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Co-Existence of Pineal Germinoma and Quasi-Moyamoya Disease: A Case Report and Review of Literature

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Abstract

Background: The coincidence of Moyamoya along with pineal germinoma is not reported in the literature.

Case description: We report an unusual presentation of a 19-year-old young man diagnosed with pineal gland germinoma and Moyamoya syndrome. He presented with Parinaud's syndrome, with radiological investigations (CT and MRI scans) showing pineal gland enhancing lesion causing obstructive hydrocephalus. Endoscopic third ventriculostomy along with lesion debulking yielded a diagnosis of pineal germinoma. Postoperatively he developed bilateral middle cerebral artery territory infarcts and became aphasic with left hemiparesis. Computed Tomography (CT) angiography revealed bilateral Moyamoya vasculopathy. Two months post-operatively he developed spontaneous left frontal lobe hemorrhage with intraventricular extension; emergent external ventricular drain inserted. The patient was discharged in a vegetative state.

Conclusion: Management of both these conditions pose a therapeutic challenge as chemo-radiation therapy for germinoma holds a risk of potential worsening of neurologic deficits related to Moyamoya.

Keywords: Moyamoya disease • Pineal gland lesion • Parinaud's syndrome • Stroke

Introduction

Moyamoya Disease (MMD) is a condition characterized by an abnormal progressive occlusion of the intracranial vessels. The term that means 'puff of smoke' denotes the characteristic angiographic findings of a multitude of tiny basal collateral vessels that are formed to sustain cerebral perfusion in response to stenosis of the supraclinoid part of the Internal Carotid Artery (ICA), as well as anterior and middle cerebral arteries. The etiology is probably polygenic and multifactorial in most patients [1-6]. Ring finger protein 213 (RNF 213) genes, located in chromosome 17q25.3, are identified as the first susceptibility gene implicated in the pathogenesis of MMD [7]. MMD follows a chronic and progressive course, with varied clinical presentation and unknown prognostic factors. The disease process usually involves bilateral hemispheres although unilateral (probable) Moyamoya has been described. Clinical presentation can be a variant of four types: "ischemic, hemorrhagic, epileptic, and other." Quasi-Moyamoya disease is a presence of Moyamoya vasculopathy along with underlying disease [5]. Atherosclerosis has found out to be the most commonly linked disease (29%), followed by Down syndrome (15.1%), von Recklinghausen disease (14%), and brain tumor (7.5%) [6]. We discuss an unusual presentation of bilateral Moyamoya disease with pineal gland germinoma, which to the best of our knowledge has not been reported previously in the literature.

Case Report

A 19-years old male patient who presented to the neurosurgery clinic with a three-week history of progressively worsening headache associated with vomiting, particularly in the morning, and walking difficulty. His prior medical and family history was unremarkable. On examination, he was awake and alert, had bilateral papilledema, convergence retraction nystagmus, and upward gaze restriction, clinical signs of Parinaud's syndrome. His gait was ataxic and there were no further neurological abnormalities. There were no signs of neurofibromatosis. His MRI brain contrast showed enhancing pineal gland lesion causing proximal obstructive hydrocephalus (Figure 1); and no evidence of prior hemorrhage or ischemic changes. MRI spinal axis showed no evidence of drop metastases. The clinical impression was of pineal germ cell neoplasm. Serum tumor markers (Alpha-fetoprotein and Beta human chorionic gonadotropin) were within normal limits. The patient underwent endoscopic third ventriculostomy and debulking of pineal lesion using a rigid endoscope through a single right frontal burr hole craniotomy. Intra-operative frozen section and final histopathological diagnosis confirmed it to be a pineal gland germinoma. Tumor cells showed positivity for SALL4 and OCT-3/4 immuno-histochemical stains. The patient had an uneventful postoperative recovery and was discharged after the removal of the external ventricular drain.

The patient presented a week later in the emergency department with sudden onset left body weakness. On examination, he had left eye abducens nerve palsy and left upper motor neuron facial palsy along with left hemiparesis. MRI brain showed acute and subacute infarcts in the right periventricular region, in the right centrum semi-ovale, and residual pineal lesion. He was started on aspirin and hyperosmolar therapy after neurology review. CT angiogram revealed narrowing of supraclinoid segments of the bilateral internal carotid artery and bilateral proximal M1 segments of the Middle Cerebral Artery (MCA) and A1 segments of Anterior Cerebral Artery (ACA) along with florid basal collateral vessels formation, overall imaging findings confirmed the presence of bilateral MMD. He continued to get worse over the next few days and was managed on the lines of stroke-related raised Intracranial Pressure (ICP). Steroids were started considering angiopathy associated inflammatory arteritis and nimodipine was started to reduce cerebral vasospasm. The repeat CT scans continued to show worsening edema and bilateral infarcts in the posterior division of MCA. Intravenous hydration was started and an autoimmune workup was sent. A detailed workup of young stroke was carried out including Antinuclear Antibody (ANA), Anti-cardiolipin Igm/ IgG, and homocysteine levels were negative.

