

Sudden Death Due to Medulloblastoma: A Case Report

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Abstract-

Purpose: Medulloblastoma is one of the notorious CNS malignancies for subtle and atypical clinical presentations, causing rapid neurological deterioration and death, especially in pediatric patients. The delay in diagnosis leads to painful remorse, conflicts, and lawsuits for parents and medical staff.

Case Report: We report a 2 year old girl with initial presentation of febrile pyuria. Soon after admission, a generalized clonic-tonic seizure attacked to her and led to an impression of febrile convulsion. However, an unusual postical slowness of pupils to light stimulation propelled a further investigation. A contrast enhanced brain computer tomography (CT) unexpectedly showed a mass occupied the fourth ventricle resulting in obstructive hydrocephalus and compressed adjacent brain stem and cerebellum. The disease rapidly progressed and she died 18 hours after an emergent decompression with extraventricular drainage (EVD) installation. Cytology of cerebrospinal fluid proved medulloblastoma.

Conclusion: This case report highlights the importance of clinical suspicion, such as a trivial but unusual presentation, a lagged pupil response to light stimulation. A brain CT scan should be done to rule out any possibility of an organic lesion. Close monitor is required in order to catch and treat medulloblastoma early. However, once discovered, the cancer has spread.

Key Words: medulloblastoma

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INTRODUCTION

Medulloblastoma is one of the most common CNS malignancies and accounts for approximately 20% to 30% of all intracranial neoplasms in children⁽¹⁾. World standardized incidence rates are 5.5 cases per million children years in boys and 3.4 per million children years in girls⁽²⁾. Peak incidences are at the ages of 3-4 years and 8-9 years⁽³⁾. Symptoms are mainly caused by

increased intracranial pressure (IICP) leading to blockage of the fourth ventricle. Therefore, when the tumor affects older children and adults, they typically become listless, with repeated episodes of vomiting and headache, which may occasionally result in a misdiagnosis of gastrointestinal disease, flu, or migraine. However, initial symptoms of the tumor in extremely young children with unfused sutures may be relatively nonspecific and include intermittent vomiting, gait dis-

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order and an inability to elevate the eyes⁽⁴⁾. Despite aggressive multimodal therapy, including surgery, irradiation, and chemotherapy, the life span of patients with medullablastoma is notoriously short and only for 1 to 5 months before a diagnosis is made.

We present a 2-year-old girl with febrile pyuria and generalized clonic-tonic seizures masquerading as febrile convulsion with suspicious urinary tract infection. Although no typical signs and symptoms of increased intracranial pressure (IICP) were noted, however, an unusual postical slowness of pupils to light stimulation propelled a further investigation. A contrast enhanced brain computer tomography (CT) showed a hyperdense, round mass in the cerebellar vermis with obstructive hydrocephalus. The disease rapidly progressed and she died 18 hours after an emergent decompression with extra-ventricular drainage (EVD) installation. Cytology of cerebrospinal fluid proved medulloblastoma. In this case, the intermittent headache and asymmetrical lagged pupil response to light stimulation may be trivial findings, but both of them are unusual presentation in a patient with seizure attack. A brain CT scan should be done if any occupying lesion is suspected.

CASE REPORT

A 2-year-old healthy girl was presented to an emergency department of a medical center for intermittent fever and lethargy for 3 days. She had complained of intermittent pain over her frontal area several times in a day with duration a couple of minutes for 1 week. She could play and eat well when the pain subsided. On physical examination, her consciousness was alert with Glasgow Coma Scales (GCS) E3V5M6. She was irritable and febrile. Her blood pressure was 112/80 mmHg, pulse rate 114 beats/min, respiration rate 20 breaths/min and body temperature 37.8°C. Her muscle power was all full; isocoria, 2.5 mm with normal light reflex, OU; Barbinski's sign absent; normal deep tendon reflex; no neck stiffness, Kerning and Brudzinski sign were both negative. Her breathing sound and bowel sound were good. No any cutaneous lesion was noted. The laborato-

ry tests revealed white blood cells 14,000/mm³, hemoglobin 13.9 g/dl, platelets 407,000/mm³. Urine analysis showed as white cell 10-20/high power field, RBC 0-2/high power field, leucoesterase 2+, nitrite -. C-reactive protein was 0.14 mg/dl. Levels of serum glucose, creatinine, sodium, and potassium were within the normal limits. Chest radiography showed normal lung marking without active lesion. Because of febrile pyuria, she was admitted under the suspicion of urinary tract infection. On admission, her consciousness was clear with good orientation. However, soon after admission, an episode of generalized clonic-tonic seizures attacked to her and then she became drowsy and lost her consciousness. Her blood pressure was 128/88 mmHg, pulse rate 120 beats/min, respiration rate 26 breaths/min and body temperature 38.5°C. A detailed physical examination showed that deep tendon reflexes were symmetrically weak. Her muscle tone was intact. No obvious pathological reflex was observed, except a delayed direct papillary light reflex of her left eye when compared to her right eye. For her fever and this trivial finding, CNS tumor or infection was suspected. A computerized

