

Vestibular Schwannoma growth during pregnancy: case report of neurofibromatosis type 2 in pregnancy

Sraavya S. Akella,¹ Jordan N. Mattson, MD,² Nina N. Moreira, MD²

Keywords: Acoustic neuroma, pregnancy, neurofibroma, neurofibromatosis type 2

Abstract

Background: Acoustic neuromas are a common sequela of neurofibromatosis type 2 and have been shown to grow at an increased rate during pregnancy.

Case: 21-year-old female, gravida 1 para 0, with history of neurofibromatosis type 2 presented for prenatal care following new onset seizures and progressive deafness. She was found to have bilateral slow-growing acoustic neuromas. Over the course of her pregnancy, her acoustic neuroma began growing and she became completely deaf. She underwent surgical decompression during her pregnancy and had a late preterm vaginal delivery due to preeclampsia with severe features. She subsequently had further operative and medical treatment of her neuromas.

Conclusion: Acoustic neuromas during pregnancy are exceedingly rare, but can be managed successfully with an interdisciplinary team approach tailored to the patients' specific clinical presentation.

¹Roy J. & Lucille A. Carver College of Medicine, University of Iowa Hospitals and Clinics, Iowa City, IA

²Department of Obstetrics and Gynecology, University of Iowa Hospitals and Clinics, Iowa City, IA

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Corresponding author: Sraavya Akella, Roy J. & Lucille A. Carver College of Medicine, University of Iowa Hospitals and Clinics, 325 Newton Road, Iowa City, IA, 52245, 515-473-5980; Sraavya.akella@uiowa.edu

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Introduction

Vestibular schwannomas are noncancerous tumors that grow on the eighth cranial nerve and are commonly seen in patients with neurofibromatosis type 2, an autosomal dominant genetic disease. The average age of symptom onset is 18 to 24 years and almost all affected individuals develop bilateral vestibular schwannomas by age 30 years.¹ Common features include tinnitus, hearing loss, balance dysfunction, as well as Bell's palsy if there is significant compression of the facial nerve.² There is evidence showing that pregnancy hastens the progression of vestibular Schwannomas, but literature and practice guidelines are lacking for the management during pregnancy.² This report describes such a rare case of vestibular schwannoma and the multidisciplinary management of its growth during pregnancy.

Case Presentation

A 21-year-old woman, gravida 1 para 0, with an established history of neurofibromatosis type 2 (NF2) with an associated seizure disorder presented for prenatal care with the high-risk

obstetrics group at our institution in 2017. In 2012 the patient was officially diagnosed with NF2 after a syncopal episode prompted head imaging which revealed multiple tumors including a large meningioma and bilateral acoustic neuromas.