The patient was discharged when his imaging showed resolution of raised Intracranial Pressure (ICP). At this stage, he was still aphasic but obeyed one-step commands had begun to move all his limbs although movements were still weak, and were worse on the left side. It was decided to start him on

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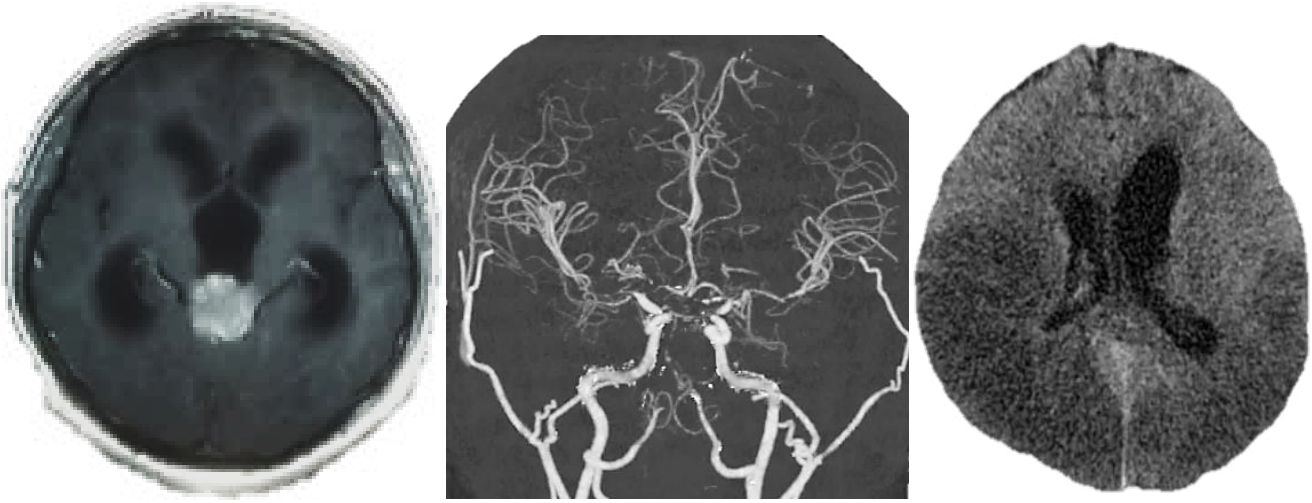
chemotherapy as per CARE protocol followed by focal radiation. He underwent two cycles of chemotherapy with carboplatin and etoposide, the first and second month after surgery. While he showed signs of further improvement in his neurological status as an outpatient, one and a half weeks after his second chemotherapy, he once again presented to the emergency department with left frontal Intracerebral Hemorrhage (ICH) (Figure 2). His platelets at admission were found to be low (50×10^9/L), possibly as a result of his chemotherapy. After platelet transfusion and hemodynamic stabilization, the right frontal external ventricular drain was passed to relieve the hydrocephalus, and tracheostomy was done simultaneously. Despite a long hospital stay, his neurological status remained poor, and he was discharged home with a tracheostomy and PEG tube. At one month follow-up, he remained in a vegetative state and further oncology therapy was discontinued.

Discussion

Quasi and definitive Moyamoya disease has no significant clinical management difference in both types of vasculopathy; the term "Moyamoya phenomenon", is a better term to convey universal meaning [3]. Brain tumor and MMD could be interlinked by any one of these mechanisms: direct compression of the carotid bifurcation by the growing basal tumor, adverse effects of radiation therapy on the tumor, association with neurocutaneous syndrome, or incidental association [8-14]. Most Moyamoya cases in the context of brain tumors are reported post-radiation, with high incidence noted in tumors adjacent to the circle of Willis like optic glioma and craniopharyngioma [15]. In our case, as no family history or clinical features of neurocutaneous syndrome were present, and no direct mass effect of the tumor on the cerebral vessels was noted, this case represents an incidental combination of two separate entities.

Germ cell tumors and Moyamoya phenomenon

There are only a few reported cases of patients with germ cell tumors and a co-existing Moyamoya phenomenon. Shibata et al. reported a case of a 15-year-old girl with suprasellar germinoma with incidental findings of MMD. She had successful surgical resection followed by chemo and radiation therapy [13]. Germ cell tumors account for 71.2% (Japan) and 80% (Korea) of all pineal region tumors; similar incidence of MMD is also noted in both Japanese and Korean populations [10]. Chiewvit et al. reported a case of 8 years old boy with biopsy-proven pineal germinoma who underwent cranial irradiation and presented 5 years later with left MCA territory infarct. CT angiography showed complete occlusion of supraclinoid part of the left ICA, suggestive of Moyamoya syndrome. Aoki et al. reports a case of 10-years-old boy who had received radiation for suprasellar germinoma, on follow-up MR angiography



(a) **(b)** **(c)**

Figure 1. (a) Preoperative MRI brain axial image showing contrast-enhancing pineal lesion with obstructive hydrocephalus **(b)** CT angiogram brain showing narrowing of bilateral distal ICA and bilateral M1 and A1 segments with multiple collateral basal lenticulostriate vessels, suggestive of 'moyamoya phenomenon' **(c)** CT brain plain axial section repeated on postoperative day 18 showing established bilateral MCA territory infarcts.

