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Posterior Reversible Encephalopathy Syndrome Developing after Aggressive Posterior Fossa Tumor Surgery

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Abstract

Posterior reversible encephalopathy syndrome (PRES) is a rare neurologic disorder, having such common radiological findings as vasogenic edema and white matter changes in watershed areas. The clinic and radiological outcome may not be reversible in 10 to 20% of patients, like in the case of our patient. Here, we discuss the pathogenetic factors that are essential in developing PRES after posterior fossa surgery. A 4-year-old female was admitted to our clinic with a recurrent/residual mass in the posterior fossa. She previously underwent posterior fossa surgery three times (for what was diagnosed as anaplastic astrocytoma through pathohistology) in another center. She was operated thrice in 5 days, and the tumor radically removed. Two days later, after the last surgery, while waking up, our patient developed seizures and altered consciousness. Her neurological condition was severe. Magnetic resonance imaging findings were compatible with those of PRES. Our patient had multiple risk factors for PRES that were as follows: multiple posterior fossa surgeries, anamnesis of chemotherapy and radiotherapy, high-dose steroid use, intracranial pressure changes, and hypertensive attacks due to surgical manipulation. In preventing the development of PRES, we should beware of sudden changes in blood pressure during surgery and meticulously manipulate the brain stem to avoid any disturbance of the central nervous system homeostasis. PRES may transform into real encephalopathy. If the patient has some of these risk factors, PRES would probably develop after surgery.

Keywords

- anaplastic ependymoma
- brain stem compression
- posterior fossa surgery
- posterior reversible encephalopathy syndrome (PRES)

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Established Facts

An already known fact is that PRES is associated with many different conditions like malignant hypertension, immunosuppressive therapy, eclampsia, electrolyte imbalances, and autoimmune diseases.

Novel Insights

New information in our case is developed PRES secondary to intracranial hypotension (after elevated intracranial pressure [ICP], aggressive tumor debulking and shunt revision which led to severe falling ICP).

Introduction

Posterior reversible encephalopathy syndrome (PRES) presents with various clinicoradiologic syndromes (headaches, seizures, vision loss, altered mental condition clinically and diffuse subcortical white matter vasogenic edema; predominantly in the parietooccipital regions, radiologically).[1] PRES is associated with many different conditions like malignant hypertension, immunosuppressive therapy, eclampsia, electrolyte imbalances, and autoimmune diseases.[2,3] A history of chemotherapy,[4] steroid use,[5] intracranial hypotension,[6] shunt revision,[7] peri- and postoperative hypertension,[8] and hypertension due to manipulation of the brain stem (especially at the ventrolateral medulla)[9–11] might contribute to PRES development.

We present a pediatric patient who previously was operated for recurrent anaplastic ependymoma. She underwent three posterior fossa- and one shunt-revision surgeries over 5 days. Subsequently, PRES developed. The patient had multiple risk factors for the development of PRES. Here, we described the pathophysiology behind PRES in our patient. Through this study, we aimed to increase awareness about PRES among neurosurgeons.

Case Report

A 4-year-old female patient who was previously operated for a fourth ventricular tumor three times, and later for placement of a ventriculoperitoneal shunt due to secondary hydrocephalus. In these surgeries, tumors extending from the foramen Luschka to the cerebellopontine angle (CPA) remained residual. As these tumors were histopathologically reported as anaplastic ependymomas, chemotherapy and high-dose steroids were accepted. Upon admission to our clinic, the patient suffered a relapse of the midline posterior fossa tumor, and also of both side tumors (these tumors increased in size) that arose in the CPA (►**Fig. 1**). Informed written consent was obtained from the parents of the patient for the publication of this case report and any accompanying images. The brain stem was compressed 270 degrees from three sides (the midline and both CPA angles). Tumors were in three different places; thus, three surgeries in different regions were performed. Neurologic examination revealed brain stem compression and long tract involvement, together with hydrocephalus. Moreover, in anamnesis, the patient had a mutism after previous surgeries, which continued 2 months. Afterward, over 5 days, three surgeries were performed, for the midline tumor and for both CPA tumors. In the first surgery, the preoperative ventriculoperitoneal shunt was revised, and the midline tumor was removed. There was no problem after the first surgery. Following the second surgery, the patient had perioperative and postoperative hypertension that was controlled under conservative treatment. Finally, following the third surgery, uncontrolled hypertension (despite medical treatment it continued 3 days) was noticed. During surgery, after manipulation of the brain stem (since the tumor arose from Luschka), intraoperative hypertension, and asystoles were observed; however, these asystoles (two times) were up to 3 seconds. The tumor was removed totally. Between every surgery, the patient was awakened for checking neurological conditions. There was no additional neurological deficit. We did not want to perform three surgeries consecutively, to better understand the problems that could arise. The patient was intubated after surgery. While intubated, but in spontaneous breathing (when she was not under anesthesia), seizures developed immediately after postoperative day (following day after surgery), one of the third surgery during the awakening phase. Antihypertensive therapy and antiepileptic drugs were commenced. Magnetic resonance imaging

