Peer Review File

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Reviewer A: An interesting study on a rare entity discussing surgical approach for these tumors.

Comment 1: The authors are discussing optic nerve (ON) gliomas, and this should be clarified. These are different than optic pathway gliomas (OPG). ON gliomas are one form of OPG. See Mishra MV 2012 in J Neuro-Oncology and Hamideh 2018 in J of Child Neurology. I understand that some tumors will extend outside the orbital region and may involve the chiasm.
Reply 1: Optic gliomas are indeed a kind of OPG, but the main case we reviewed was optic gliomas, and some of them are OPG (extending to the whole optical pathway and invading the intraorbital optic nerve). All cases involving OPG contain intraorbital optic gliomas, because we mainly want to elaborate a surgical method for intraorbital optic gliomas, which can reduce postoperative complications of ocular function.

Comment 2: The authors should state in each group how many tumors confined to the ON only and how many extended to the chiasm. In lines 179-187 the authors mention extension of tumors but not clear. See comments 14 below.
Reply 2: We have modified our text as advised (see Page 4, line 63-75).

Comment 3: Need to clarify if these are for tumors where upfront surgery was used? Or any tumor? In other words, did these patients receive any therapy (chemotherapy or radiation or others) before tumor resection?
Reply 3: None of our patients had received radiotherapy or chemotherapy (both before and after surgery), which made our baseline for inclusion relatively reasonable. At the same time, it is also a crucial point that most of these patients in China are extremely difficult in economy. Few patients can afford the cost of multiple chemotherapy. They often consider the treatment of life-saving surgery at the last moment of the disease. This is why most of our patients who have surgery are patients without vision.

Comment 4: The fact that only two cases recurred is amazing and this I think unusual for ON gliomas that extend to the chiasm (35 cases per authors on line 181). This outcome with surgery alone is unusual and I think the patients received surgery.
Reply 4: We were also surprised after follow-up of these cases. The tumors involving

the chiasmatic region had been resected conservatively, for the sake of the contralateral vision, the tumors might even be left behind. However, during follow-up, we found that there was no obvious tumor growth or recurrence in MRI. Our surgical pathology was mostly grade I and II gliomas. Two cases of recurrence were grade IV gliomas.This is also the purpose of writing this article. We have also discussed MDT. It is true that the recurrence rate of patients undergoing surgery in our center is extremely low. This is also the technical basis for us to dare to preserve the optic nerve sheath and simply resect the tumor in the later stage. It is also the surgical method we want to express in this article.

Comment 5: Need to also mention treatments received after surgery? What was the standard of care at their hospital after surgery? Observation and then treat at relapse?

Reply 5: For postoperative patients, we did not recommend continuing chemotherapy, only long-term follow-up MRI, and in our median follow-up time, we did not find that this kind of tumor is easy to relapse after surgery.

Comment 6: What was the vision status in these tumors? This is important and related to suggestion # 4. Is the standard at Tongren Hospital for ON gliomas upfront resection regardless of vision status? Although resection is curative it still means blindness to that eye. So many teams will avoid resection if there is decent vision in that eye. See Hamideh et al 2018 in J of Child Neurology. So, were these resected tumors in eyes that are blind or light perception only or counting fingers?

Reply 6: Although we enrolled surgical patients, it is not necessarily that OPG needs surgical treatment. We also recommended patients to take chemotherapy at the early stage of OPG diagnosis. However, most of the patients who return to the Department of Neurosurgery do not receive chemotherapy. The patients admitted to the Department of neurosurgery are those who must undergo surgical treatment after screening by the Department of Ophthalmology and oncology. The first diagnosis of these patients was in the Department of Ophthalmology and neurology Surgery was here to assist ophthalmologists to complete the operation task. We recommended an operation that can relatively protect the postoperative eye function when we have to operate. (after all, no vision recovery after surgery and eye dysfunction will bring more serious consequences). In other words, the vision of these patients was almost lightless vision. At the same time, some patients with residual visual acuity but severe exophthalmos have also undergone surgery. For patients with relatively good vision and vision larger than the number of fingers in front of their eyes, we did not give surgery and recommended chemotherapy.

Comment 7: So, we need to know previous treatments (if any) before surgery and any treatments after surgery?

Reply 7: We recommended chemotherapy or follow-up for OPG with good preoperative vision. For the postoperative patients in our center, we did not recommend chemotherapy, but only follow-up MRI for 1 month, 3 months, 6 months, 1 year and 3 years (we were shocked that the recurrence rate of patients undergoing surgery was extremely low).

Comment 8: Need to know the pathology of the tumors? How many grade I glioma and how many grade II or grade III or grade IV?

grade I 50 (58.1% 50/86) II 30 (34.9% 30/86) III 4 (4.7% 4/86) IV 2 (2.3% 2/86)

Reply 8: This may be related to the fact that most of the patients we treated were NF1 patients (43.0% 37 / 86). The tumor grade was relatively low, and the main patients were benign tumors.

