Recurrence of Supratentorial Ependymoma in a Brazilian Child: case report and 3D model reconstruction

ABSTRACT
Ependymomas are tumors resulting from neoplasms in ependymal cells. They represent the third most common tumor of the central nervous system in pediatric patients, occurring more frequently intracranially, in addition to having a high rate of local recurrence. Three-dimensional reconstruction is an emerging technology that promises benefits to professionals, patients, and students. We report the case of a 3-year-old female patient with a recurrent left frontal ependymoma, as well as its unique 3D reconstruction. The primary lesion was clinically manifested by gait imbalance, and recurrence was identified by resonance magnetic imaging. This type of tumor requires resection surgery as main treatment, and total removal is associated with lower mortality and low recurrence rate. Despite that, in the present study, the primary lesion was partially resected, which represents a tendency to recurrence. The case was presented through a 3D reconstruction of the recurred intracranial lesion and the postoperative period, based on image exams of the patient, to discuss the surgical approach. In addition, the 3D model is an innovation that allows preoperative practice by neurosurgeons and improves the clinical understanding of the patient and their family by enabling the observation of structures. Also, it aids in medical education by ensuring 3D visualization, essential for the study of anatomy. Therefore, the present work adds to the scientific literature new possibilities offered by 3D reconstruction technology.

Keywords: Ependymoma; Case report; Recurrence; Three-dimensional printing

RESUMO
Ependimomas são tumores decorrentes de neoplasias em células ependimárias. Representam o terceiro tumor mais comum de sistema nervoso central em pacientes pediátricos, ocorrendo com maior frequência intracranialmente, além de apresentarem alta taxa de recorrência local. A reconstrução 3D é uma tecnologia emergente que promete beneficiar profissionais, pacientes e estudantes. Relatamos o caso de uma paciente de três anos de idade com um ependimoma frontal esquerdo recidivante, acompanhado de sua reconstrução 3D. A lesão primária se manifestou clinicamente por desequilíbrio de marcha e a recorrência foi identificada por ressonância magnética. Tal tipo de tumor requer como tratamento principal a cirurgia de reseccão, sendo a retirada total associada a menor mortalidade e a baixa taxa de recidiva. Apesar disso, no presente estudo, a lesão primária foi parcialmente retirada, o que representa uma tendência à recorrência. O caso foi apresentado através de uma reconstrução 3D da lesão intracraniana e do
Ependymomas are tumors originating from ependymal cells, which can arise throughout the whole neuraxis. In children, ependymomas predominantly occur intracranially\(^1\), commonly located around the ventricular region\(^2\). In pediatric patients, they are the third most common tumor of the central nervous system (CNS), corresponding from 6 to 10% of the cases\(^3\). Regarding the location, intracranial ependymomas are classified as posterior fossa ependymomas and supratentorial ependymomas, which occur in two-thirds of the cases\(^4\). The ependymoma recurrence or progression can occur in up to 72% of the cases and is usually identified within the first five years after surgical resection\(^5\).

Three-dimensional (3D) printed models are templates created by 3D reconstruction of real structures constituted by different materials, such as nylon, gypsum, aluminum, textile materials, and polylactic acid (PLA), which are stacked layer by layer through computer control\(^6\). Several methods could be used to create a 3D model. The most common are surface scanning, photogrammetry, computer tomography (CT) or magnetic resonance imaging (MRI) reconstruction, and digital modeling\(^7\). 3D models of anatomical structures are arising as important tools for surgery planning and medicine teaching\(^7-9\).

This article, written following CARE guidelines, addresses the case of a 3-year-old female patient with recurrent supratentorial ependymoma and presents a unique 3D reconstruction model of the intracranial lesion, in order to discuss the surgical approach and the new possibilities offered by these technologies.

