Primary Pineal Neuroblastoma in Adults: A Rare Case Report and Literature Review

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1 INTRODUCTION

Neuroblastoma is an embryonic tumor derived from the neural crest with migratory neuroectodermal cells (1). It is one of the most common extracranial solid tumors in infants and children. More than 90% of neuroblastoma cases occur in children under 5 years old (2,3). The clinical signs and symptoms of neuroblastoma are highly dependent on the origin and spread of the tumor (4). Neuroblastoma with a primary lesion in the central nervous system is defined as primary central nervous system neuroblastoma (PCNSN), which is rare and carries a poor prognosis (5). In PCNSN, primary tumors located in the pineal gland are exceedingly rare, and there is no previous report thus far. Here, we report an adult patient diagnosed with primary pineal neuroblastoma who received surgical resection and postoperative radiotherapy.

2 CASE HISTORY/EXAMINATION

A 56-year-old female suffering from sudden dizziness and limb fatigue was admitted to our hospital on May 20th, 2020. She had a history of type 2 diabetes for 2 years and took metformin orally. She had no family history of malignant tumors. Physical examination was unremarkable. Cranial magnetic resonance imaging (MRI) showed a 2 cm $\times$1.8 cm tumor in the pineal region, obstructive hydrocephalus and interstitial brain edema (Figure 1). Chest and abdominal imaging examinations were normal. No significant abnormalities were found in routine blood examination, biochemistry, coagulation or other laboratory examinations.

3 METHODS

After routine preoperative examination, radical resection of the tumor in the pineal region was performed on May 23rd, 2020. During the operation, a tough mass with a diameter of approximately 2 cm was found in the pineal region, which blocked the midbrain aqueduct and squeezed the great cerebral vein and bilateral internal cerebral veins. Dizziness symptoms were significantly relieved after surgery, and the patient recovered well without any neurological symptoms. Postoperative pathological diagnosis confirmed pineal neuroblastoma, with immunohistochemical staining of Syn (+), NSE (+), GFAP (+), ATRX (+), S100 (+), p53 (+, approximately 5%), EMA (-), desmin (-), TTF-1 (-), oligo-2 (-), NeuN (-), CD99 (-), H3K27M (-), SALL4 (-), and β-catenin (-). Figure 2 shows representative pathological images. No mutations in the BRAF, TERT and IDH1/2 genes were detected (Figure 3).

Cranial MRI after one month of surgery showed no residual tumor in the pineal region. Obstructive hydrocephalus and interstitial brain edema were also relieved (Figure 4).

Afterwards, the patient was treated with brain and spinal cord radiotherapy (54 Gy) for one month. Grade 3 neutropenia occurred during radiotherapy and recovered after treatment with recombinant human granulocyte stimulating factor. The patient was followed up regularly after treatment. The patient's diagnosis

and treatment process is shown in Figure 5.

4 OUTCOME AND FOLLOW-UP

In conclusion, PCNSN is a rare tumor whose clinical manifestations and imaging characteristics are non-specific. We mainly make clinical diagnoses through comprehensive consideration (especially pathology). When we diagnose PCNSN, we should perform a comprehensive and systematic examination to exclude brain metastasis of neuroblastoma. The final diagnosis is mainly based on pathology, especially immunohistochemistry. There are no standard treatment guidelines for this treatment; surgery is the main method; postoperative combined chemotherapy is feasible; and whether radiotherapy is performed after surgery is controversial, especially in infants. The overall prognosis of patients with this tumor is very poor. The relatively good prognosis of younger children has the characteristics of high recurrence and high dissemination and metastasis rates, but there is great clinical heterogeneity. As clinicians, we should choose the treatment method according to the clinical symptoms of patients, hoping to achieve maximum remission and improve the prognosis of patients with the treatment method of minimal side effects.

5 DISCUSSION

PCNSN is an undifferentiated neuroectodermal tumor derived from embryonic neural tube reproductive stromal cells, with a low incidence rate (0.28 cases per 1000000 person-years) and poor prognosis (2,6). In general, PCNSC is more frequent in young children (especially those aged less than 1 year old) but rare in adults, and the incidence rate gradually decreases with age (7). In a retrospective study using the Surveillance Epidemiology and End Results (SEER) database, adults (aged [?] 40 years) comprised only 8.2% of all PCNSN cases (8). Since the first report, almost no cases of adult neuroblastoma in the pineal region have been reported.

PCNSN is mostly located in the supratentorial brain parenchyma, temporal lobe, frontal lobe and parietal lobe. It may also be located in the lateral ventricle, pineal gland and spinal canal and can occupy space in the sellar region. The gross pathological specimens showed that the tumor had a rich blood supply and clear boundaries. PCNSNs often present as hemorrhage, calcification, cystic degeneration and necrosis in the tumor, and the tumor surface can be covered with a layer of pseudocapsules. It is characterized by poorly differentiated neuroepithelial cells with a fibrous matrix, a homogenous rosette, necrosis and calcification (6,7). Under light microscopy, tumor cells are usually described as small, rounded, blue cells with rosette patterns (Homer Wright Pseudorosettes) (7). Under the electron microscope, the presence of neurosecretory granules is helpful for the diagnosis (8). Immunohistochemistry showed that the cells could show weak expression of synaptophysin (Syn) or glial fibrillary acidic protein (GFAP) with a fibrous matrix, homogenous rosettes, necrosis and calibration; however, Ki-67 was highly immunolabelled (6). The gross pathology and immunohistochemistry of the patient we have demonstrated seems to be consistent with this finding.