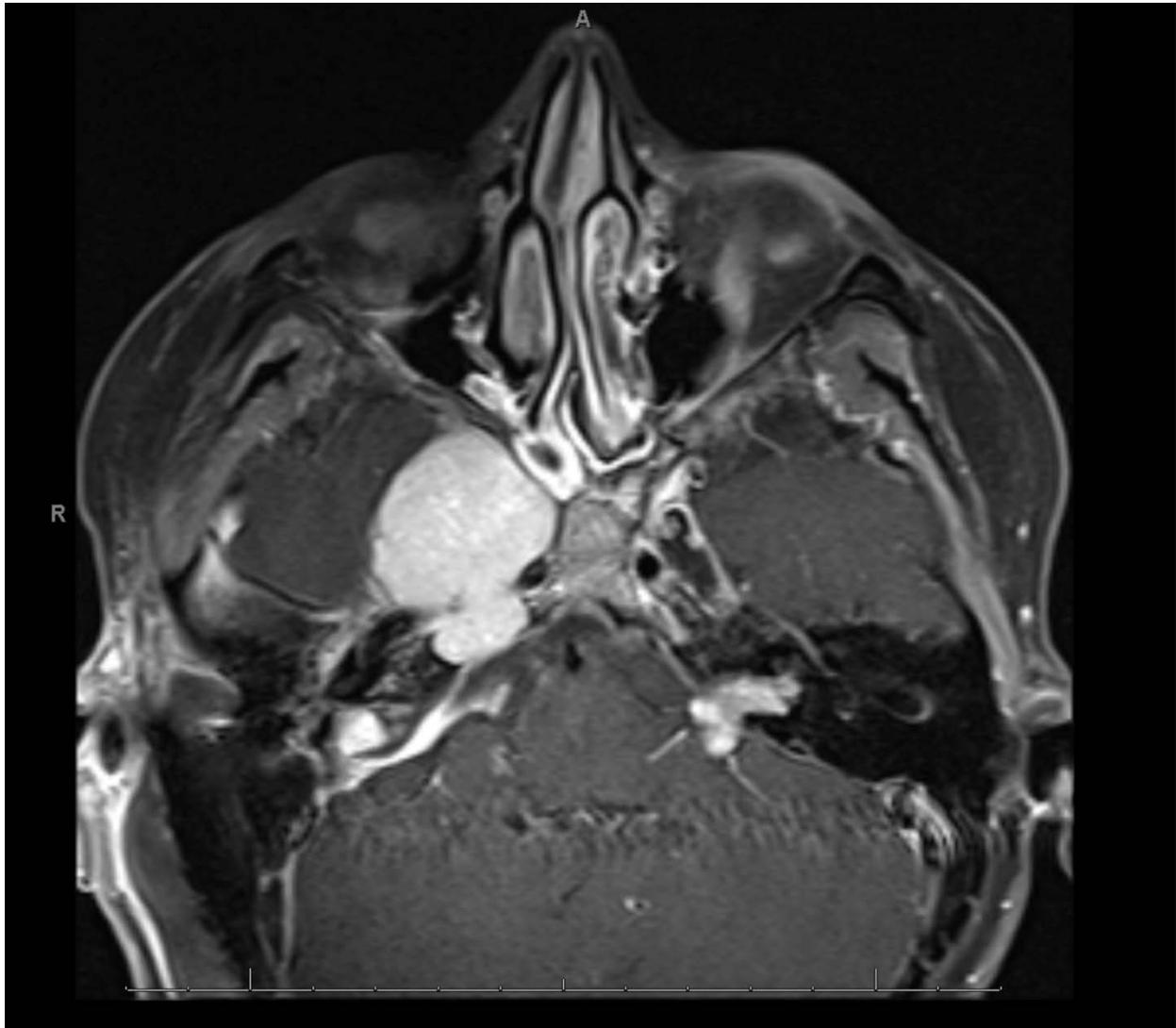


Figure1. Axial T1 post-gadolinium contrast MRI of orbit depicting preoperative right cavernous sinus meningioma with involvement of right trigeminal nerve schwannoma

The patient underwent removal of the meningioma in October 2012 and resection of the larger right-sided acoustic neuroma in January 2013 with post-operative sequelae of partial right-sided facial paralysis. Within one month following the acoustic neuroma resection, her family relocated to Iowa and she was transferred to our

institution. She presented to Ophthalmology with complaints of progressive vision loss and an orbit MRI showed right cavernous sinus meningioma (0.9 x 2.5 x 1.6 cm) with normal orbits, globes, and optic nerves, a slight increase in size of left-sided acoustic neuroma, and a right trigeminal schwannoma (Figure 1).

