CASE REPORT

Papilloedema and Increased Intracranial Pressure as a Result of Unilateral Jugular Vein Thrombosis

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ABSTRACT

Intracranial hypertension and papilloedema are known to develop secondary to cerebral sinus or bilateral jugular vein thrombosis. However, in rare cases, unilateral jugular vein thrombosis may lead to increased intracranial pressure and papilloedema with resultant headache and vision changes. We describe a 45-year-old patient with squamous cell carcinoma of the larynx that developed right jugular vein thrombosis after chemoradiation therapy with cetuximab. This was later complicated by intracranial hypertension and papilloedema. The normal cerebral venous drainage, the potential role of chemoradiation therapy on the aetiology of jugular vein thrombosis, and the mechanism of increased intracranial pressure secondary to unilateral jugular vein occlusion are discussed.

Keywords: Headache, idiopathic intracranial hypertension, jugular vein thrombosis, papilloedema

INTRODUCTION

Papilloedema is one of the clinical features of intracranial hypertension that usually presents with headache that increases when supine, transient visual obscuration, pulsatile tinnitus, nausea, and vomiting. It may require immediate reduction in intracranial pressure (ICP) to prevent further damage on the optic nerve and permanent loss of vision. We understand that the optic nerve is commonly affected in increased ICP because the elevated cerebrospinal fluid (CSF) pressure causes distension of the subarachnoid space, with circumferential compression of the optic nerve leading to papilloedema. We present a case that developed papilloedema and elevated ICP secondary to unilateral jugular vein thrombosis.

CASE REPORT

A 45-year-old man finished 2-month radiotherapy and cetuximab for squamous cell carcinoma of the larynx (stage T3N1M0) in June 2013. In July 2013, 6

weeks after completion of treatment, he developed swelling of the right side of face and neck, and was subsequently diagnosed with right internal jugular vein thrombosis. He was started on enoxaparin 10 mg subcutaneously every 12 hours (q12h). In December 2013, he started having headache and blurry vision. Optic nerve optical coherence tomography (OCT) in March 2014 showed bilateral, asymmetric papilloedema that was worse on the left side. Brain magnetic resonance imaging (MRI) in April 2014 showed bilateral optic nerve sheath widening, and bulging of left papilla (Figure 1A–C) in keeping with elevated ICP.¹ He presented to the neurology clinic in June 2014 with headache and decreased vision in the left eye. Examination at that time showed decreased temporal field vision and Frisen grade II papilloedema in the left eye. Eye movements, muscle strength, and reflexes were normal. He had decreased pinprick sensation at his feet. Lumbar puncture at that time showed opening pressure of 35 cm of H₂O with CSF protein 62 mg/dL, glucose 60 mg/dL, white blood cell (WBC) 0 cells, red blood cell (RBC) 2 cells. Brain MR venogram in September 2014 was negative

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FIGURE 1 MRI T2 sequence shows bilateral optic nerve sheath widening (arrows) (A and C) and bulging of left papilla (short black arrow) (B). Magnetic resonance venogram shows right jugular vein thrombosis (white arrow) (D). CT angiogram shows right jugular vein occlusion (E) and prominent collateral circulation (F). Right eye fundus prior to procedure shows no papilloedema (G); left eye fundus prior to procedure shows papilloedema (H).

for cerebral venous sinus thrombosis and showed right jugular vein thrombosis (Figure 1D). Computed tomography (CT) angiogram in September 2014 showed right internal jugular vein occlusion from its origin to its distal most extracranial segments with numerous prominent right-sided collateral veins (Figure 1E and F). After his neurology visit, he started acetazolamide but did not tolerate it and in September 2014, topiramate 100 mg twice a day (bid) was started instead. On neuro-ophthalmic examination in September 2014, corrected visual acuity with glasses was 20/25 in the right eye and 20/40 (no improvement with pin hole) in the left eye. Fundoscopy showed Frisén grade II papilloedema in left eye and was grade 0 in the right eye (Figure 1G and H). Intraocular pressure was within normal range on both sides. Humphrey automated perimetry showed non-specific superior nasal scotoma. By October 2014 his headache and blurry vision had worsened, and ventriculoperitoneal shunt placement

was performed. Afterwards, his vision and headache improved.

