Case Report

Pseudotumor cerebri in carcinoma cervix: "A diagnostic dilemma"

Kiran Kumar B R[1], Chendil V[2], Rajesh Javarappa[2], Amrut S Kadam[3]

From [1]Senior Resident, [2]Assistant Professor, [3]Professor and Head, Department of Radiation Oncology, Bangalore Medical College and Research Institute, Bengaluru, Karnataka, India

ABSTRACT

Pseudotumor cerebri, commonly known as idiopathic intracranial hypertension or benign intracranial hypertension, is a rare syndrome that presents mainly as a result of raised intracranial pressure (ICP). The diagnosis of this condition is established by the exclusion, with the aid of radiological imaging, and examination of cerebrospinal fluid. Due to the aggressive nature of this disease, both signs and symptoms may be intermittent, making definitive diagnosis difficult. Here, we present the case of a 60-year-old female with Stage III carcinoma cervix that was treated with concurrent chemoradiation with weekly cisplatin. She completed the concurrent chemoradiation and developed intermittent seizures, headache, weakness of lower limbs, and visual disturbances. A diagnosis of pseudotumor cerebri was entertained using the modified Dandy Criteria. Pseudotumor cerebri should be considered in cancer patients presenting with raised ICP of sudden onset in the absence of clinical and radiological evidence of brain metastases.

Key words: Carcinoma Cervix, Chemoradiation, Cisplatin, Pseudotumor cerebri

Pseudotumor cerebri or idiopathic intracranial hypertension (IIH) is a rare syndrome in which patients have the signs and symptoms of raised intracranial pressure (ICP) but have no radiographic evidence of a lesion in the brain. It was first described by a German physician, Quincke in the 1890s [1]. Dr. Dandy, a neurosurgeon, proceeded to describe the clinical course of 22 patients over a 7-year period in the 1920s and 1930s. All patients in this group presented with symptoms of increased intracranial tension, headache, blurred vision, and vomiting. Fundoscopy of all cases revealed papilledema and, in many cases, retinal hemorrhages were also present, indicative of long-standing severe intracranial hypertension, confirmed by raised pressures on lumbar puncture. In that document, Dandy explained that the elevations in pressure seem to come and go overtime, and are rarely constant. From this report, arose the original Dandy criteria which includes symptoms of increased intracranial tension; headache, blurred vision,vomiting and papilledema for the diagnosis of benign intracranial hypertension (BIH).

The original criteria were modified by Smith in 1985 and are currently known as the revised Dandy criteria which have been uniformly adopted as a diagnostic paradigm for BIH [2,3]. The annual incidence of this benign condition has been reported to vary from 0.9 to 2.2 cases per 100,000 populations, occurring predominantly in females [4,5] but can occur at any age [6]. Headache is the major presenting symptom. Other symptoms include dizziness, nausea, and vomiting, and visual and neurological deficits [6,7]. The diagnosis of this condition is established by the exclusion of other diseases that have similar symptoms with the aid of computerized tomography (CT) scan, magnetic resonance imaging (MRI), and cerebrospinal fluid (CSF) assessment [8,9]. We report a case of pseudotumor cerebri in a carcinoma cervix patient who was undergoing chemoradiation treatment with cisplatin. To the best of our knowledge, this disease has never been described in carcinoma cervix patients.

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CASE REPORT

A 60-year-old female presented with a chief complaint of bleeding per vagina. On evaluation, she was diagnosed to have squamous cell carcinoma cervix Federation of Gynecology and Obstetrics Stage IIIB. She was treated with definitive chemoradiation with weekly cisplatin. She received external beam radiation therapy with a dose of 50 Gy in 25 fractions and weekly cisplatin 40 mg/m^2. She completed the concurrent chemoradiation uneventfully and was planned for a brachytherapy procedure. She developed intermittent seizures, headache, weakness of lower limbs, and bilateral visual disturbances.

On examination, her blood pressure was 120/80 mmHg and body mass index was 21 kg/m^2. She had bilateral papilledema on ophthalmologic evaluation. Urgent MRI scan of the brain revealed no focal intracerebral or cerebellar lesion (Fig. 1). Routine laboratory tests, which included complete blood counts, serum electrolytes, renal function tests, liver function tests, and

Correspondence to: Kiran Kumar B R, Department of Radiation Oncology, Bangalore Medical College and Research Institute, Bengaluru-560 002, Karnataka, India. E-mail: drkiranbr@yahoo.com.

random blood sugar, were all normal. CSF analysis was normal for biochemical content and no evidence of atypical elements. There were no focal neurological deficits. We also tested the autoimmune antibody series and paraneoplastic syndrome-related antibody in the CSF to determine the causes of the neurological symptoms, but both tests yielded negative results.

In view of the patient's alertness, symptoms of ICP (headache and vomiting), absence of focal brain lesion, or neurological deficit, a diagnosis of pseudotumor cerebri was made using the modified Dandy criteria (Table 1). She was commenced on parenteral dexamethasone and acetazolamide. The patient's prognosis was poor and her relatives decided to give up on treatment, choosing to return to their hometown. The patient was lost to follow-up.

