Case Report

Cerebral venous sinus thrombosis with venous hemorrhagic infarct in a patient with high-grade glioma of the left thalamus

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ABSTRACT

Cerebral venous sinus thrombosis (CVST) is an uncommon type of venous thromboembolism whose diagnosis is often difficult due to its vague and non-specific clinical findings. Sometimes, the diagnosis is delayed as the symptoms were considered to be attributable to the underlying etiology, especially in patients with brain tumors such as high-grade glioma (HGG). We described the case of a 60-year-old male patient who presented with headache, generalized seizures, and right hemiparesis soon after receiving brain radiation and temozolomide therapy for HGG of the left thalamus. Initially, his symptoms were considered to be due to his underlying tumor but the subsequent imaging revealed left transverse, left sigmoid, and superior sagittal sinus thrombosis with venous hemorrhagic infarct of the left occipitoparietal lobe. The patient was started on anticoagulant therapy and symptoms resolved completely within a month. Clinicians should always consider CVST in the differential diagnosis of non-specific neurological symptoms, especially in patients with underlying brain tumors.

Key words: Cerebral venous sinus thrombosis, High-grade glioma, Venous infarct, Thalamus

The patients with high-grade glioma (HGG) carry a high risk of venous thromboembolism (VTE) [1-3]. Cerebral venous sinus thrombosis (CVST) is an uncommon type of VTE whose diagnosis is often difficult due to its vague and non-specific clinical findings [1,4,5]. Sometimes, the diagnosis is delayed as the symptoms were considered to be attributable to the underlying etiology, especially in patients with HGG [5,6]. This case report highlights the case of a 60-year-old patient whose diagnosis of CVST was delayed as the symptoms were thought to be of the underlying brain tumor.

CASE REPORT

A 60-year-old male, with no medical history, was diagnosed with HGG of the left thalamus for which he received definitive radiotherapy (60 Gy/30#) and concurrent chemotherapy with temozolomide and tolerated it well. Two days after receiving the last dose of chemoradiation, the patient developed a severe headache and two episodes of generalized seizures. His symptoms were thought to be due to his tumor and were admitted for supportive care. After 2 days, the patient developed right-sided hemiparesis with altered sensorium.

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On examination, the patient's vitals were stable.

The patient was taken for magnetic resonance imaging which revealed T2 and fluid-attenuated inversion recovery hyperintensities in the superior sagittal sinus, left transverse, and sigmoid sinuses with loss of flow void. Magnetic resonance venogram demonstrated a lack of flow in the left transverse and sigmoid sinus (Fig. 1). Large altered signal intensity was seen in the left parieto-occipital lobe associated with gyral edema and bleed blooming on gradient recalled echo and restricted diffusion on diffusion-weighted imaging. The previous left thalamic glioma with mild edema and mass effect was also noted (Fig. 2). A diagnosis of CVST with venous hemorrhagic infarct was made.

Tests for clotting abnormalities were done before anticoagulant therapy. Plasma D-dimer was elevated to 2741.90 ng/mL (normal range of 0–500). Protein C, S, antithrombin III, and fibrinogen levels were normal. The patient was started on dose-adjusted low-molecular-weight heparin as per the patient's weight and neurorehabilitation was started.

Symptoms resolved completely within a month. Subsequent computed tomography scan showed residual thrombus which is stable and the hemorrhagic infarct was dissolved. The patient was discharged with residual right hemiparesis and oral anticoagulants. The patient's informed consent was obtained for writing this report.

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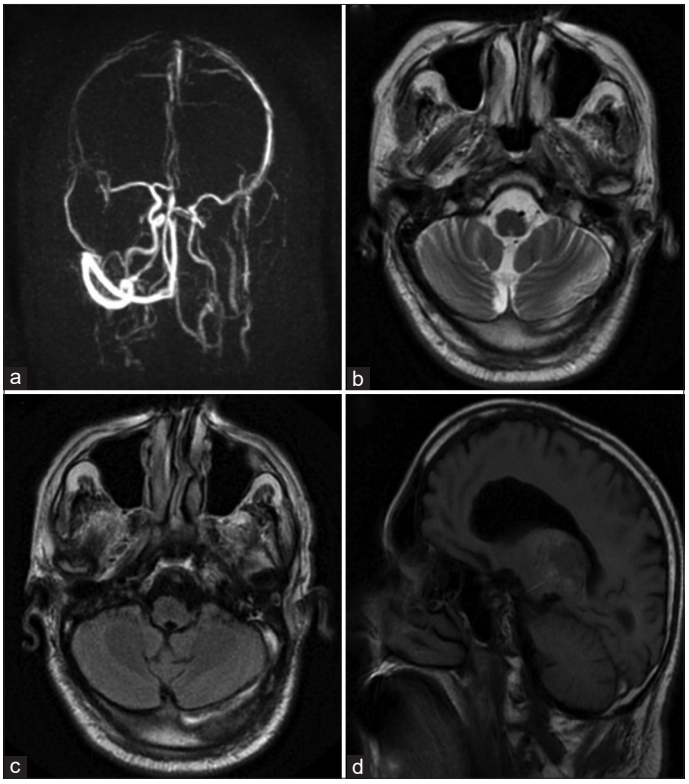

Figure 1: Magnetic resonance imaging demonstrating (a) filling defect of the left transverse and sigmoid sinus; (b) absence of flow void of the left transverse and sigmoid sinus on axial T2, (c) axial fluid-attenuated inversion recovery (FLAIR), and (d) of superior sagittal sinus on sag FLAIR sequence

