

Case Report

A Case of Nongerminomatous Germ Cell Tumor of the Pineal Region: Risks and Advantages of Biopsy by Endoscopic Approach

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A 21-year-old male was admitted to our department with headache and drowsiness. CT scan and MRI revealed acute obstructive hydrocephalus caused by a pineal region mass. The serum and CSF levels of beta-human chorionic gonadotropin (beta-hCG) were 215 IU/L and 447 IU/L, respectively, while levels of alpha-fetoprotein (AFP) were normal. A germ cell tumor (GCT) was suspected, and the patient underwent endoscopic third ventriculostomy (ETV) with biopsy. After four days from surgery, the tumor bled with mass expansion and ETV stoma occlusion; thus, a ventriculoperitoneal shunt was positioned. After ten months, the tumor metastasized to the thorax and abdomen with progression of intracerebral tumor mass. Despite the aggressive nature of this tumor, ETV remains a valid approach for a pineal region mass, but in case of GCT, the risk of bleeding should be taken into account, during and after the surgical procedure.

1. Introduction

Primary intracranial germ cell tumors (GCTs) are 3.1% of all primary brain tumors [1]; they affect pediatric population (mean age of 16.1 years) with a male:female ratio of 4:1 and are located in midline structures such as suprasellar and/or pineal region [2]; tumors contemporary located at suprasellar and pineal regions called synchronous GCT are 13% of all GCTs; these lesions are germinoma (60–80% of patients) with high sensitivity to radiotherapy [3], teratoma (18%), endodermal sinus tumors (7%), embryonal carcinomas (5%), and choriocarcinomas (5%). Teratoma is also divided into mature, immature, and anaplastic [4]. The clinical presentation is mainly related to the tumor location [5]: suprasellar lesions cause diabetes insipidus (DI), hypopituitarism, or bilateral temporal hemianopsia, whereas lesions of the pineal region produce signs of increased intracranial pressure (ICP) due to obstructive hydrocephalus, Parinaud's syndrome, ataxia, behavioral changes, and seizure. The time of diagnosis is related to the presenting symptoms: signs of increased ICP are associated to earlier diagnosis, while endocrine dysfunction or behavioral alteration is associated with delayed diagnosis [6].

Despite specific CT and MRI features for each GCT, histologic types have been described in literature [7, 8], and these tumors are associated with increased markers such as alpha-fetoprotein (AFP), beta-human chorionic gonadotropin (beta-hCG), and placental alkaline phosphatase (PLAP), a definitive histologic diagnosis is necessary to plan proper treatment [9–11]. Mature teratomas are treated with surgical resection, while other GCT needs a combination of surgery, radiotherapy, and chemotherapy according to the tumor type [12, 13]. Germinoma and mature teratomas have the best prognosis.

2. Case Presentation

A 20-year-old male was admitted to our department in January 2017 with a four-day history of headache and drowsiness. The computed tomographic (CT) scan and magnetic resonance imaging (MRI) demonstrated acute obstructive hydrocephalus due to a mass in the pineal region (maximum diameter of 1.5 cm) with signs of previous hemorrhage and without significant contrast enhancement (Figure 1). An external ventricular drain (EVD) was positioned with neurological improvement.

