Case Report

A case of germinoma located in the fornix inducing transsynaptic atrophy of the Papez circuit

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A B S T R A C T

Germinoma is a rare CNS germ cell tumor preferentially affecting children and young adults. Intracranial germinomas arise typically in the neurohypophysis and pineal region and occasionally in the basal ganglia and thalamus. Germinomas in the basal ganglia and thalamus are characterized by the ipsilateral cerebral and brainstem hemiatrophy with slowly progressive neurological deficits, which is due to tumor infiltration into the thalamocortical and corticospinal tract and induction of anterograde and retrograde Wallerian degeneration. We report an 11-year-old boy with a mass located in the fornix incidentally discovered on the first work-up of his minor head injury. Imaging findings revealed the ipsilateral atrophy of the mammillary body and the fornix. Stereotactic brain biopsy was performed and the final diagnosis was germinoma. The ipsilateral atrophy of the mammillary body and the fornix implied the transsynaptic degeneration via the Papez circuit. We discuss the unique nature of germinomas and underlying pathological mechanisms.

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I n t r o d u c t i o n

Germinomas are primary CNS germ cell tumors that typically arise in the neurohypophysis and pineal region, although they may develop in atypical locations such as the basal ganglia and thalamus. Germinomas in the basal ganglia and thalamus represent 5%-10% of all intracranial germinomas [1] and cause ipsilateral cerebral and brainstem hemiatrophy due to the anterograde and retrograde Wallerian degeneration induced by tumor infiltration into the thalamocortical and corticospinal tract [2,3].

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Here we present a case of germinoma arising from the fornix. MR imaging findings revealed the ipsilateral atrophy of the fornix and the mammillary body, which is suggestive of transsynaptic degeneration via the Papez circuit. The tumor was small and the atrophy was insidiously progressed with no major symptoms.

Case report

An 11-year-old boy visited a nearby hospital with a transient headache after he had got minor head injury during skateboarding. Computed tomography (CT) of the head was performed, and a mass 1.6cm in diameter was incidentally detected in the anterior horn of the left lateral ventricle (Fig. 1). The patient was referred to our hospital for further examination and treatment. The patient showed no symptoms or neurophysiological abnormalities on admission. Blood and cerebrospinal fluid tests, including alpha-fetoprotein (AFP) and human chorionic gonadotropin beta (hCG-β) values, were normal. The mass showed iso-signal intensity compared to the cortex on T1- and T2-weighted MR imaging (Fig. 2A & B), high signal intensity on diffusion-weighted imaging at b = 1000 s mm⁻² (Fig. 2C), and low ADC values (Fig. 2D). Gadolinium-based contrast enhanced T1-weighted imaging (Fig. 2E) revealed slight enhancement. Coronal MR images (Fig. 2F-L) showed that the mass was arising from the left fornix and the ipsilateral fornix and mammillary body were smaller in size. No abnormalities were observed in the neurohypophysis or pineal gland. Intraventricular endoscopy revealed a mass arising from the left fornix, which was soft and easy to bleeding (Fig. 3). Stereotactic brain biopsy was performed successively. Histopathological examination revealed the tumor was composed of round to polygonal cells with large nuclei and tumor-infiltrating lymphocytes (Fig. 4A & B). Immunohistochemical examination demonstrated PLAP(+), c-kit(+), OCT3/4(+), SALL(+), AFP(+), ß-HCG(+), CD30(-), CD30L(-), CD99(+), p53 (weakly positive) and Ki-67 (60%-70%). Based on these results, the patient was diagnosed with germinoma. He received chemoradiotherapy and achieved clinical remission. Six months later, follow-up MR imaging showed no recurrence and no significant change in atrophy.

Discussion

Germinoma is the most common subtype of CNS germ cell tumors and estimated in the annual incidence rate of 0.12 cases per 100,000 population aged under 15 in Japan [4]. Germinomas are thought to originate from primordial germ cells entrapped during embryonic migration and predominantly arise from the midline structures such as the pineal gland and neurohypophysis. The basal ganglia is the third most common location of intracranial germinomas [4,5] and germinomas arising in the basal ganglia and thalamus can infiltrate the thalamocortical and corticospinal tract and induce ipsilateral cerebral and/or brainstem hemiatrophy by Wallerian degeneration.

Histologically, germinomas consist of 2 cell populations: large and undifferentiated cells that resemble primordial germinal elements and tumor-infiltrating lymphocytes. Tumor cells in germinoma have high levels of Ki-67, a marker of cell proliferation, and have a high proliferative capacity. However, tumor growth is suppressed by tumor-infiltrating lymphocytes. Tumor-infiltrating lymphocytes are characteristic of germinoma and the initial diagnosis can therefore be mistaken for inflammatory diseases [6]. A recent study showed that the germinomas with a longer clinical course are more strongly growth-suppressed by lymphocytes and likely to be smaller in size [7]. We consider that the immune response between the tumor cells and tumor-infiltrating lymphocytes in the neural tract can lead to insidious axonal damage and transsynaptic atrophy.

The Papez circuit is a fundamental system associated with memory and emotion. Sensory information from the cerebral cortices converges in the hippocampus, and the output is transferred to the mammillary body via the fornix. This information passes through the projection fibers to the anterior nucleus of the thalamus and around the cingulate gyrus. The atrophy of fornix and mammillary body secondary to transsynaptic degeneration can occur in various etiologies: Wernicke encephalopathy, hippocampal sclerosis, thalamic infarction, herpes simplex encephalitis, and surgical injury. Glioma and lymphoma can involve in the Papez circuit [8]; however, the speed of the tumor growth will overwhelm the secondary degeneration induced by the tumor infiltration into the circuit with some neurological symptoms and signs. In contrast, germinomas are more likely to cause damage of

Fig. 1 – CT imaging. An axial image of plain CT scan shows a mass (white arrow) 1.6 cm in diameter with high-density compared with the brain parenchyma in the anterior horn of the left lateral ventricle.
Fig. 2 - MR imaging. Axial MR images (A-E) reveal that the mass (white arrow) shows an iso-signal intensity compared to the cortex on T1- and T2-weighted images (A, B), high signal intensity on the diffusion-weighted image at b = 1000 s mm⁻² (C), and low ADC values (D). Gadolinium-based contrast enhanced T1-weighted image (E) shows a faint enhancement. T2-weighted coronal images (F-K) show the tumor (T) arising from the left fornix and the atrophy of the ipsilateral fornix (F) and the mammillary body (M). Coronal image of high resolution CISS MR acquisition (L) presents more clearly.
Fig. 2 – Continued
neuronal circuit in the same location because of its localized and long-lasting nature.

In conclusion, we report a case of germinoma located in the fornix with ipsilateral atrophy of the fornix and mammillary body, suggestive of transsynaptic degeneration via Papez circuit. The nature of germinoma’s insidious infiltration into the surrounding neuronal tract can cause transsynaptic degeneration and make it distinctive and challenging of its diagnosis.

**Patient consent**

Written informed consent was obtained from the patient.

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