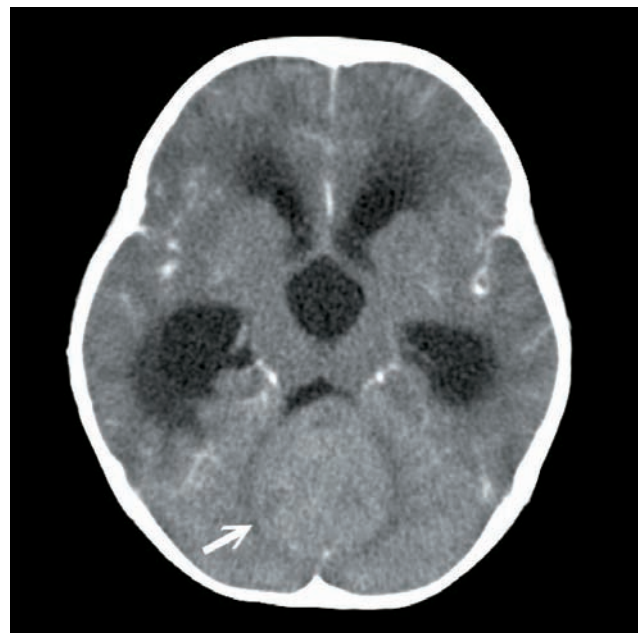


Figure 1. Contrast enhanced brain computer tomography. A minimal enhanced mass (arrow) occupies the fourth ventricle and leads to obstructive hydrocephalus and the compression of brain stem and cerebellum.

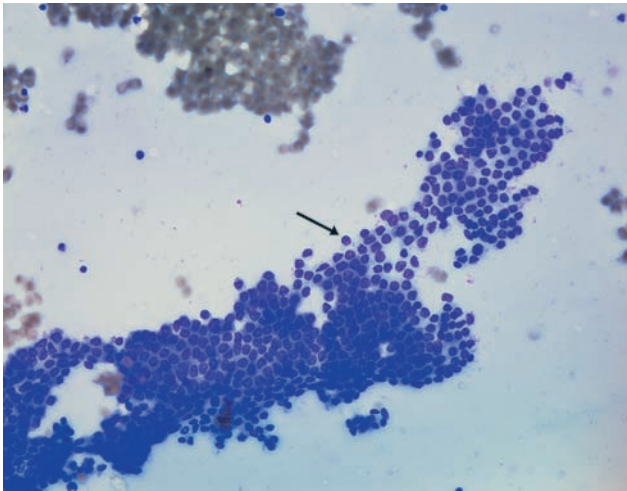


Figure 2. Air drying smear of cerebrospinal fluid consists of sheets of monomorphic cells (arrow) with indistinct borders, hyperchromatic nuclei and a high nuclear cytoplasmic ratio, compatible with classic medulloblastoma.

tomography scan showed a hyperdense, round mass with tiny calcified spots which occupied the fourth ventricle resultant obstructive hydrocephalus with subependymal CSF absorption and compression of adjacent brain stem and cerebellum (Figure 1). An emergent extraventricular drainage was performed to relieve her high intracranial pressure. She did not show any signs of recovery and died soon after admission 18 hours later. The cytology analysis of cerebrospinal fluid proved medulloblastoma (Figure 2).

DISCUSSION

When a patient with a brain tumor presents atypical and subtle symptoms, such as headache and vomiting in the emergent room, it may inevitably become a claim of negligence against the doctor if sudden death occurs. Medulloblastoma is such a case. Early in the course of illness, symptoms are always non-specific. Later all presentations may become much more typical, such as headaches related to increase intracranial pressure, primarily occurring on awakening, accompanying symptoms including vomiting, and some degree of truncal unsteadiness. Other clinical manifestations include head tilt, stiff neck, and body weight loss. Except for an inter-

mittent headache, none of these symptoms were not prominent in this girl. Her fever and pyuria normally and naturally led to a suspicious urinary tract infection. However, there was no bacteria growth in blood, urine, and cerebrospinal fluid samples in this case. Therefore, we speculated that her fever might not be caused by infection but by tumor progression.