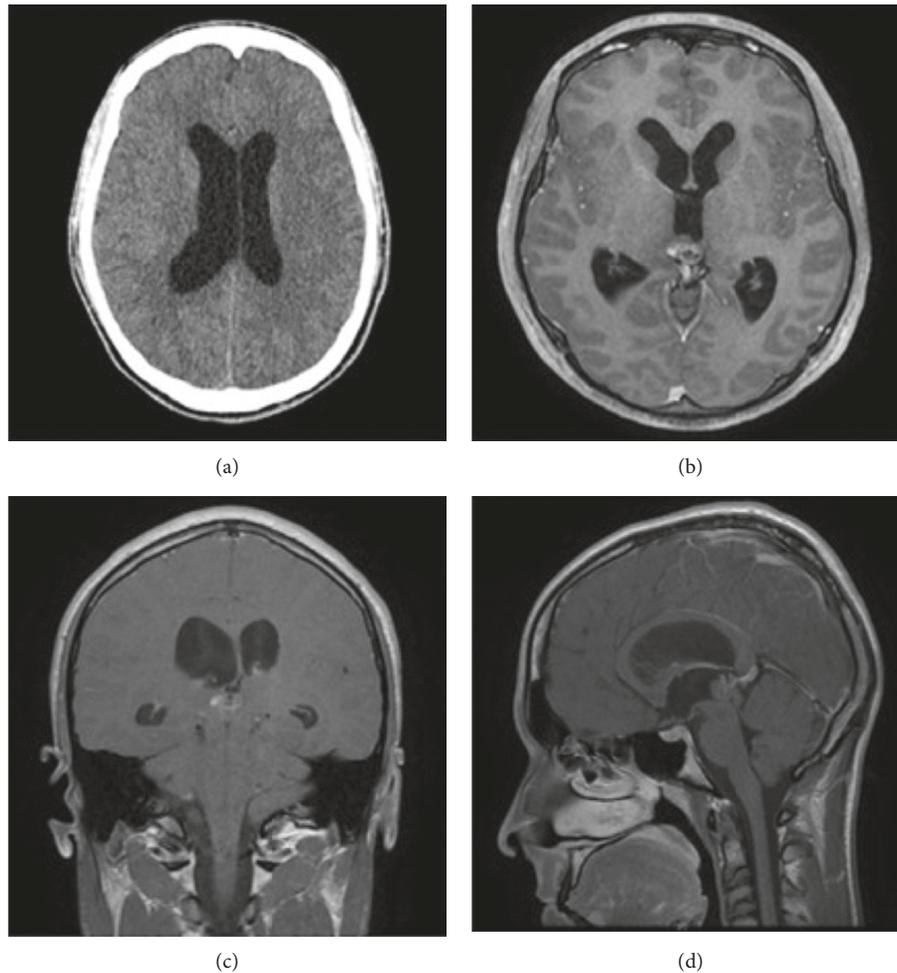


FIGURE 1: CT scan and MRI at admission documented acute obstructive hydrocephalus caused by a pineal region mass.

The serum and CSF levels of beta-hCG were 215 IU/L and 447 IU/L, respectively; the serum and CSF levels of AFP were within normal range. The full-body CT scans, spine MRI, and testicular ultrasounds were negative. Tumors of the pineal region may vary from benign to malignant lesions and are classified into four categories: GCT, pineal cell tumors (such as pineocytoma, pinealoblastoma), glial cell tumors, and miscellaneous tumors [14, 15]. In this patient, the lesion site, his age, and tumor marker levels strongly suggested a GCT. Given the high level of beta-hCG and normal level of AFP, a germinoma, choriocarcinoma, or mixed type tumor was taken into account. The patient underwent endoscopic third ventriculostomy (ETV) with biopsy of the anterior part of the lesion which appeared as a purplish and friable mass in the posterior part of the third ventricle; a good hemostasis was obtained without evidence of intraventricular and/or mass hemorrhage. EVD was left in place. The histological exam of the surgical specimen documented neural tissue with ependymal cells, macrophages, and cells of germ line without neoplastic elements. The CT scan four days after surgery demonstrated no signs of hemorrhage. On the fifth day after surgery, EVD was closed but 24 hours later, the patient showed neurological worsening with drowsiness and cognitive function decline; thus, EVD was reopened (Figure 2).



FIGURE 2: Acute obstructive hydrocephalus 24 hours after EVD closure.

Because of the onset of bacterial meningitis (*Staphylococcus haemolyticus* isolated from CSF specimen), EVD was substituted and clinical picture improved with antibiotic therapy after ten days. MRI on the twelfth day after surgery

