men.[8] It was therefore very unusual for this patient to develop a gliosarcoma at the age of 12. In fact, a literature review by Mallick *et al* found a total of only 25 reported cases of paediatric gliosarcoma.[9] Another study by Karremann *et al* determined the relative incidence of gliosarcomas among paediatric glioblastomas to be 1.9% (4 out of 206 cases found in their glioblastoma multiforme database).[7] It was also observed that while most tumours were found in the temporal lobe in adults, the frontal lobe was more frequently affected in paediatric patients, as seen in this case. Gliosarcomas typically appear as rapidly growing, heterogeneously enhancing intra-axial masses.[10] Signs of increased intracranial pressure (vomiting, headache and macrocephaly) were the leading symptoms of gliosarcoma in paediatric patients.[7] Although aggressive, gliosarcomas rarely invade into the orbit. A PubMed search of the keyword 'gliosarcoma' with 'orbit' was performed and the query

yielded two citations, of which only one was relevant. Nguyen *et al* reported the first case of intracranial gliosarcoma with multicompartment invasion of the adjacent parenchyma, skull base, extracranial soft tissues and orbit in a 44-year-old woman.[10] Therefore, the 12-year-old man in this case report is the second case of gliosarcoma with invasion into the orbit to be reported, and the first case among paediatric gliosarcomas to be reported.

Unfortunately, the prognosis of gliosarcomas is extremely poor, with a median survival in untreated patients of 4 months.[8] At the time the patient was examined by ophthalmology, he was already at the point of comfort care only. In fact, the prognosis for most invading tumours with orbital involvement is generally poor.[11] Exceptions include spheno-orbital meningiomas and chondrosarcomas. A review of tumours invading the orbit by Jorgensen and Heegaard reported the most common symptoms of tumours invading the eye to be proptosis.[11] Associated symptoms included diplopia and decreased vision. Although not the most common, pain was still frequently seen. However, it was reported to be more commonly associated with certain tumours over others (eg, glioblastomas, osteosarcomas and rhabdomyosarcomas).[11] As seen in this patient, the pain can be severely debilitating and impact a patient's quality of life. Because of the high recurrence and mortality rates of tumours that invade the orbit, treatment options are limited. Retrobulbar chlorpromazine offers a relatively quick, easily performed procedure that in this case provided immediate and permanent pain control.

Learning points

- This case report suggests the benefit of using retrobulbar chlorpromazine injections in patients suffering from tumour invasion to the orbit.
- Unfortunately, because this patient passed away soon after the injection, the long-lasting effects of chlorpromazine injections in tumours invading the orbit are unknown.
- Additionally, potential side effects of the injection could not be adequately documented. Some common side effects documented in previous case reports included periocular inflammation leading to chemosis, proptosis, limited ocular motility and facial swelling.[2]
- To conclude, retrobulbar chlorpromazine injections have the potential to alleviate pain associated with tumours invading the orbit and can be heavily considered when the tumour has a poor prognosis.

Contributors FJ and AR both directly participated in the planning, execution and analysis of this case report.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent for publication Next of kin consent obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

ORCID iD
Andrew Reynolds http://orcid.org/0000-0003-1612-3956

REFERENCES

1 Xavier TVH, de Oliveira TR, Mendes TCBS. Treatment of patients with painful blind eye using stellate ganglion block. *Braz J Anesthesiol* 2016;66:75–7.
2 Chen TC, Ahn Yuen SJ, Sangalang MA, *et al*. Retrobulbar chlorpromazine injections for the management of blind and seeing painful eyes. *J Glaucoma* 2002;11:209–13.
3 McCulley TJ, Kersten RC. Periocular inflammation after retrobulbar chlorpromazine (thorazine) injection. *Ophthalmic Plast Reconstr Surg* 2006;22:283–5.
4 Estafanous MF, Kaiser PK, Baerveldt G. Retrobulbar chlorpromazine in blind and seeing painful eyes. *Retina* 2000;20:555–8.
5 Fiore C, Lupidi G, Santoni G. Effet de l'injection retrobulbaire de chlorpromazine dans le glaucome absolu. *J Fr Ophtalmol* 1980;3:397–9.
6 Bastrikov NI. [Symptomatic treatment of terminal painful glaucoma by the retrobulbar administration of aminazine]. *Vestn Oftalmol* 1989;105:47–9.
7 Karremann M, Rausche U, Fleischhack G, *et al*. Clinical and epidemiological characteristics of pediatric gliosarcomas. *J Neurooncol* 2010;97:257–65.
8 Han SJ, Yang I, Tihan T, *et al*. Secondary gliosarcoma: a review of clinical features and pathological diagnosis. *J Neurosurg* 2010;112:26–32.
9 Mallick S, Gandhi AK, Sharma DN, *et al*. Pediatric gliosarcoma treated with adjuvant radiotherapy and temozolomide. *Childs Nerv Syst* 2015;31:2341–4.
10 Nguyen Q-BD, Perry A, Graffeo CS, *et al*. Gliosarcoma with primary skull base invasion. *Case Rep Radiol* 2016;2016:1–6.
11 Jørgensen M, Heegaard S. A review of nasal, paranasal, and skull base tumors invading the orbit. *Surv Ophthalmol* 2018;63:389–405.