A 2-years-old Afro-descendant female patient was presented at the hospital with a one-week evolution of unbalanced gait and fever. She had a negative cancer family history and previously presented an adequate neuropsychomotor development for her age. The family denied additional symptoms and past interventions. In physical examination, gait disturbance with left lateralization was identified. Laboratory tests showed a lack of alteration. A cranial CT imaging was requested and evidenced a heterogeneous expansive intraparenchymal lesion in the left frontal lobe, of solid aspect, with multiple cystic areas, predominance of T2 hyper signal and T1 intermediate signal, and size of approximately 8.2 x 7.2 cm in the axial plane and 5.8 cm in the craniocaudal extension, causing adjacent vasogenic edema, midline deviation, and uncal herniation signals. She was diagnosed with left lateral ventricle ependymoma that has expanded to the left frontal lobe. The tumor was partially resected by frontoparietal craniotomy. During surgery, the patient suffered a cardiac arrest for less than two minutes. However, in the postoperative period, she showed gait improvement and no focal deficits. The histopathological exam of the lesion indicated a primary nervous system hypercellular neoplasia constituted by epithelioid and polygonal cells with mild atypia, with solid base architecture and pseudorosettes, with great extension of necrosed area, suggestive of anaplastic ependymoma, grade...
III. Her first post-surgery head MRI showed no evidence of residual expansive process.

Her follow-up was conducted by head MRI every three months, and by that, the tumor recurrence was observed. At 3 years old, in the fourth MRI, it was revealed a lesion with solid-cystic content, expanded to the left frontal horn, measuring approximately 4.2 cm x 2.6 cm in its bigger axis (Figures 1 and 2).

She was admitted to Santo Antônio Hospital at Irmandade Santa Casa de Misericórdia’s Hospital complex. By the time of her admission, she was in good general condition, lucid, and time and space-oriented, did not present any alterations in laboratory tests and neurological examinations, with a maximum score (15 out of 15) on the Glasgow Coma Scale.

The patient underwent a second left frontoparietal craniotomy and tumor resection was conducted without complication.

during the procedure. After the procedure, the patient was admitted to the intensive care unit (ICU), and maintained under analgesic effect without neurological deficits. The patient underwent intracranial pressure monitoring with cerebrospinal fluid (CSF) drainage. ICU discharging happened in two days. In the physical exam, the patient was awake, alert, oriented, and hemodynamically stable. She was breathing spontaneously and had no fever. Furthermore, neurological examination indicated an absence of meningism and focal deficits, preserved verbal and motor responsiveness, preserved pupillary light reflexes, symmetrical facial mimicry, and preserved gross sensibility. Postoperative histopathological and immunohistochemical examination of the lesion confirmed the suspected diagnosis, relapsed frontal ependymoma, but indicated a grade II neoplasm (Figure 3). Postoperative MRI showed no signs of residual disease, and the patient was forwarded to radiotherapy adjuvant treatment, in order to prevent minimal residual lesion.

Figure 1. T1 MRI sequence. Diffusion-weighted (DWI) showing lesion on axial plane. A 3D MRI reconstruction with digital sculpting showing a lesion on the left lateral ventricle.

Figure 2. Three-dimensional reconstruction of the pre-procedure MRI showing the tumor recurrence before the second resection.
Case Report

We reported a case of a supratentorial ependymoma in a young girl. Despite surgical resection, recurrence was identified after one year. The histopathological exam conducted after the first procedure classified the tumor as a grade III ependymoma. Curiously, after recurrence, a second surgical resection was performed, and the postoperative histopathological exam indicated a grade II ependymoma.

Ependymomas are rare malignant tumors arising from the ependymal lining of the ventricles and spinal canal. Approximately 90% of ependymomas occur intracranially, of which one-third are supratentorial and two-thirds are in the posterior fossa. Although they can occur at all ages, they are more common in children, comprising up to 10% of pediatric intracranial tumors. Ependymomas are the third most common pediatric nervous system tumor, behind only astrocytoma and medulloblastoma, and its incidence peaks between ages 0 to 4. It is slightly more common in males than in females. At the presentation, the incidence of metastasis is rare, albeit the chances of recurrence are high, as we will discuss in this report. The most common histological type, according to World Health Organization (WHO) classification, is ependymoma grade II.

In young children, the clinical presentation is usually nonspecific, with the most common symptoms being irritability, lethargy, and growth problems. Furthermore, there is a correlation between the location of the ependymoma and the symptoms presented: in supratentorial ependymomas, the most common symptoms usually are headache, seizures, weakness, intracranial hypertension, and focal neurological signs. Curiously, the patient we reported presented only an unbalanced gait, in contrast to the literature.