This was the limitation of this article, because the pathological grade of most tumors was benign, we rarely encounter high-grade OPG in clinic. But this did not affect the conclusion of the article and the surgical techniques we want to promote.

Comment 9: Were the resection margins free of tumor? especially in the 65 cases (line 181) who had tumor isolated in the ON only. These tumors can be cured with resection only and I agree the recurrence rate is low (if low grade glioma).

Reply 9: We consulted the director of the Department of Pathology (one of the authors). At the same time, we did microscopic examination on the cutting edge of the optic nerve sheath in some patients we suspected. It was true that there is no tumor invading the optic nerve sheath. This was also the pathological basis for us to retain the optic nerve sheath in the later stage. Of course, this was also related to our higher benign rate of tumor.

Comment 10: How many of these cases were Neurofibromatosis 1?

Reply 10: There were 43 cases of NF1 (43.0% 37 / 86).

Comment 11: How many had bilateral ON glioma?

Reply 11: Only 1 case (1.2% 1 / 86) involved bilateral optic pathway.

Comment 12: The authors need to use range in a simpler way. For example, Lines 79 to 82 “The median surgical age was 6 years old, with the youngest patient being three years old and the oldest patient being 16 years old. The median follow-up time

was 78.5 months, with the shortest time being 43.8 months and the longest time was 134.3 months". This could be stated as Median surgical age was six years (range, 3-16 years) and median follow-up time was 78.5 months (range, 43.8-134.3 months). Please see many other examples in the paper especially same page.
Reply 12: We have modified our text as advised (see Page 3-4).

Comment 13: How many are alive at follow up?
Reply 13: Up to the time period mentioned in the article, all patients survived.

Comment 14: The two patients who relapsed as GBM what was the original tumor? Did they receive radiation?
Reply 14: The original tumor was grade IV tumor, the patients did not receive radiotherapy before operation, after operation and during follow-up. The two patients were all rural patients in China, and their economic conditions were extremely poor.

Comment 15: Why did the patients receive MRI and CT? Most places will perform only MRI.
Reply 15: In our center, CT scan of optic nerve tube was used to evaluate the inward growth trend of OPG, and to differentiate it from other optic nerve tumors that affect bone. For example, the optic nerve tube of optic nerve sheath meningioma is very different from that of optic nerve glioma. The optic nerve tube is thickened, and the suspected tumor has intracranial spread.

Comment 16: Lines 181-182: 64 + 35 + 1 = 100 and not 86?
Reply 16: Because there were many patients with several clinical manifestations coexist, rather than only one form, such as exophthalmos patients may be accompanied by vision without light perception, so the overall data was greater than 86 cases.

Comment 17: Can the authors provide data on symptoms duration? And were there delays in diagnosis?
Reply 17: The age of first diagnosis was 11.8 ± 8.8 years.The age of operation was 12.5 ± 9.2 years. It can be explained that the vision preservation period of the patients without chemoradiotherapy is about one year.

Comment 18: Can the authors include some recommendations about the need to protect the remaining eye? For example protective glasses as any trauma the only

remaining good eye means blindness.

Reply 18: In the patients we followed up after operation, there was no vision loss in the healthy eye. We guess that there was no special recommendation for the healthy eye, so we just need to follow up. But the operation side of the eye should pay attention to postoperative eye function exercise and corneal protection, after all, vision can not be restored and accompanied by eye movement dysfunction, this was a situation we do not want to see, which seriously affects the children's social and psychological health.

Comment 19: References 4 and 31 need to be fixed. The spaces between authors names needs fixing.

Reply 19: We have modified our text as advised .

Comment 20: Figure 1: the child is 1 year old. The authors mention in the text the youngest age was 3 years old?

Reply 20: It was a mistake in writing.We have modified our text (see Page 3, line 56)

Comment 21: The authors mention causes of exclusion but how many were excluded for each cause?

Reply 21: If the ophthalmology oncology clinic was included, the number of patients will be larger, but there was no surgical and pathological results, which can not prove that it must be OPG,that was a limitation. We only mention neurosurgical patients referred from ocular tumors. About 15 patients were considered to have fair vision and did not receive surgery. We recommended chemotherapy for these patients and lost follow-up (no further visit). The operation rate was about (85.1% 86 / 101)

Comment 22: What was the total CNS tumors at that hospital during the study period? This will help understand the % of ON gliomas in CNS tumors at that hospital.

Reply 22: It's a pity that our center's CNS treatment is not as good as the neurosurgery department of Beijing Tiantan Hospital. Our center's neurosurgery department relies more on the neurosurgery support from the national key discipline of Ophthalmology of Beijing Tongren Hospital. The proportion of CNS is very low, and there are few such patients.