DISCUSSION

Pseudotumor cerebri, otherwise known as IIH, is a disorder of unknown etiology. Historically, IIH was first described by Quincke in the late 19th century [1]. The criteria for the diagnosis of IIH are based on the modified Dandy criteria [10].

Symptoms of IIH often mimic brain metastasis, with headache being the most common presentation in over 90% of patients [11]. Other symptoms may include dizziness, nausea, vomiting, and seizure. Papilledema is often diagnostic of this condition in the setting of IIH. It is of clinical note that IIH without papilledema had also been reported in the literature [12].

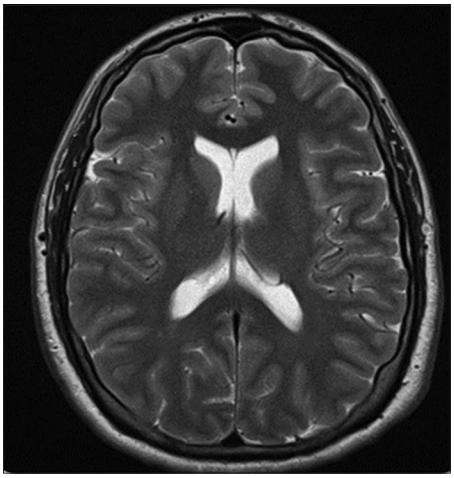

Figure 1: Magnetic resonance imaging of the brain

Table 1: Modified dandy criteria for the diagnosis of idiopathic intracranial hypertension

1	Signs and symptoms of increased intracranial pressure
2	Awake and alert patient
3	No abnormal neurological findings except papilledema or a sixth nerve palsy
4	Normal CT/MRI except for empty Sella syndrome or small ventricles
5	Documented increased CSF opening pressure (>200 mm of water in non-obese and >250 mm of water in obese patient), with normal CSF composition
6	No other known cause of raised intracranial pressure

Obesity and female sex are the recognized predictive factors for the onset of this rare disease [13]. The relationship between obesity and IIH is poorly understood, with several etiological hypotheses proposed, including increased central venous pressure, various hormonal and metabolic changes that are commonly found in obese patients [13].

The pathogenesis of IIH is not fully elucidated. ICP is determined by CSF formation and absorption, but it is unclear whether there are any physiological regulatory mechanisms operating at the choroid plexus or arachnoid villi and granulations. Under normal circumstances, ICP is maintained by cerebral arterial pressure, which is subject to cerebral autoregulation such that it remains constant over a wide range of systemic arterial blood pressure. ICP is also greatly influenced by cerebral venous pressure. Various perturbations can favor an increase in ICP, such as: (i) An increased cerebral volume as a result of increased interstitial fluid volume, increased blood volume, and increased tissue volume; (ii) increased CSF volume as a result of increased CSF production rate and increased CSF outflow resistance; (iii) increased cerebral arterial pressure as a consequence of loss of autoregulation; and (iv) increased cerebral venous pressure [13]. Early in 1995, King *et al*. discovered an elevation in cranial venous pressure in patients with IIH, which led to a growing recognition that local venous obstruction played an important role in the pathogenesis of IIH [14]

Brain CT and MRI are valuable tools in the diagnosis of IIH because brain metastases in patients with extracranial neoplasms are easily excluded by their use [8]. Therapy is directed at reducing intracranial CSF pressure, management of symptoms, and preservation of vision. The traditional treatment of repeated lumbar puncture and surgical shunting has been supplanted by medical therapy and weight loss. Medical treatment (non-operative) with acetazolamide and parenteral steroid was successful in the patient, as in other reports, recovery was complete with no residual morbidity [15].

Studies have documented acetazolamide's success in the management of symptoms and stabilizing vision in 47–67% of patients [15,16]. Acetazolamide, a carbonic anhydrase inhibitor, is thought to work by inhibition of carbonic anhydrase, leading to a reduction in the transport of sodium ions across the choroid plexus epithelium. There are no standard doses of acetazolamide for the management of intracranial hypertension, acetazolamide 500 mg 2 times daily, gradually titrating by 250 mg every week up to a maximum dosage of 4 g/day, has been suggested [15,16].

To the best of our knowledge, BIH has never been described in cervix cancer patients. In this patient, no causative or associated factors could be found except for the administration of Cisplatin. Chemotherapy drugs have been associated with BIH and may be a contributory cause in this patient [17]. In the present case, BIH occurred after completion of treatment with cisplatin that was given for 5 cycles (cumulative dose: 200 mg/m^2). Cisplatin is associated with neurotoxicity. Seizures and leukoencephalopathy have also been described [18,19].

Pseudotumor cerebri remains a diagnostic challenge to most physicians. Furthermore, these findings can wax and wane

overtime. Due to the nature of this disease, both signs and symptoms may be intermittent, making definitive diagnosis difficult. Newer imaging studies, particularly the magnetic resonance venogram along with a constellation of correlative findings and associated diseases, have given new impetus in the diagnosis, treatment, and pathophysiology of this disease.

CONCLUSION

Pseudotumor cerebri should be considered in cancer patients presenting with raised ICP of sudden onset in the absence of clinical and radiological evidence of brain metastases. We advise early intervention in patients with pseudotumor cerebri to prevent morbidity.

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