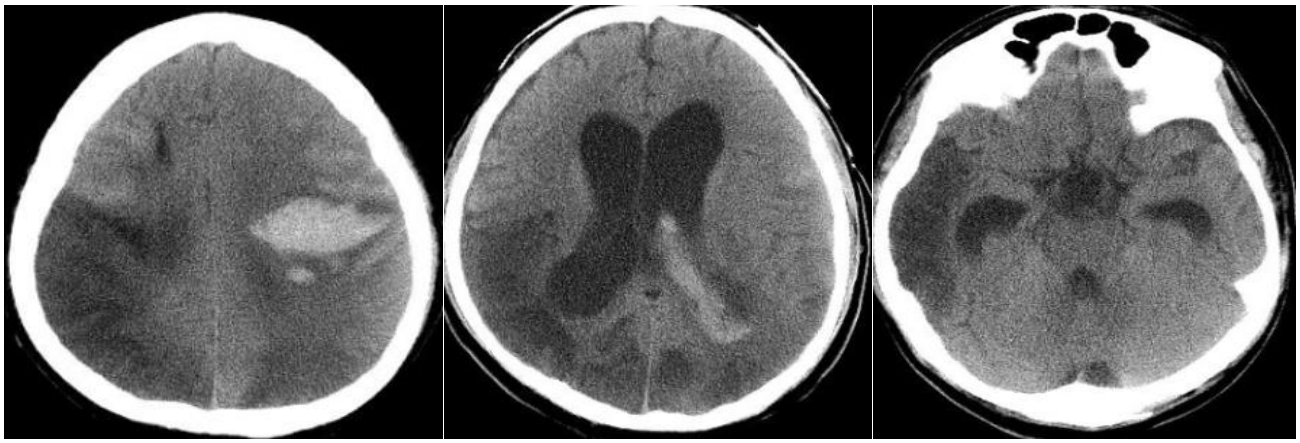


Figure 2. (a) Axial CT scan of brain showing interval development of a large intraparenchymal hematoma in the left frontal lobe along centrum semiovale and corona radiata, previous findings of bilateral frontoparietal lobe infarcts redemonstrated. **(b)** Same scan showing intraventricular dissection of hemorrhage within the occipital horn of the left lateral ventricle. **(c)** Enlargement of bilateral temporal horns of lateral ventricles signifying hydrocephalus.

5 years later, he had developed bilateral carotid occlusion with Moyamoya-like collateral vessels. Wang et al. noted a significant association between increasing the radiation dose and a shorter interval in the development of radiation-induced vasculopathy in pediatric brain tumor patients. In our patient, bilateral MCA territorial infarcts developed 15 days after surgery before radiation therapy could be started, which contrasts with the cases reported previously. The management strategy of these two distinct pathologies remains undetermined. As germinoma is a malignant but highly curable tumor with chemo and radiation therapy need to be administered despite the risks. Moyamoya syndrome is associated with dysfunctional cerebral autoregulation. Perioperative blood pressure control is vital during brain tumor surgery as hypertension is a common adaptive mechanism to maintain cerebral perfusion and countering raised ICP and poorer autoregulation during surgery among patients with bilateral vasculopathy is significantly associated with postoperative transient ischemic attack or strokes.

In our case, it was unusual for the patient to present with acute infarcts, and later an acute intracerebral hemorrhage despite having a chronic pathology that was stable for so many years. There can be several hypothetical explanations for it. We assume that the patient had a chronic raised ICP due to the pineal gland tumor obstructing his CSF flow and perhaps it was the sudden change in CSF dynamics after the ETV that in some way caused his Moyamoya disease to become symptomatic. Another reason could be the perioperative fluid balance as the patient received peri-operative mannitol, which coupled with sub-arachnoid blood from the surgery, could have caused vasospasm in the abnormal vessels. It could be speculated that the inflammatory response of germinoma to adjacent vessels might have worsened the Moyamoya angiopathy with subsequent infarct formation. The patient's second presentation with ICH can be explained based on chemotherapy-induced endothelial toxic effects and bone marrow suppression that caused thrombocytopenia. In this context, early initiation of chemotherapy proved to have deleterious consequences for the patient.

Conclusion

To our knowledge, this is the first reported case of the co-existence of pineal gland germinoma and the Moyamoya phenomenon in the absence of radiation therapy. For effective management of these conditions and to prevent complications, awareness regarding preoperative detection, clinical course of both conditions with benefits and adverse effects of each therapy is recommended.

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