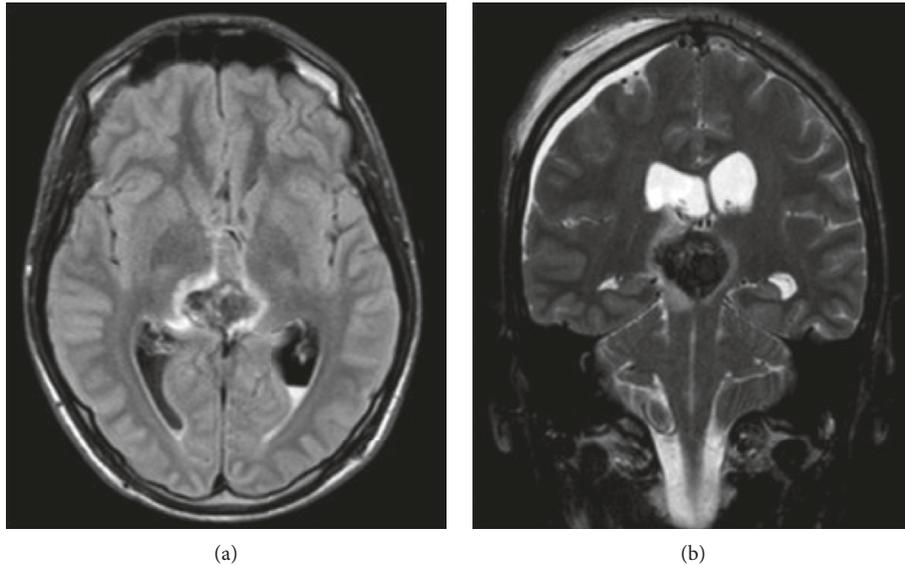


FIGURE 3: Intratumoral hemorrhage with mass expansion and complete occlusion of the third ventricle.

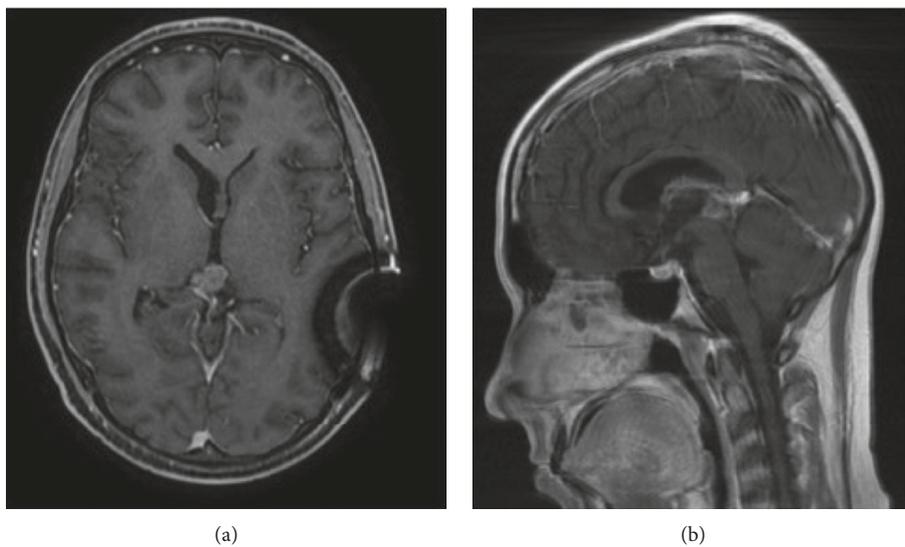


FIGURE 4: MRI after chemotherapy shows residual tumor mass. For this lesion, the patient underwent stereotactic radiosurgery.

demonstrated intratumoral hemorrhage with significant mass expansion, with blood in the third ventricle, and with mesencephalic aqueduct (Figure 3). The ventriculoperitoneal (VP) shunt was positioned one month later after complete infection recovery. The patient underwent four cycles of bleomycin/etoposide/cisplatin (BEP) regimen, and the MRI at four months from surgery (Figure 4) showed reduction of mass volume and normal size of brain ventricles. After four cycles of chemotherapy, beta-hCG serum level decreased, but complete normalization was not obtained (serum level was 26 vIU/L). The neurologic status after treatment of hydrocephalus and first-line chemotherapy was good and patient underwent stereotactic radiosurgery for the residual mass. Although in non-germinomatous GCTs the whole brain radiotherapy would

be indicated, the patient, also for the absence of histologic diagnosis, refused a whole irradiation due to its high morbidity compared to the stereotactic radiosurgery. Anyway, two months later, he started to complain general malaise and gait imbalance, and the full-body CT scan showed increased intracerebral tumor mass with a new focal lesion and systemic metastasis involving the lungs, liver, and adrenal gland (Figures 5 and 6); the serum levels of beta-hCG were 12.713 UI/L. A liver biopsy was obtained, but no malignant cells were found.

A second line of chemotherapy was started with partial decrease of serum beta-CGH until 1.883 UI/L without any decrease of cerebral or systemic lesions. At the present, after 10 months from admission, the patient is still alive with a poor prognosis.