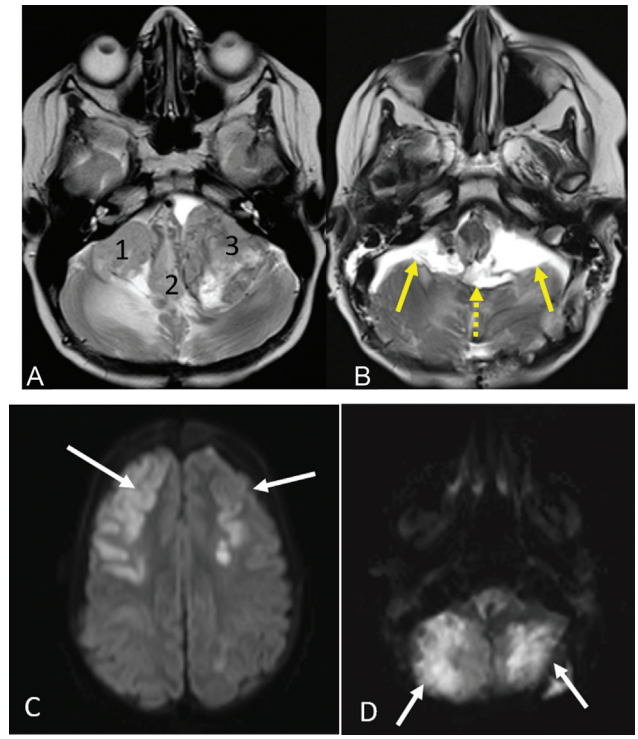

Fig. 1 Preoperative and postoperative images. (**A**) Axial T2 sequence magnetic resonance imaging (MRI) showing midline (number 2) and bilateral cerebellopontine angle (CPA) (number 1 and 3) tumor. (**B**) Axial T2 sequence MRI showing totally resection of fourth ventricle (*dotted arrow*) and bilateral CPA (*solid arrow*). (**C**) Postoperative diffusion MRI showing bilateral vasogenic edema in frontal region. (**D**) Postoperative diffusion MRI showing bilateral vasogenic edema in cerebellum.

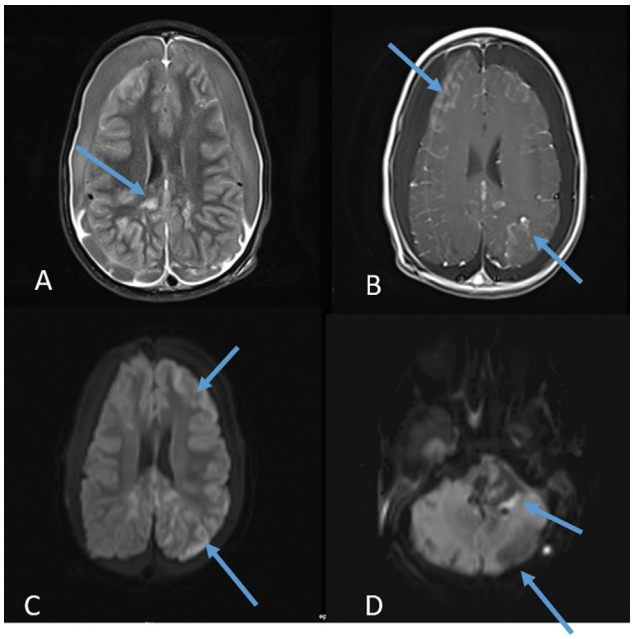

Fig. 2 Postoperative late magnetic resonance imaging (MRI), developing necrotic changes. (**A**) Fluid-attenuated inversion recovery sequence MRI showing cytotoxic edema (*blue arrow*). No periventricular lucency and bilateral subdural hygroma formed, these signs showing intracranial pressure drop. (**B**) T1 sequence MRI with contrast enhancement showing cytotoxic edema in frontal and parietal regions (*blue arrows*). (**C**) Diffusion MRI showing cytotoxic changes in frontal and parietal regions (*blue arrows*). (**D**) Diffusion MRI showing cytotoxic changes in cerebellum (*blue arrows*).

(MRI) revealed bilateral vasogenic edema in the frontal, temporal, deep white matter, and parietooccipital regions and also the cerebellum (►**Fig. 1**). Before this condition, there was not any awareness. Two weeks after the admission MRI, a transformation of vasogenic edema into cytotoxic edema was observed (►**Fig. 2**). There was not any vascular damage during surgery; after the surgery area of our surgery was clear without any symptoms of ischemia related to damage of posterior fossa. The patient is currently in a coma without spasticity, maybe mutism. Two months after the surgery, she opened eyes and performed some movements in her extremities. Afterward, she transferred to the rehabilitation center. Probably patient again had mutism and the same time altered level of consciousness due to PRES.

