Successful treatment of hemorrhagic congenital intracranial immature teratoma with neoadjuvant chemotherapy and surgery

Case report

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Congenital intracranial immature teratomas carry a dismal prognosis, and the usefulness of chemotherapy for these tumors has not been elucidated. The authors report on the successful management of a case of congenital intracranial immature teratoma by using neoadjuvant chemotherapy and surgery after the failure of an initial attempt at resection.

The patient was an infant who had begun vomiting frequently at the age of 12 days and had been admitted to a hospital at the age of 18 days with continued vomiting, increased head circumference, and disturbance of consciousness. A CT scan of the brain revealed a large mass in his posterior fossa and hydrocephalus. Surgery was performed on an emergent basis, but only minor tumor resection could be performed due to massive intraoperative hemorrhage. The histopathological diagnosis was immature teratoma. Postoperatively, the infant was in critical condition due to severe postoperative complications, and when he was transferred to the authors’ institution 43 days after birth, his respiratory condition was still unstable because of lower cranial nerve palsy. Chemotherapy with carboplatin and etoposide resulted in moderate shrinkage of the tumor. Further chemotherapy led to improvement in the patient’s general condition and weight gain, which allowed for a second attempt at resection. During this second surgery, which was performed when the child was 8 months of age, after 8 courses of chemotherapy, the tumor was completely resected with little bleeding. Histological findings from the second operation were consistent with mature teratoma.

This case indicates that upfront chemotherapy may be effective for the initial management of such cases. Although the objective response to the treatment was modest, chemotherapy reduced the hemorrhagic nature of the tumor, facilitated improvement of the patient’s general condition, and allowed for successful resection.

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KEY WORDS • congenital brain tumor • immature teratoma • neoadjuvant chemotherapy • pediatric neurosurgery • oncology

The prevalence of congenital brain tumors has been reported to be in the range of 1.7–13.5 per 100,000 live births.2,6,20 These lesions represent 0.5%–1.9% of all pediatric brain tumors2,6 and are generally associated with a poor prognosis.10 Central nervous system neoplasms are the cause of 5%–20% of deaths during the fetal and neonatal period.35 Teratomas account for the largest group of congenital brain tumors, followed by astrocytomas, medulloblastomas, and choroid plexus papillomas.10 Congenital intracranial immature teratomas are sometimes large enough to endanger life, and they are usually hemorrhagic, preventing easy surgical removal and resulting in a dismal prognosis.9,19 We report the successful management of a case of congenital intracranial immature teratoma of the posterior fossa by using neoadjuvant chemotherapy and a second surgery after an initial resection, which was incomplete because of the hemorrhagic nature of the tumor.

Case Report

This male infant was born at a gestational age of 38 weeks by a normal vaginal delivery after an uneventful...
gestation and regular prenatal examinations. His Apgar score was 9 at 1 minute after birth and 10 at 5 minutes. His body weight at birth was 3056 g, and his head circumference was 35 cm (1.1 SDs above the mean). His parents reported that he had experienced frequent vomiting and head circumference enlargement since the 12th postnatal day. He was admitted to a local hospital on the 18th postnatal day because of extreme lethargy. CT of the brain revealed a large mass located in the posterior fossa with high-density dots within the lesion, suggesting calcification, as well as obstructive hydrocephalus (Fig. 1A and B). Surgery was undertaken, but only a limited tumor resection could be performed because of massive bleeding from the mass (Fig. 1C and D). Histopathological examination revealed an immature teratoma composed of immature cartilage, bone, muscle, and neural tube–like components with glial cells (Fig. 2A and B). Postoperatively, the child was in critical condition because of severe complications, including respiratory failure and disseminated intravascular coagulation secondary to intraoperative bleeding. After a gradual recovery, he was transferred to our hospital for further treatment on the 43rd postnatal day.

On the day of admission to our hospital, the patient’s head circumference was 41.8 cm (3.6 SDs above the mean). On neurological examination, he was alert but demonstrated impairment of left eye abduction and also showed left facial nerve palsy. MRI of his brain revealed a large residual tumor with several areas of hemorrhage (Fig. 3A). His respiratory condition remained unstable, and he developed aspiration pneumonia, experiencing several episodes of respiratory arrest during hospitalization at our hospital. After a multidisciplinary discussion, a trial of chemotherapy with a moderate dose of carboplatin (18.6 mg/kg per day) on Day 1 and etoposide (5 mg/kg per day) on Days 1 and 2 was decided upon. An MRI study performed after 2 courses of chemotherapy revealed a 23% reduction in the size of the tumor (Fig. 3B). Additional courses of chemotherapy led to signifi-

Fig. 1. A and B: Nonenhanced CT images obtained before the first surgery showing hydrocephalus and a large mass with multiple small calcifications located in the posterior fossa. C and D: Nonenhanced CT images obtained after the first surgery showing massive intratumoral hemorrhage.

Fig. 2. A and B: Photomicrographs of tumor specimen from the first operation showing the composition of the immature teratoma. Neural tube–like components can be seen in A and immature muscle in B. C and D: Photomicrographs of specimen from the second operation showing only differentiated components such as bronchus (C) and epidermis and dermis (D). H & E, original magnification ×400 (A and C) and ×200 (B and D).