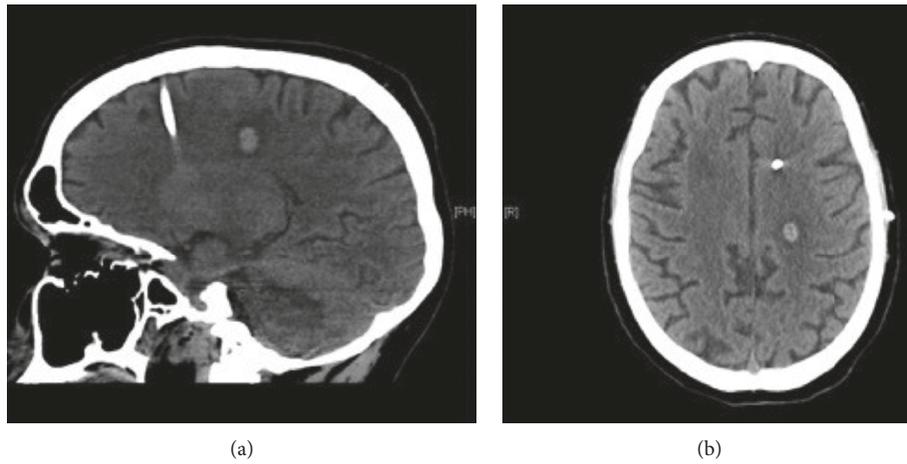


FIGURE 5: CT scan showing the new cerebral focal lesion.

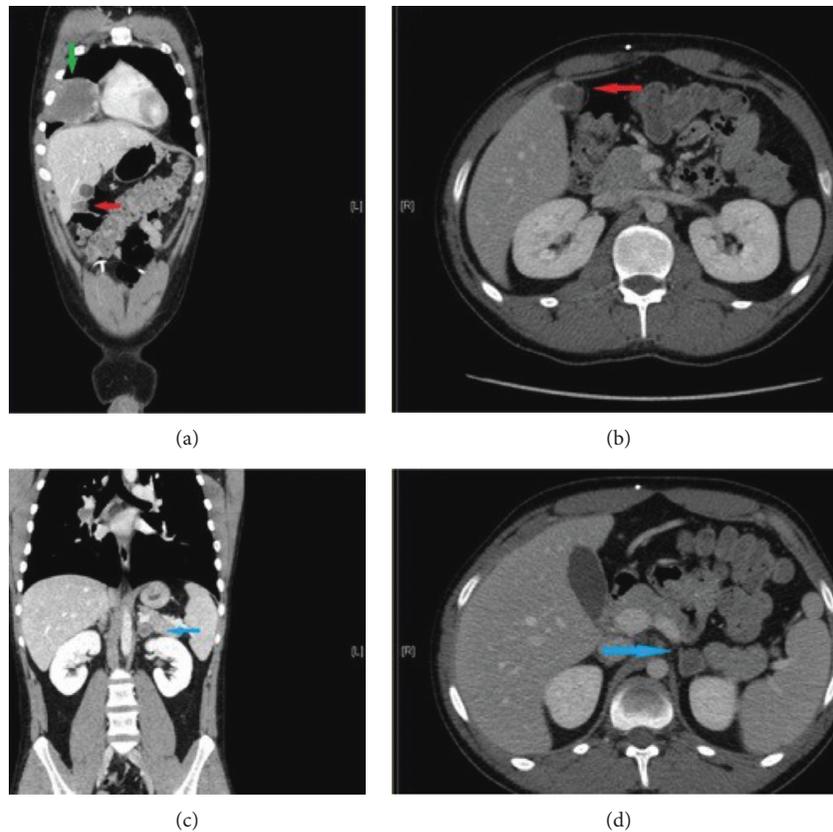


FIGURE 6: CT scan of the thorax and abdomen showing the lung (green arrow), liver (red arrow), and left adrenal (blue arrow) lesions.

3. Discussion

Taking into account the range of tumors which may occur in the pineal region, histologic diagnosis is necessary to get a correct management. Specimens for diagnosis can be obtained by an open procedure, a stereotactic biopsy or an endoscopic approach [14, 16]. Open procedure is generally avoided because many lesions of the pineal region show high response rates to radiotherapy and/or chemotherapy, so aggressive surgical removal is debated. Despite data from

literature confirming that stereotactic biopsy is a safe and effective procedure, endoscopic biopsy (Figure 7) is preferred because it allows both biopsy with direct visualization of the tumor and treatment of obstructive hydrocephalus by third ventriculostomy [17–20]. Moreover, most tumors are mixed type ones and the direct visualization of the lesion allows a multiple sampling that increases the probability of a correct histological diagnosis. It has been suggested that endoscopic biopsy should be reserved only for cases of GCTs with normal serum markers because, in case of marker