The clinical symptoms of patients with PCNSN are often related to the location and size of the tumor, and whether there is local or distant metastasis, there are a wide range of clinical manifestations (4). There are some special clinical manifestations that can suggest that patients suffer from neuroblastoma, such as paralysis of the lower limb related to the intraspinal epidural extension of a primary paraspinal tumor (4%), severe diarrhea (4%) caused by vasoactive intestinal peptide (VIP) produced by tumor cells that is ineffective for standard treatment, acute cerebellar encephalopathy (2%-8%), claude bernard-horner syndrome (1%-7%), arterial hypertension, flushing, and occasional sweating (0-2%) due to increased catecholamine concentrations (3). The preoperative imaging diagnosis of PCNSN is extremely difficult, and it is easily misdiagnosed as medulloblastoma and ependymoma. There is currently no consensus on the treatment of PCNSN. Surgery plays a momentous role in the treatment of this disease. For young patients, planned staged tumor resection can be carried out. According to the age of the patients, radiotherapy alone, chemotherapy alone or combined with radiotherapy and chemotherapy were selected. It has been proven that combined chemotherapy is effective for neuroblastoma. Radiotherapy, as an auxiliary method of the primary site, is the standard treatment for high-risk neuroblastoma and can effectively reduce the recurrence of the primary site (9).

Studies have shown that tumors easily spread through cerebrospinal fluid, and the local recurrence and distant brain and spinal cord metastasis rates are relatively high (10,11). Therefore, preventive brain and spinal cord radiotherapy may be reasonable. However, the side effects of radiotherapy on the central nervous system remain a major problem, especially for infants and children with developing central nervous systems. Problems such as radiation necrosis of the brain parenchyma may lead to late cognitive loss and other side effects (12,13). Surgery, cerebrospinal radiotherapy and chemotherapy have prolonged the median survival of patients (4,14). (10) Amor reported a patient with primary central nervous system neuroblastoma treated with synchronous radiotherapy and chemotherapy as an adjuvant therapy, and there was no recurrence after 14 months of radiotherapy. To date, surgery is the first choice for the treatment of PCNSN, and combined chemotherapy is performed after surgery, followed by craniospinal radiation and additional chemotherapy (10,15).

PCNSN is a rare and invasive tumor whose treatment is affected by age, tumor histological type, tumor expansion and tumor location. Owing to local tumor recurrence and pia mater implantation, the prognosis is relatively poor. The patient we reported had a primary adult central neuroblastoma originating from the pineal gland. The incidence rate is extremely rare, and there are almost no relevant reports in the literature. She received postoperative whole brain and whole spinal cord radiotherapy after surgery, with relatively good tolerance, which can provide a basis for the treatment of adult PCNSN.

6 CONCLUSIONS

So far, there is no consensus on the optimal treatment for PCNSN. However, complete surgical resection is the best option, and postoperative radiotherapy and/or chemotherapy based on the patient's surgical and physical condition is also necessary.

ETHICS STATEMENT

We have passed local ethical review. Written informed consent was obtained from the individual(s) for the publication of any potentially identifiable images included in this article.

AUTHOR CONTRIBUTIONS

Yao Tang composed the manscript. Linjuan Li and Xiaofen Li provided images and tables. Youling Gong reviewed and edited the manuscript. All authors have agreed to the final version of the article.

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CONFLICT OF INTEREST STATEMENT

All authors declare no conflicts of interest.

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Key clinical message

Primary pineal neuroblastoma is one of the extremely rare and poorly prognosis tumors and have not been reported so far. Here, we report an adult patient diagnosed with primary pineal gland neuroblastoma who underwent surgical resection and postoperative radiation therapy. Provide optional direction for the treatment of this disease.

Project names	Results	Normal walues
Leukocyte count(WBC)	6.40	3.5-9.5×10ˆ9/L
Platelet count(PLT)	247	100-300×10ˆ9/L
Hemoglobin(HGB)	130	115-150g/L
Alanine aminotransferase(ALT)	41	¡40IU/L
Aspartate aminotransferase(AST)	30	¡35IU/L
Creatinine(Cre)	52	48-79umol/L
Prothrombin time(PT)	8.5	9.6-12.8 second
Glycosylated hemoglobin	7.7	4.5-6.1%
Alpha-fetoprotein(AFP)	1.14	¡7ng/ml
Chorionic gonadotropin(β-HCG)	1.15	¡3.81mIU/ml

Table 1. Laboratory examination data at the time of hospitalization.

Figure 1. Magnetic resonance imaging of the head before operation showed pineal space occupying lesions (about 2cm*1.8cm in size), obstructive hydrocephalus and interstitial brain edema. The arrow indicates the location of the space occupying lesion.((A). Sagittal Position. (C). Coronal Position. (B/D).Horizontal Position.)

Figure 2. Postoperative pathological results. ((A/B). Microphotographs of PCNSN(H and E ×200). (C-I).The positive immunohistochemical results of Syn, NSE, GFAP, ATRX,S100,P53 and Ki-67(about 5%). (J-R).The negative immunohistochemical results of EMA, desmin,TTF-1,Oligo-2,NeuN,CD99,H3K27M SHLL4 and β-catenin.)

Figure 3. No mutations in BRAF, TERT and IDH1/2 genes were detected.((A).BERF. (B)TERT. (C/D).IDH1/2.)

Figure 4. Magnetic resonance imaging of the head after operation showed that the pineal region was changed after operation, and there were no tumor residues. The obstructive hydrocephalus and interstitial brain edema were obviously alleviated contrasted to those before operation.((A). Sagittal Position.(B/C/D).Horizontal Position)

Figure 5. Diagnosis and treatment algorithm based on this case report.

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