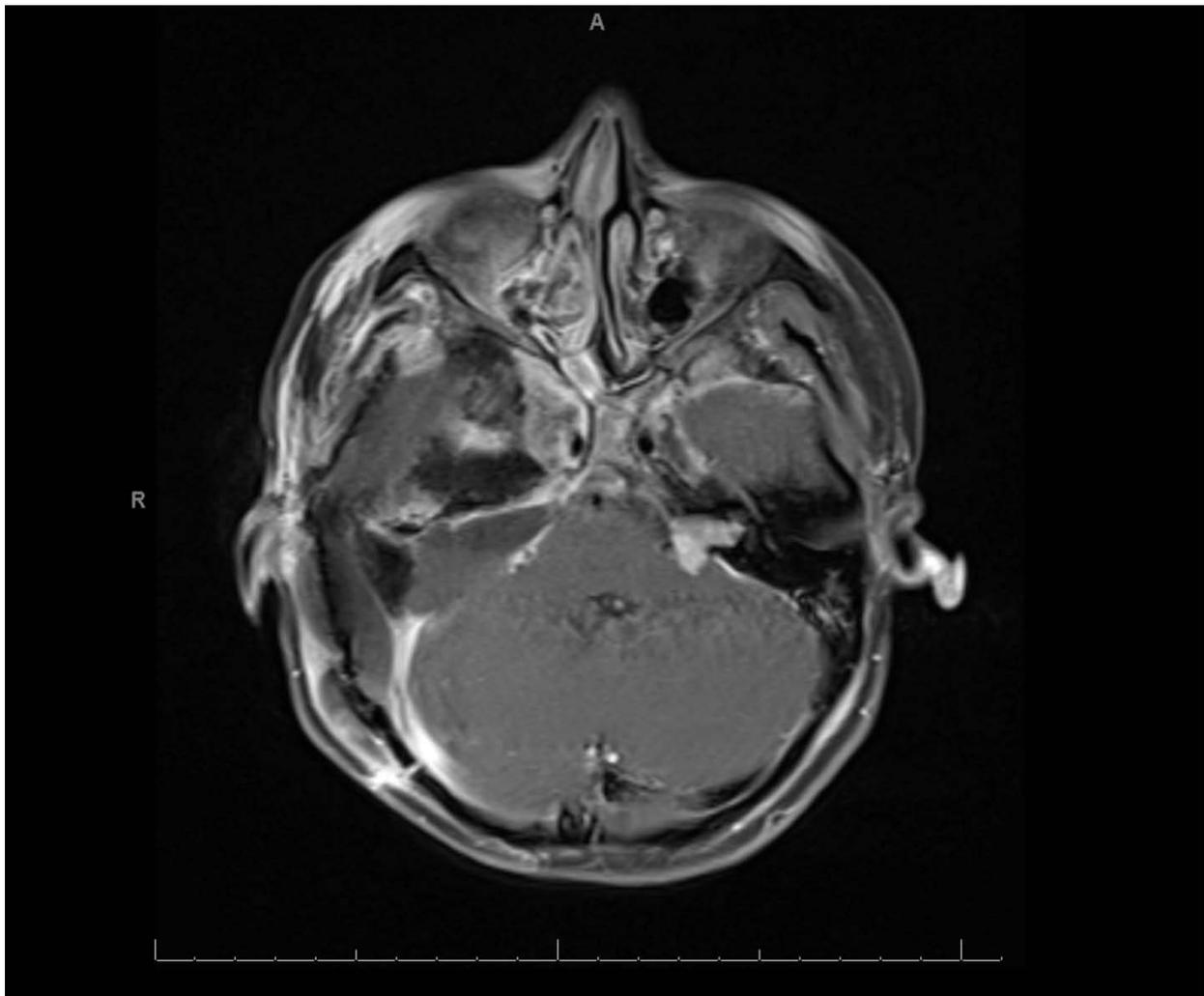


Figure 2: Axial T1 post-gadolinium contrast MRI of postoperative brain depicting significant debulking of tumor with residual soft tissue mass adjacent to right cavernous sinus.

In April 2013, neurosurgery and ENT jointly resected the trigeminal schwannoma which was found to be emanating from V3 portion of the fifth cranial nerve. Immediate postoperative imaging revealed significant debulking with small soft tissue mass adjacent to right cavernous sinus concerning for residual tumor (Figure 2). At this time, she was also noted to have multiple small bilateral schwannomas along C5-C7, T1, T2, L2-L5, S1 and S2 nerve roots. At 5 months follow-up she had persistent paresthesia in V2 and V3 distribution with continued decline in hearing. She continued follow-up with ENT with MRI and audiograms every 3 months to monitor tumor growth and hearing loss. She had significant sensorineural hearing loss in her right ear (which was not tested by audiogram regularly for this reason), however her left ear was showing progressive decline on audiograms. In March 2014, due to worsening hearing in the left ear (both subjective and objective decline in word recognition from 88% to 68% over two weeks), she was started on Bevacizumab therapy which resulted in symptomatic improvement.

She initially presented to our obstetrics department for high-risk assessment and preconception counseling in June 2017. She was given extensive counsel regarding the probability of an increase in tumor size and the development of new tumors during pregnancy. She was also alerted to the risk of losing her vision or hearing permanently. Since her tumor resection in 2013, regular MR imaging was done and her pre-pregnancy tumor burden included bilateral trigeminal and vestibular schwannomas and right frontal

meningioma, all stable over the prior 3 years. In addition, she underwent genetic counseling at which time she was informed that the risk of her offspring inheriting the mutation is 50%. She decided to pursue fertility and presented at 7 weeks gestation with a planned and viable intrauterine pregnancy that was discovered during hospitalization for her first seizure in October 2017. Workup at that time found some epileptiform activity which was interpreted as likely secondary to her prior brain surgeries and she was discharged with levetiracetam 500 mg BID. She declined any prenatal screening.