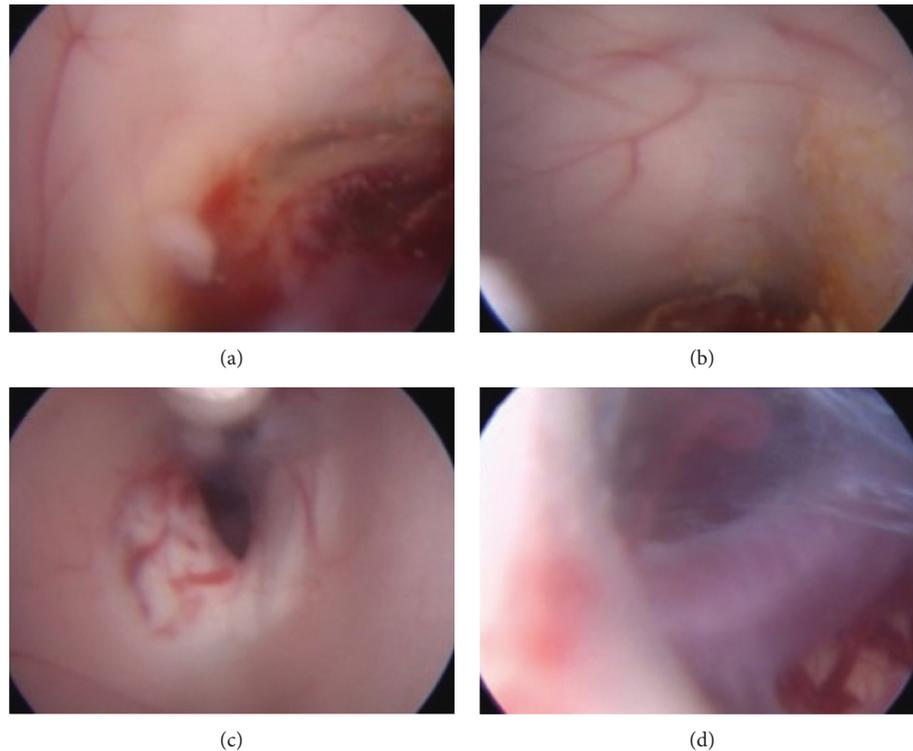


FIGURE 7: Endoscopic third ventriculostomy procedure. (a) Anterior view of the tumor. (b) Subependymal spread. (c) Stoma. (d) Stoma with basilar artery view.

increase, the histologic exam taken in isolation may lead to incorrect diagnosis of benign lesion if the malignant cells are not present in the specimen [21]. We agree with many authors, and we believe that both markers and histologic diagnosis should be carefully valued to identify the type of tumor even in patients with elevated tumor markers [22]. In patients with increase hCG serum level, some authors prefer to start with chemotherapy without biopsy because of the high diagnostic specificity for choriocarcinoma [23–28]; anyway, the initial serum level of hCG in our case (215 UI/L) was significantly lower than the values reported in literature, so the biopsy was mandatory. It is well known that cerebral GCS has a high probability of hemorrhage during stereotactic, minimally invasive, and endoscopic procedures [29–32]. In our case, we observed hemorrhage between the fifth and the twelfth day after surgery, and so we confirm the high risk of intraventricular hemorrhage of this lesion. We also supposed that the bleeding into the ventricles was the cause of ventriculostomy failure. In this case, the position of the VP shunt is safe even in case of previous CSF infection [33]. This is described also for other internal devices such as spinal and orthopedics prosthesis before proper antibiotic therapy [34–36]. Nongerminomatous primary intracranial GCTs are high aggressive tumor with a 3-year survival rate ranging from 27.3% for pure malignant tumor to 70% for mixed type with some elements of pure malignant tumor and both cerebrospinal fluid (CSF) and blood dissemination may occur; metastasis through a VP shunt has also been described [37]. In this case, we supposed a blood dissemination of tumor because of the absence of spinal metastasis,

which are related to CSF way, and/or intraperitoneal lesions. Finally, because nongerminomatous GCT has poor prognosis compared with germinoma, whole brain irradiation is required to prevent the relapse either locally or metastatic disease in particular CSF spread. The whole brain radiotherapy treatment has been proposed but patient refused it.

4. Conclusion

In cases of pineal region tumor, ETV and biopsy are valid options as primary surgical approach, but, because of the hemorrhage high risk, third ventriculostomy failure may occur, so a careful clinical follow-up is necessary for the prompt positioning of a ventricularperitoneal shunt.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

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