The rate of recurrence or progression of the intracranial ependymoma varies from 43 to 72%. Data show that patients with full resections followed by radiation have a global survival of 67 to 93% and progression-free survival of 51 to 82%. In the reported case, none of those treatment modalities were accomplished, which probably contributed to the early recurrence of the tumor. In 80% of the cases, the ependymoma recurrence occurs locally, and, in most of the cases, it happens within the first 5-years after the treatment of the initial tumor, which is in accordance with our patient’s case. Factors related to the ependymoma recurrence are the extension of the surgical resection and the timing of adjuvant therapies. In that regard, incomplete resection, as first happened in our patient’s case, is an important cause of recurrence observed in 50% of ependymoma patients. Extensive resections seem to be an important prognosis factor, and tumor complete resection has been associated with a longer time without progression (12.7 years). In pediatric patients, 50% or more experience recurrence, and even with full resection and radiotherapy, it happens with 40% to 50% of them. Furthermore, up to 30% of patients experience a second relapse.

Regarding the prognosis, the survival rate after ependymoma recurrence is low. The risk of mortality is even higher in patients that had the recurrence identified because they presented symptoms compared to those who had it identified by imaging follow-up, which might indicate that our patient has a chance of a better prognosis, once her recurrence was diagnosed by a follow-up MRI. The poor outcomes at the
relapse may be associated with elements that affect the overall treatment of pediatric ependymoma, which include diverse tumor biology with absence targeted therapies, no effective chemotherapy options, and younger age at recurrence.

The recurrence in our patient occurs in the supratentorial region and, according to Byer’s systematic review, this location is associated with lower overall survival (8.3 months) compared to 20.1 months when it happens infratentorially. Furthermore, as reported by this review, patients younger than 3-year-old demonstrate a median overall survival of 31 months compared to 17.5 months for those who recurred after 3-year-old, as in our case.

As for the treatment applied after the relapse, our patient underwent surgery and adjuvant radiotherapy. Unfortunately, it was also observed in the review that individuals who underwent surgery at recurrence had a median overall survival of 24.2 months. In comparison, the patients that received radiation therapy had 29.2 months of median overall survival and those who received chemotherapy had a median of 19.3 months associated with overall survival.

In 2015, a new molecular classification for ependymomas was proposed, in which ependymomas are initially divided into their three anatomical compartments, supratentorial (ST), posterior fossa (PF), and spinal (SP), followed by further stratification into nine total subgroups according to genetics and DNA methylation. According to this classification, supratentorial ependymomas are stratified into supratentorial subependymomas (ST-EPN-SE), RELA fusions (ST-EPN-RELA), and YAP1 fusions (ST-EPN-YAP1). In the ST group, studies have shown that YAP1 fusions foretell an excellent prognosis, with 5-year PFS and OS of 66 and 100%, respectively, whereas the presence of RELA fusions, which occurs in more than 70% of cases, correlates with some of the poorest outcomes (5 years PFS and OS of 29 and 75%, respectively). Despite this, these differences have not yet been translated into significant differences in the therapeutic management of these injuries. Unfortunately, in the reported case, RELA fusion was not researched. This information would allow a better future risk stratification, which could be relevant in the decision to administer more aggressive treatment in patients with a dismal prognosis that characterizes cases of RELA fusions.

Tumor resection surgery is considered the main pillar of pediatric ependymoma management. In this way, the total resection is associated with a lower mortality rate, longer survival, and longer time without disease progression. On the other hand, the subtotal is associated with a higher rate of mortality and recurrence. In some cases, resection is incomplete due to excessive bleeding, the need for two different accesses for surgery, the absence of accurate correlation between imaging and intraoperative findings, and the excessive duration of the surgery. Those findings could explain the impossibility of total resection in our patient’s first surgery.