Over the course of the pregnancy, the patient was followed closely by otolaryngology (ENT) in addition to the high-risk obstetrics (MFM) team at our institution. As ENT had been monitoring her at regular 3-month intervals with audiograms and brain MRI since 2013, they continued the same protocol. Brain MRI at 9w6d showed grossly stable bilateral vestibular schwannomas, right frontal meningioma, and bilateral trigeminal schwannomas in comparison to the pre-pregnancy MRI three months prior. Her hearing progressively declined clinically over the course of pregnancy with intermittent episodes of blurred vision that were self-resolving and first reported at her 20wk appointment. Repeat MRI at 22 weeks' gestation, roughly three months after her last MRI, demonstrated significant growth of the right vestibular schwannoma (increased to 4.0 x 2.4 cm from 2.7 x 1.7 cm) now resulting in brainstem compression. Audiogram done at this time showed 0%-word recognition score (WRS) in patient's left ear compared with 68% 10

months earlier. Given contraindications for the use of bevacizumab during pregnancy, a two-week course of 60 mg of prednisone daily was started to symptomatically improve hearing. However, this was unsuccessful, and the patient's hearing continued to deteriorate. An emergency room MRI was completed at 25 weeks for worsening symptoms including headaches, vomiting, taste changes and difficulty swallowing. This revealed stable schwannoma size with vasogenic edema in cerebellar hemispheres and vermis. Given the fact that the patient was at 25 weeks, delivery was not seen as a suitable option.

A multidisciplinary case conference was set up and consensus opinion of participating consultants (ENT, neurosurgery, MFM, and anesthesia) was to proceed with surgical decompression of the brainstem with a goal to allow the patient to advance to term delivery. Fetal nonstress tests were conducted pre- and post-operatively without any intraoperative fetal monitoring as maternal hemodynamic stability was felt to be an adequate reflection of fetal wellbeing. The patient underwent successful resection of the right vestibular schwannoma at 26w2d gestational age. The surgery was completed by both ENT and neurosurgery in the left-lateral tilt position under general endotracheal anesthesia with a translabyrinthine approach. She had a two-day neurosurgical ICU stay for maternal neurological monitoring. She showed appropriate postoperative recovery and was discharged on postoperative day 3. After surgical intervention, the majority of her symptoms improved, except her

hearing loss.

The patient's pregnancy was further complicated by preeclampsia with severe features due to severe range blood pressures that developed at 30 weeks' gestation. She was admitted at that time and remained hospitalized until delivery at 34 weeks. Due to known spinal tumors, she was unable to undergo epidural anesthesia and opted therefore for vaginal delivery with fentanyl PCA for pain control. She was induced at 34 weeks and went through vaginal delivery without complications. Her clinical course was further complicated by postpartum preeclampsia for which she was treated with labetalol. She was discharged on hospital day 2. Her baby boy was born with APGARs of 2 and 5 at 1 and 5 minutes and was admitted to the NICU due to respiratory distress and prematurity. He made appropriate improvements and was fit for discharge by day of life 26. Outpatient follow-up with pediatric genetics was arranged for testing and monitoring of the infant for NF2.

Our patient followed up with ENT and neurosurgery 7 weeks post-partum for further assessment of her tumor growth. At that time, a plan was made to pursue cochlear implantation (CI) followed by resection of the left acoustic schwannoma so that if meaningful hearing was retained, a selective debulking of her tumor could be done. If there was no meaningful hearing retained, CI could be removed and the tumor fully resected. She underwent cochlear implantation approximately two months postpartum and noted improvement in hearing subjectively. Finally, at 4 months postpartum, she

underwent tumor debulking with a retrosigmoid approach and electrocorticographic monitoring with 80% successful tumor debulking. This was completed with an interdisciplinary team composed of otolaryngologic and neurosurgical specialists.

Discussion and review of the literature

Neurofibromatosis Type 2 (NF2) is characterized by noncancerous tumors of the nervous system, and commonly present with vestibular schwannomas that develop along the auditory nerve. NF2 is inherited in an autosomal dominant pattern though approximately 50% of individuals with NF2 have a de novo variant.³ Vestibular schwannomas present with symptoms of tinnitus, hearing loss, and balance dysfunction. Schwannomas may also develop in other peripheral nerves and affected individuals may also develop meningiomas, ependymomas and, rarely, astrocytomas.³ The average age of onset of symptoms in afflicted individuals ranges from 18 to 24 years and almost all affected individuals develop bilateral vestibular schwannomas by age 30 years. Diagnosis of NF2 in the pediatric population is often delayed due to a rather non-specific presentation; children often present with dermatological and ocular signs rather than with hearing loss.¹ In this case, our patient presented classically in her teenage years with vestibular schwannomas as well as meningiomas and other scattered neuromas.