It was nearly impossible for any clinician to draw her initial clinical presentations, including pyuria, fever, a generalized clonic-tonic seizure to a brain tumor. Retrospective review this case, we think that the occurrence of tonic-clonic seizures in this girl was a critical point in the course of this illness. Theoretically, tonic-clonic seizures can be a sign of CNS occupying lesion(s) or febrile convulsion when the patient is suffering from a fever, but postictal presentations may elicit diagnostic clues. For instance, several ophthalmological signs, such as nystagmus and 6th cranial nerve palsies, and papilledema are reported in patients with medulloblastoma⁽⁵⁾. In fact, all these signs did not appear in this case. Comparing to her right eye, the asymmetrical slowness of direct papillary light reflex over her left eye was relatively subtle. We did not know whether this finding is due to her innateness or the postictal changes or the progress of uncus herniation. The electrophysiological tests, such as electroencephalography (EEG), may record seismological data, like epileptiform discharges and differentiate these conditions. However, her deterioration at a rapid pace and expiration within several hours after admission caused no plenty of time for this test.

A huge mass in the cerebellum, obstructing the outlet of the IV ventricle was shown in her brain CT (Fig. 1). Differential diagnoses of these imaging findings include medulloblastoma, pilocytic astrocytoma, ependymoma and atypical teratoid tumor^(6,7). The incidence of pilocytic astrocytoma is about 30-40% and the common locations of this tumor are the cerebellar vermis or hemispheres. Imaging studies demonstrate the structure of this tumor is cystic with an enhancing mural nodule on CT and the solid component is highly vascular with a deficient blood-brain barrier and therefore enhances avidly and homogeneously⁽⁵⁾. Ependymomas account for about 10% of pediatric posterior fossa

tumors with well-defined margins and originate from the floor or the roof of the fourth ventricle. Being invasive and malicious, ependymomas tend to extend into the cerebellopontine angle and extrude through the foramina of Luschka and Magendie, causing severe obstructive hydrocephalus and dissemination⁽⁵⁾. Medulloblastoma is the most common infratentorial malignant tumor for patients under 15 years of age, accounting for 15% to 25% of pediatric brain tumors⁽⁷⁻⁹⁾. The typical appearance of the childhood medulloblastoma on CT is a hyperdense midline vermian mass abutting the roof of the fourth ventricle, with perilesional edema, variable patchy enhancement and hydrocephalus⁽⁵⁾. Only a careful pathology analysis can achieve a corrective diagnosis in spite of similarities and differences in the imaging scan among these tumors. However, once discovered, the tumor has spread.

Medulloblastoma mostly locates in the 4th ventricle and tends to extrude into neighbor cerebellar tissue for its aggressive behavior and invasive nature. It is notorious for having a shorter onset of symptoms, typically less than 1 month when compared to other cerebellar tumors⁽⁵⁾. Although surgery may improve survival in the children with medulloblastoma if the tumor is resectable, however, there were approximately 15% of cases showing brain stem infiltration and CSF dissemination when a diagnosis is made⁽⁹⁾. To the worse, when patients are in a life-threatening condition, IICP related signs and symptoms, such as progressive hypertension, bradycardia and diminished respiratory effort may or may not appear and all these lethal manifestations become prominent as compensatory mechanisms collapse⁽¹⁰⁾. Only one third of cases demonstrate typical presentations⁽¹¹⁾. In this case, her young age (less than 3 years of age), huge tumor size (more than 1.5 cm²), and the tumor seeding are reflecting poor prognosis⁽⁹⁾.

Even with adequate resection, 20% to 30% of children with medulloblastoma will experience tumor progression within 2 years, including sudden death⁽⁹⁾. Sudden death due to clinically undiagnosed medulloblastoma in infancy and childhood is underestimated, because infants and children may present normal or minimal symptoms and signs⁽¹²⁾, and only an autopsy can

prove it⁽¹³⁾. In this case, the mass in the fourth ventricle obstructed subependymal CSF absorption and compressed adjacent brain stem and cerebellum. Such a huge lesion may be the cause of her rapid deterioration and death. Moreover, CSF sample for pathology analysis proved tumor seeding, which supported that the concept that "once discovered, the medulloblastoma has spread".

In conclusion, clinical presentations of a child with medulloblastoma are always non-specific, even mimicking other diseases, such as gastrointestinal disease, flu, or migraine. If a child less than 3-year-old presents with pyuria and consequent occurrence of tonic-clonic seizures, all these might set up the first-line clinicians to mistakenly diagnose the child as having febrile convulsion with suspicious urinary tract infection. Brain imaging, such as CT or MRI, can identify latent organic-occupying lesion if any unusual presentations, such as nystagmus, 6th cranial nerve palsies, papilledema, and a delay response to light stimulation are noted. Misdiagnosis can be potentially harmful and lead to a tragedy and lawsuits.

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