3D model
In order to enlarge the surgical and anatomical understanding of the case, we developed a 3D reconstructed model of the intracranial lesion. The 3D model was created by 3D image segmentation from the CT images, using the open-source 3D slicer software. Following, the model was exported as a stereolithographic archive to ZBrush (Pixologic) to be improved. In Zbrush, polypainting was performed using image references from the surgery. The model was 3D printed with PLA filament on a Creality Ender 3 printer (Figure 4). The total cost of the 3D printing was R$ 50,00.

Figure 4. Three-dimensional printed model of relapsed resected lesion.
Research has shown that 3D models of intracranial injuries offer several benefits for neurosurgeons. They facilitate the observation of the spatial relationship between the injury and the surrounding tissues, allow better planning of the surgical procedures, and enable training in surgical techniques, offering effective simulations of the surgeries. A 2019 study simulated 49 highly complex neurosurgeries using 3D models with different colors and textures to mimic tissues, vessels, and tumors, and concluded that simulations allow the surgeon to practice different approaches to the same operation and select the one in which the risks are smaller, more predictable or better known.

Furthermore, 3D models also facilitate communication between the surgeon and the patient, allowing a better understanding of the clinical picture through reliable visual structures, which is especially important in pediatric patients. Compared to imaging examinations, which are mostly 2D black-and-white images, and hard to explain, pre-operative communication using 3D-printed models helps patients, especially those without medical background, to have a more thorough understanding of the disease and surgical plan, including the difficulty, risk and possible complications of surgery. As such, it improves communication efficiency, shortens the communication time, and is favorable for doctor-patient relationship. Additionally, this method reduces patient anxiety because of the enhanced understanding, since the feeling is mostly caused by the unknown.

Three-dimensional models are also an important tool for anatomy and medical education. Since anatomy is an inherently three-dimensional subject, the learning of the 3D relationships of structures is essential. Research has found that a poor understanding of 3D anatomy at the undergraduate level compromises the training of postgraduates in the use of 3D clinical imaging technologies. In this context, the addition of 3D models in the learning process of anatomical and surgical subjects is significantly beneficial, especially when complicated anatomic structures are involved, which is true in neurological pathologies.

A meta-analysis published in 2020 analyzed the application of 3D models in anatomy teaching and concluded that it was associated with a significant increase in terms of test scores, answering accuracy, and student satisfaction, in comparison to the conventional use of 2D or cadaveric resources. In the studies that compared specifically 3D printed models with conventional nervous system models, the post-training test scores of the 3D group were also higher than the conventional group.

Moreover, 3D printed models provide active control over the object, stimulating both kinaesthetic and visual learning, which improves the ability to identify anatomical features from a variety of orientations. Therefore, the 3D reconstruction images and models that we created might increase the comprehension of the reported case and could be used as examples in neuroanatomy or surgery classes.

Limitations
The present study includes some limitations. The major refers specifically to the selected case, which is not an outstanding unusual history, despite the uncommon initial clinical manifestations and the early recurrence.

Additional limitations are related to the 3D printed model creation process. We developed a new perspective for the case, through a 3D reconstruction of the intracranial lesion. The 3D printed model was created by 3D image segmentation from the CT images, a method that can capture internal and external features and is usually highly accurate. However, the selected method also presents important limitations, since it requires manual segmentation for small structures reconstruction, a time-consuming and not always completely accurate technique. In addition, our study comprehends a neurosurgical case in which the 3D model was produced only after the procedure. Therefore, the direct medical applications could not be evaluated, as it could be used in surgical planning and improvement of patient understanding, as already discussed.

CONCLUSION

Even though our study reports a usual case and the 3D model used is dependent on the operator, we reported a non-atypical
Case Report


Catão JR, Debastiani MS, Everling MDB, Ko T, Herwig GK et al. - Recurrence of Supratentorial Ependymoma in a Brazilian Child: case report and 3D model reconstruction

We report a case of intracranial ependymoma in a child. However, we elaborated a new perspective on the anatomical and surgical aspects of its pathology through a 3D-reconstruction of the brain, a technology which could improve the patient comprehension and the medical planning around intracranial lesions. Our case report also provides extra information on 3D-reconstruction and can be helpful as readers can observe the anatomy of the case and its specificities, providing a more immersive reading and deeper learning.

REFERENCES


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