There is some evidence showing that pregnancy accelerates clinical progression and radiographic growth of

neuromas in NF2, as seen in our patient.² One study of 103 patients showed that vestibular schwannomas occur more frequently in women and tend to be larger and more vascular in females.⁴ Two leading hypotheses regarding the mechanism of tumor growth during pregnancy consider the role of increased hormone receptors and increased blood volume during pregnancy.⁵ Several studies have investigated the expression of estrogen receptors in vestibular schwannoma. Brown et al. found an upregulation in estrogen receptors in sporadic vestibular schwannoma specimens compared with normal nerve samples in sixteen patients.⁶ This study directly contradicts findings by Beatty et al., who found no statistically significant association between the presence or quantity of estrogen or progesterone receptors in pregnancy and in progression of vestibular schwannomas.⁷ Multiple studies have shown that these tumors are large and more vascular during pregnancy and some contain estrogen receptors.⁸

The management of acoustic neuromas in pregnancy depends on the stage of pregnancy and the location and size of the tumors. Maternal benefits must be weighed against fetal risk of harm when deciding on management strategies. Surgical resection of tumors is considered safe during the second trimester of pregnancy.⁸ A retrospective cohort study of nine women with a skull base tumor during pregnancy demonstrated successful emergent skull base surgery in the second trimester.⁹ First trimester surgery carries an increased risk of spontaneous abortion, while third trimester surgery carries an

increased risk for preterm delivery.⁹ Our patient underwent tumor resection during late second trimester due to worsening symptoms. Given that she was not experiencing symptoms from her spinal tumors and other intracranial tumors, those were deferred to postpartum management.

Acoustic neuromas presenting without evolving neurological deficit can be managed via close observation and treatment can be deferred to the postpartum period.² Some patients with acoustic neuromas might experience hearing loss during pregnancy due to growth of the tumors.¹⁰

Medical treatment has become available recently by employing targeted therapies such as Bevacizumab, a recombinant monoclonal antibody which inhibits vascular endothelial growth factor (VEGF). Bevacizumab has been shown to result in radiographically reduced tumor size and to delay hearing loss in patients with vestibular schwannomas.¹¹ However, Bevacizumab is an IgG antibody and crosses the placenta. Due to lack of sufficient information with respect to its use during pregnancy, the team opted to proceed with caution and discontinue this treatment during this patient's pregnancy. In anticipation of the effects caused by withholding her Bevacizumab during pregnancy, the patient had been counseled with respect to the likelihood of tumor growth and prepared her for a possibility of further vision and hearing loss possibly necessitating surgical resection.

Another important consideration when managing a pregnant patient with NF2 and acoustic schwannomas is the need

for an interdisciplinary approach to care. Complicated cases with tumor progression at a rate which causes worsening symptoms, require close communication and cooperation among ENT, neurosurgery, maternal-fetal medicine, anesthesiology, genetics, and social work in order to achieve the best possible outcomes.¹² Lastly, the mode of delivery depends on the intracranial pressure (ICP). It is intuitive to emphasize that patients with increased ICP should not push during the second stage of labor to avoid brainstem herniation. Our patient, though intermittently experiencing symptoms of increased ICP, was able to tolerate Valsalva maneuver (e.g. with bowel movements) during her antepartum stay and was hence permitted to push during labor.

Of note, epidural anesthesia is considered a contraindication in this setting because neurofibromas may involve the spinal cord and nerve roots. However, reported cases have employed successful epidural analgesia after having ruled out spinal neurofibromas by CT scan, and this option can be considered on a case-by-case basis.^{13,14} In our case, epidural analgesia was contraindicated due to spinal tumors seen on MRI.

In conclusion, acoustic neuromas during pregnancy are very rare, but can be managed successfully with an interdisciplinary team approach tailored to the patient's specific clinical presentation.