Comment 23: In table 1 what does P 25, P 75 mean?

Reply 23: Because the overall age span is large, the data is difficult to achieve normal distribution, and can not use the mean plus standard deviation, so the skew

distribution data representation method is adopted, that is, median (P25, p75) represents, P25, p75 represents the 25th and 75th percentiles of percentiles.

Comment 24: Not sure what is the point of the last table (STROBE Statement)? What is it for? Also, why it is an image?
Reply 24: The last table(table2) showed complications and recurrence of two groups. We submit it in the form of a form, not an image.

Reviewer B
Comment 1: The manuscript "Comparison of two surgical methods for the treatment of optic pathway gliomas in the intra-orbital segment: an analysis of long-term clinical follow-up which evaluates the surgical outcome" provides a comparison of two surgical approaches to optic pathway glioma.
Optic pathway glioma are common pediatric brain tumors that frequently threaten vision but rarely threaten life. Approximately half of the cases are associated with NF1 and the goal of treatment is to preserve or improve vision. Chemotherapy may preserve vision, and treatments such as Avastin (bevacizumab) have recently been shown to potentially improve vision, even in significantly impaired eyes (Avery, JAMA Ophthalmology 2014). Radiation is rarely if ever used in NF1 because of the predisposition of cancer seen in NF1 patients. Surgery is rarely used and indicated only for unusual circumstances such as disfiguring proptosis in a nearly blind eye or enlarging tumor with mass effect on critical structures (Avery Neuro-Ophthalmol 2011; de Blank Journal of Neuro-Ophthalmology 2017). In these cases, a trial of chemotherapy may reduce proptosis and preserve remaining vision before losing vision to a surgical intervention. Unfortunately, the relatively minimal place for surgical intervention in OPG is not conveyed in this manuscript.
Reply 1: Most of the patients we treated were exophthalmos, which seriously affected the function and almost had no light perception in visual evaluation. As a neurosurgeon, all the patients we treated were carefully evaluated by ophthalmologists. About 43.0% (37 / 86) of the patients we enrolled were NF1 related patients. As a benign tumor, our operation was suitable for patients with no vision and affected eyes The patients whose bulbar function involved the intracranial visual pathway at the same time.

Comment 2: To adequately describe the patients treated with surgery, this manuscript would need to describe prior therapies attempted, current visual acuity and recent change in visual acuity, and NF1 status. Without these details, the description of surgery in these patients appears cavalier and without significant

thought to other potential therapies that may have preserved vision and quality of life.

Reply 2: None of our patients had received radiotherapy or chemotherapy (both before and after surgery), which made our baseline for inclusion relatively reasonable. At the same time, it is also a crucial point that most of these patients in China are extremely difficult in economy. Few patients can afford the cost of multiple chemotherapy. They often consider the treatment of life-saving surgery at the last moment of the disease. This is why most of our patients who have surgery are patients without vision.

Comment 3: All in all, this manuscript gives the unfortunate and incorrect impression that surgery is a common therapy for OPG and that its use is reasonable except in the most extreme cases where other therapies have failed. This is unfortunate, as surgery will frequently result in complete loss of vision in the affected eye.

Reply 3: Indeed, it seems very cruel, but it is in line with certain national conditions. At the same time, it is precisely because of this kind of surgery that postoperative blindness is inevitable, so choosing a better surgical method to preserve the residual eye movement function is the significance of this article.

Comment 4: Parts of the introduction and discussion describing OPGs appear incorrect, as well. And parts of the author's language usage ("none incision") were confusing.

Reply 4: We have modified our text as advised in parts of the introduction and discussion.And the "none incision" has also been modified.

Comment 5: The authors have clearly put a lot of work into this manuscript. As it is currently written, I worry that it will mislead readers about the role of surgery in OPG. If the authors plan to revise and submit this manuscript, I hope they will emphasize the relatively small role for surgery in OPG and better describe the clinical features and prior therapies of their patients.

Otherwise, the description of these patients appears well out of the norm for clinical management of OPG.

Reply 5: In fact, in China, OPG chemotherapy costs a lot, and many long-term chemotherapy also brings side effects and economic distress to patients. Although we enrolled surgical patients, it is not necessarily that OPG needs surgical treatment. We also recommend patients to take chemotherapy at the early stage of OPG diagnosis. However, most of the patients who return to the Department of Neurosurgery do not

receive chemotherapy. The patients admitted to the Department of neurosurgery are those who must undergo surgical treatment after screening by the Department of Ophthalmology and oncology. The first diagnosis of these patients is in the Department of Ophthalmology and neurology Surgery is here to assist ophthalmologists to complete the operation task. We recommend an operation that can relatively protect the postoperative eye function when we have to operate. (after all, no vision recovery and eye movement dysfunction will bring more serious consequences: including psychological factors, social factors, etc.)