Fig. 3. Contrast-enhanced axial T1-weighted MR images. A: Image obtained after admission to our hospital, showing the residual tumor with subacute hemorrhage. B: Image obtained after 2 courses of chemotherapy, showing modest reduction in tumor size. C: Image obtained just before the second operation, showing that the tumor size remained stable after 8 courses of chemotherapy. D: Image obtained after the second operation, showing complete resection.
cant improvement in the infant’s general condition, increased weight gain, and a gradual improvement in his respiratory function.

The child underwent removal of the residual tumor at the age of 8 months, after completion of 8 courses of chemotherapy (Fig. 3C). Preoperatively, the tumor size appeared unchanged compared to the size in the MRI study performed after 2 courses of chemotherapy, but complete resection was achieved with minimal bleeding (Fig. 3D).

The histological characteristics of the lesion were consistent with mature teratoma composed of fully differentiated tissue elements, such as cartilage, bone, fat, skin, and epithelia, with no malignant type of germ cell tumors, including immature teratoma (Fig. 2C and D). Because of prolonged hydrocephalus, the infant required placement of a ventriculoperitoneal shunt after tumor removal, but his postoperative course was otherwise uneventful. The child is currently in complete remission at 3 years of age.

Discussion

We report on the successful management of a congenital intracranial immature teratoma with neoadjuvant chemotherapy and surgery. The initial surgery, performed before chemotherapy, had resulted in incomplete resection because of massive intraoperative bleeding, a common and often fatal complication of surgery in neonatal patients with brain tumors.10

Teratomas are the most frequent congenital brain tumors and account for 30%–50% of all such lesions.6,10,18 These tumors are sometimes diagnosed in utero by prenatal ultrasonography.10,22 Features leading to ultrasonographic detection are macrocephaly, fetal hydrocephalus, and polyhydramnios.10,20,24 There is also a high incidence of breech presentation when these tumors are present.10 The tumors are most commonly detected during the third trimester, and in some cases, ultrasonography findings are normal until 2 weeks before the third trimester.5,23,25 The patient in our case had no pertinent prenatal history or abnormal ultrasonographic findings, such as head circumference enlargement or ventricular dilation, and he had a normal delivery. His head circumference at birth was within normal limits.

Congenital intracranial teratoma generally arises from the supratentorial area.24 The exact anatomical location of the tumor cannot be determined in at least one-third of reported cases because so much of the brain is replaced with tumor and identifiable anatomical landmarks are lost.3,4,10,13,25 In patients for whom the locus of origin can be identified, the cerebral hemispheres are the most common primary site, followed by the third ventricle and pineal region.6,10 Large tumors may erode through the skull and extend into the orbit, oral cavity, or neck.2,5,10,13,22 The location of the tumor in our case was the posterior fossa, a relatively uncommon site for congenital teratomas.

Survival of infants with congenital intracranial teratomas is quite poor;10 more than 90% of those affected die before delivery or shortly afterward,9 and in a previous review of the literature the reported 1-year survival rate was 7.2%.34 There have been reports of cases in which patients have survived for a long time following complete resec-

tion,1,13,14,22 and the prognosis is considered to be greatly improved if complete resection can be achieved.2,5 For predicting outcome, the location and size of the mass are more important than the histological grade.10,20 Because intracranial teratomas are usually hemorrhagic tumors, a large amount of intraoperative blood loss is often inevitable during resection, sometimes reaching and even exceeding the infant’s blood volume.10 Therefore neurosurgeons tend to hesitate when considering extensive surgical removal.

Irradiation is generally contraindicated for congenital immature teratomas because of its consequences on normal brain growth and development in neonates.20 It is recognized that, in older children, chemotherapy with platinum agents is effective for intracranial immature teratomas.11,15,16 It is also known that neoadjuvant chemotherapy can induce differentiation of malignant germ cell tumors into mature teratomas.8 The apparent tumor maturation presumably reflects the selective chemo-ablation of their actively proliferating components.19 Shaffrey et al. reported 2 cases of immature teratoma that differentiated into mature teratoma.21 In this report, maturation of the tumor following chemotherapy occurred in one case and spontaneous maturation, which is extremely infrequent, was observed in another patient who did not receive any treatment except surgery. Waiting for months for spontaneous maturation of congenital immature teratoma without treatment may be justified in some cases, but it seems reasonable to treat patients with chemotherapy if their tumors are too hemorrhagic to allow a second surgery, as in our case.

There have been very few reports of successful chemotherapy for congenital immature teratomas,17 but the optimal chemotherapeutic regimen for this type of tumor has yet to be established.5 In our case, the dosage of chemotherapeutic agents was determined according to a regimen for retinoblastoma7 that is commonly used in neonates.

Given the minimal information available in the literature concerning the response of congenital immature teratoma to chemotherapy, our experience with this case suggests that even moderate chemotherapy tolerable by seriously ill patients with this type of tumor may be effective as an initial treatment. Although the response of the tumor to the treatment was modest, it is obvious that this chemotherapeutic treatment could have diminished the aggressiveness and hemorrhagic nature of the tumor; thereby improving the child’s general condition and facilitating complete resection. Interestingly, a similar approach has recently been advocated for congenital glioblastoma.12

Conclusions

Our experience confirms that a subset of congenital intracranial teratomas can be successfully managed. In this case, chemotherapy allowed complete resection. In cases of unresectable tumors or for patients in poor clinical condition who are not candidates for major surgery, neoadjuvant chemotherapy could lessen the aggressiveness of the tumor and offer the opportunity to perform subsequent surgery.
Chemotherapy for neonatal immature teratoma

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Disclosure

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in the paper.

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