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References

1. Anand G, Vasallo G, Spanou M, Thomas S, Pike M, Kariyawasam DS, Mehta S, Parry A, Durie-Gair J, Nicholson J, Lascelles K, Everett V, Gibbon FM, Jarvis N, Elston J, Evans DG, Halliday D. Diagnosis of sporadic neurofibromatosis type 2 in the paediatric population. *Arch Dis Child*. 2018 May;103(5):463-469. <https://doi.org/10.1136/archdischild-2017-313154> Epub 2018 Mar 13. PubMed PMID: 29535107.
2. Gaughan RK, Harner SG. Acoustic neuroma and pregnancy. *Am J Otol*. 1993 Jan;14(1):88-91. PubMed PMID: 8424484.
3. Evans DG. Neurofibromatosis 2. 1998 Oct 14 [updated 2018 Mar 15]. In: Adam MP, Ardinger HH, Pagon RA, Wallace SE, Bean LJH, Stephens K, Amemiya A, editors. *GeneReviews*® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2018. Available from <http://www.ncbi.nlm.nih.gov/books/NBK1201/> PubMed PMID: 20301380.
4. Kasantikul V, Netsky MG, Glasscock ME 3rd, Hays JW. Acoustic neurilemmoma. Clinicoanatomical study of 103 patients. *J Neurosurg*. 1980 Jan;52(1):28-35. <https://doi.org/10.3171/jns.1980.52.1.0028> PubMed PMID: 7350277.
5. Kachhara R, Devi CG, Nair S, Bhattacharya RN, Radhakrishnan VV. Acoustic neurinomas during pregnancy: report of two cases and review of literature. *Acta Neurochir (Wien)*. 2001;143(6):587-91. <https://doi.org/10.1007/s007010170063> PubMed PMID: 11534675.
6. Brown CM, Ahmad ZK, Ryan AF, Doherty JK. Estrogen receptor expression in sporadic vestibular schwannomas. *Otol Neurotol*. 2011 Jan;32(1):158-62. <https://doi.org/10.1097/MAO.0b013e3181feb92a> PubMed PMID: 21099731; PubMed Central PMCID: PMC3073320.
7. Beatty CW, Scheithauer BW, Katzmann JA, Roche PC, Kjeldahl KS, Ebersold MJ. Acoustic schwannoma and pregnancy: a DNA flow cytometric, steroid hormone receptor, and proliferation marker study. *Laryngoscope*. 1995 Jul;105(7 Pt 1):693-700. <https://doi.org/10.1288/00005537-199507000-00005> PubMed PMID: 7603272.
8. Doyle KJ, Luxford WM. Acoustic neuroma in pregnancy. *Am J Otol*. 1994 Jan;15(1):111-3. PubMed PMID: 8109621.
9. Priddy BH, Otto BA, Carrau RL, Prevedello DM. Management of Skull Base Tumors in the Obstetric Population: A Case Series. *World Neurosurg*. 2018 May;113:e373-e382. <https://doi.org/10.1016/j.wneu.2018.02.038> Epub 2018 Feb 14. PubMed PMID: 29454125.
10. Van Gompel JJ, Agazzi S, Carlson ML, Adewumi DA, Hadjipanayis CG, Uhm JH, Olson JJ. Congress of Neurological Surgeons Systematic Review and Evidence-Based Guidelines on Emerging Therapies for the Treatment of Patients With Vestibular Schwannomas. *Neurosurgery*. 2018 Feb 1;82(2):E52-E54. <https://doi.org/10.1093/neuros/nyx516> PubMed PMID: 29309638.

11. Beni-Adani L, Pomeranz S, Flores I, Shoshan Y, Ginosar Y, Ben-Shachar I. Huge acoustic neurinomas presenting in the late stage of pregnancy. Treatment options and review of literature. *Acta Obstet Gynecol Scand.* 2001 Feb;80(2):179-84.
<https://doi.org/10.1034/j.1600-0412.2001.080002179.x> PubMed
PMID: 11167216.
12. Dounas M, Mercier FJ, Lhuissier C, Benhamou D. Epidural analgesia for labour in a parturient with neurofibromatosis. *Can J Anaesth.* 1995 May;42(5 Pt 1):420-2; discussion 422-4.
<https://doi.org/10.1007/BF03015490>
PubMed PMID: 7614652.
13. Sakai T, Vallejo MC, Shannon KT. A parturient with neurofibromatosis type 2: anesthetic and obstetric considerations for delivery. *Int J Obstet Anesth.* 2005 Oct;14(4):332-5.
<https://doi.org/10.1016/j.ijoa.2005.02.007> PubMed PMID: 16140520.