DISCUSSION

This is a case of papilloedema in the setting of complete occlusion of right jugular vein without cerebral sinus or bilateral jugular vein thrombosis. The aetiology of the jugular vein thrombosis is likely related to cetuximab therapy and radiation. Cetuximab is a monoclonal antibody used in the treatment of colorectal cancer and squamous cell carcinoma of head and neck. It acts by inhibition of cell growth, induction of apoptosis, and decreased production of vascular endothelial growth factor (VEGF). Reduced VEGF leads to endothelial dysfunction, defects in the interior vascular lining, exposing subendothelial collagen. A meta-analysis found that people treated with anti-EGFR monoclonal antibodies

such as cetuximab had a 32% higher risk of developing venous thromboembolism.² In addition, radiotherapy also contributed to thrombosis by injuring the vasa vasorum, leading to intimal proliferation. In the literature, we found a case of lower extremity deep vein thrombosis while on cetuximab treatment, perhaps related to hypomagnesemia and dehydration, which precipitated the thrombus formation.³

Our case is peculiar because papilloedema and increased ICP developed with only unilateral jugular vein thrombosis. The venous drainage of the brain involves predominantly both internal jugular veins and compensatory nonjugular venous drainage system (vertebral plexus and pterygopalatine plexus).^{4,5} If there is an obstruction of one internal jugular vein (IJV), the other vein should be able to compensate with the formation of some collaterals and the nonjugular venous system. This physiologic adaptation is also seen in cases of bilateral radical neck dissection for metastatic head and neck cancers in which both jugular veins are sacrificed. Some patients are able to tolerate this procedure without increase in intracranial pressure.⁶ In the literature, patients with elevated ICP in the setting of jugular vein thrombosis either have unilateral jugular vein thrombosis with associated cerebral venous sinus thrombosis or bilateral jugular vein thrombosis,⁷ different from our case. However, there are cases of papilloedema after unilateral jugular vein resection, usually of the right side.⁸ The cause of the papilloedema in those patients is thought to be a hypoplastic or small-calibre left transverse sinus that is not able to drain cerebral venous blood completely, as the transverse sinus is right, left, and co-dominant in 59%, 25%, and 16% of normal people.⁹ We think that our patient had a dominant right transverse sinus. When he developed right IJV thrombosis, this resulted in insufficient cerebral venous drainage from the non-dominant left transverse sinus and led to increased ICP. We also wonder if chemoradiation therapy with cetuximab may have resulted in an insufficient compensatory response in his nonjugular vein system. Of note, brain MR venogram was done in September 2014, approximately 9 months after symptoms onset. Although the left transverse sinus is patent in the MRV and we cannot exclude that it was not atrophic previously because there was no prior MRV or angiography for comparison, we still feel that it could have dilated in response to the increased intracranial pressure, given that transverse sinus are collapsible veins and right-sided dominant transverse sinus is more frequent in the population. In unilateral transverse sinus thrombosis, it has been shown with duplex sonography that venous flow increases in the opposite transverse sinus.¹⁰

Another interesting feature of our case is that papilloedema was asymmetric despite having symmetric optic nerve sheath dilatation in MRI imaging

(Figure 1A–C). Although unusual, unilateral papilloedema has been described in cases of elevated intracranial pressure including pseudotumor cerebri.¹¹ MRI of cases with asymmetric papilloedema has shown no differences in optic nerve sheath dilatation.¹¹ The exact mechanism of asymmetric papilloedema is unknown, although it is postulated that involves compartmentalisation of the subarachnoid space around the optic nerve with CSF flow between the intracranial and perioptic compartments that is not continuous nor bidirectional. Variations in the lymphatic capillaries in the meninges of the optic nerve, trabecula, and septa in the optic nerve subarachnoid space can cause these differences in CSF pressure transmission, resulting in asymmetric papilloedema.^{12–14} Our patient did not appear to have optic nerve anatomic anomaly, although as mentioned above, the absence of MRI optic nerve anomaly in some cases of asymmetric papilloedema has been described before.¹¹

This case teaches us that in a patient presenting with persisting headache and papilloedema, increased ICP should be considered a possibility, even if papilloedema is only unilateral and one jugular vein is still patent, as prompt diagnosis and treatment can improve visual outcomes.

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