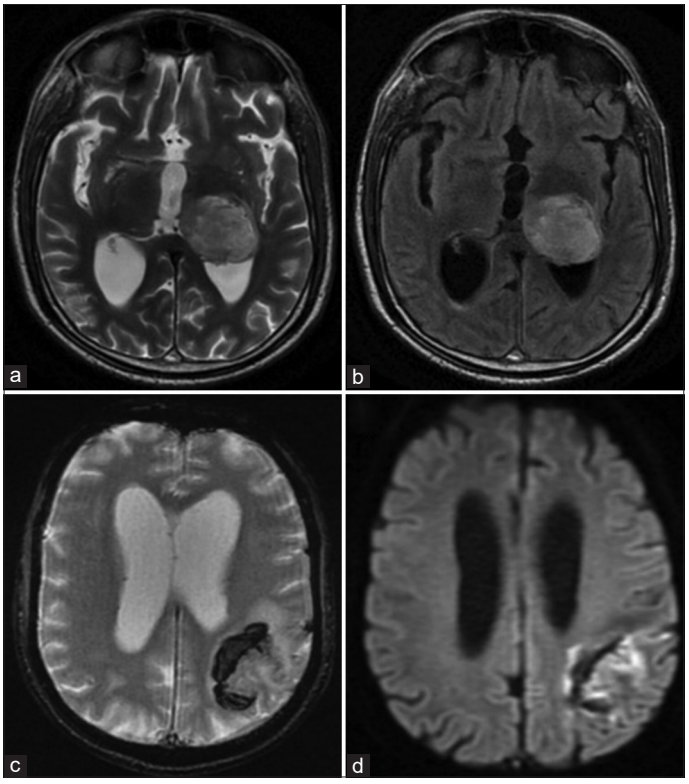

Figure 2: Magnetic resonance imaging demonstrating (a) well-defined mass with mixed intensity on T2 and (b) hyperintense on fluid-attenuated inversion recovery; (c) altered signal intensity in the left parieto-occipital lobe with bleed blooming on gradient recalled echo and (d) restricted diffusion on diffusion-weighted imaging suggestive of hemorrhagic venous infarct

DISCUSSION

CVST is an uncommon type of VTE [1-4]. The incidence of CVST was about 0.3–4% in cancer patients, with cancer increasing risk for CVST roughly 5-fold [5,7]. Extracranial VTE events such as deep venous thrombosis and pulmonary embolism have been widely reported in HGG; however, the incidence of CVST in HGG patients is not well established in the literature [4,5]. According to a recent study, the incidence of CVST in glioblastoma multiforme patients was reported to be 7.4% [3].

The pathogenesis of CVST is complex and is not well-defined in cancer patients. CVST can be a direct complication of tumor infiltration or compression on a sinus where the pathogenesis is prolonged and the occlusion may be asymptomatic [8]. When seen perioperatively, it is more commonly a direct consequence of surgical manipulation resulting in an acute presentation [8].

CVST results in venous hypertension and the resultant cerebral edema can cause a range of symptoms such as nausea, vomiting, headache, seizures, and focal neurologic deficits [4,5,9]. These symptoms are highly non-specific and are usually attributed to the underlying brain tumor; this is the reason why many reports estimated an approximate 7-day delay between the onset of symptoms and the diagnosis [9]. CVST can potentially lead to serious complications. About 50% of patients with CVST develop infarction and/or hemorrhage [9]. The underlying venous hypertension was thought to be the main driver causing reduced effective drainage of affected brain tissue resulting in venous congestion with subsequent oxygen debt and eventual infarction. Furthermore, increased venous pressure can lead to rupture of venules/capillaries resulting in hemorrhage [10]. These complications have major implications for patient morbidity and mortality. Considering the remote location of the tumor from the CVST site and no surgical history, these two etiological factors were not relevant to our case.

When tumor compression or surgical manipulation is absent, cancer-related prothrombotic states are thought to be responsible for the development of CSVT. Elevated plasma D-dimer levels, inflammatory cytokines, as well as the downregulation of the thrombomodulin and the protein C system were a few markers of hypercoagulable state of cancer [1,5]. Plasma D-dimer levels were elevated in our patient, thus hypercoagulable state might have contributed to the occurrence of CVST.

Treatment of HGG also influences the risk of thrombosis [3,5,10]. Focal brain radiation with concurrent chemotherapy with temozolomide is the standard treatment of HGG. In general, chemotherapy was found to be an independent risk factor for extracranial thrombosis in HGG [1,4,6,10]. No such cases have reported the occurrence of CVST directly attributable to temozolomide. However, there is one study reporting CVST in a patient with a brain tumor treated with temozolomide, focal brain radiotherapy plus bevacizumab where the possible risk of thrombosis was attributed to the anti-angiogenic agent [3]. Our patient did not receive bevacizumab therapy.

Depending on the field and dosage, radiotherapy may also increase the risk of thrombosis, although a clear association

has not been shown [4]. The risk of thrombosis attributable to radiotherapy, especially in HGG, is unclear. This could likely be due to the absence of an untreated control group as most of the patients with HGG receive radiotherapy [2]. The other most notable causes of CVST such as puerperium, hormone therapy, genetic thrombophilia, head trauma, and intracranial infections were not found in our patient [5,6]. Although our patient developed CVST soon after receiving the complete chemoradiotherapy, its possible etiological role is highly unlikely as there are no such cases reported so far. Considering the elevated levels of D-dimer, the occurrence of CVST in our patient was thought to be due to a hypercoagulable state secondary to HGG.

CONCLUSION

Clinicians should not assume the neurological symptoms in patients with HGG to be attributable to the underlying tumor and must always consider CVST in the differential diagnosis. With timely diagnosis and treatment, it is possible to achieve an excellent outcome for most patients with CVST.

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