Discussion

Aim in surgery of ependymoma is the extent of resection and safe surgery to prevent neurological deficit. This type tends to infiltrate adjacent brain, have a higher proliferation rate, and moreover lead to dissemination causing drop metastasis in the central nervous system. As we know, the extent of resection is recognized as the mainly prognostic marker in adults and in children.[12] Therefore, there is no other treatment option for ependymoma. We aimed to remove the entire tumor; therefore, radical surgery was planned.

The pathophysiology of PRES is still unclear. PRES is generally associated with immunosuppressive therapy, eclampsia, hypertension, and kidney disease. Furthermore, PRES after brain and spinal surgery has been described.[2,3,13] In five patients, it developed after supratentorial tumor surgery.[14] Fifteen cases were reported after subarachnoid hemorrhage.[7] Eleven cases were declared secondary to cerebrospinal fluid (CSF) leakage and eleven cases, including this one, following posterior fossa tumor surgery have been reported.[2,3,13,15] Probable mechanisms of PRES related to the difference between CSF pressure and cerebral arterial pressure. If the arterial pressure markedly exceeds the CSF pressure in the posterior circulation, disruption of the blood–brain barrier occurs. The factors leading to this condition are yet unknown.

Various pathogeneses have been described in literature. The two main theories, which attempted to explain PRES, were that malignant hypertension caused disturbances in cerebral autoregulation, hyperperfusion of the brain, endothelial injury, and, consequently, vasogenic edema. PRES is also seen in patients with a normal blood pressure. In case of a normal blood pressure, PRES occurs as a result of endothelial dysfunction owing to systemic toxicity, like chemotherapy in cancer treatment, autoimmune disease, toxemia of pregnancy, infection, and sepsis.[16]

The second theory is cerebral vasoconstriction and hypoperfusion as a result ischemia of the brain and vasogenic edema.[17,18]

In the follow-up period, we noticed on MRI pachymeningeal thickening and enhancement, enlarging subdural space that is compatible with intracranial hypotension. Also, when we look and see those problems mainly in watershed areas. We looked into literature and concluded that in our case developed PRES secondary to intracranial hypotension (after elevated intracranial pressure [ICP], aggressive tumor debulking, and shunt revision which led to severe fall in ICP). We were not aware of this situation before. We wrote this article to increase awareness.

Moreover, theories linked to brain stem manipulation were described, as manipulation surgically rostral ventral lateral medulla (RVLM), raised venous pressure, and the secretion of vasoactive neuropeptides due to Cushing's reflex which a reaction to secondary hydrocephalus.[2,3,13] The RVLM is regarded as a pressor center. Some authors have proposed hypertension as a result of surgical manipulation of tumor and structures of the central nervous system like the ventrolateral medulla.[9,10] Our patient had surgeries in both CPA localizations, especially in the region of the RVLM; moreover, we manipulated this area perioperatively.

Prior to our case report, 12 previous cases of PRES developing after posterior fossa surgery have been reported. We observed that eight of these cases had large (giant)-sized tumors, whereas in four of them there were no data on the size of the tumor. Five of these patients underwent recurrent operations. All of the patients had an elevation of the ICP preoperatively. We believe the main pathogenic factor that the patients were preoperative ICP elevation, and if the tumor was located in the fourth ventricle or had a CPA localization, surgical manipulations of this area, rapid decompression and a sudden change in the ICP may be key factors in the development of PRES. We observed that all of

the patients recorded in literature who developed PRES had at least one of the risk factors.

From the literature review, the general outcome in PRES seems to be a return to the baseline neurological status. In neurosurgical patients, it could be difficult to differentiate between neurologic deficits occurring due to primary lesions, after the surgical procedure, or as a result of the PRES itself. Also, we stated that the clinic and radiological outcome may not be reversible in 10 to 20% of patients, as in the case of our patient. We should remember that PRES in pediatric patients had a 15% mortality rate.[19] In our patient, the vasogenic edema became cytotoxic. This factor showed that not all cases of PRES in patients exhibit a reversible character. If the patient has a severe dysfunction of homeostasis, the ensuing encephalopathy could be irreversible.

Adding to literature, as rare cases of PRES are also important, because the etiology and pathophysiology are poorly understood, and will probably be explained better after an adequate number of cases.

Conclusion

Acute changes in the ICP secondary to radical tumor excision and shunt revision might have contributed to the development of PRES in our patient, who had a recent history of chemotherapy and high-dose of corticosteroids.

We should meticulously manipulate brain stem and its environs, especially in region of the RVLM and the fourth ventricle. Beware of sudden and severe changes in the blood pressure and ICP (especially acute drops) during posterior fossa surgery. Rapid decompression of posterior fossa tumors in the presence preoperative ICP elevation may be key factor in the development of PRES after aggressive posterior fossa surgery.

Ethical Approval

Informed written consent was obtained from the parents of the patient for publication of this case report and any accompanying images.

Authors' Contributions

Orkhan Mammadkhanli and Gokhan Bozkurt were involved in the conception and design; acquisition, analysis, and interpretation of data; drafting; revising; and final approval of the manuscript. Mahmut Ozden contributed to the acquisition, analysis, and interpretation of data.

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Conflict of Interest

None declared.

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