Letters to the Editor

After ruling out the possibilities of drug toxicity (from history and checking prescriptions), Wilson's disease, autoimmune etiologies, and other metabolic conditions, the patient was evaluated with an EEG, which revealed the classical periodic discharges. The levels of IgG measles antibodies were very high in cerebrospinal fluid and serum samples, which was consistent with a diagnosis of SSPE. Thus based on a classical EEG and raised antimeasles antibody titer, a diagnosis of SSPE was made with this uncommon initial presentation.

In developing countries like India where measles is still prevalent, one should be aware that of the atypical presentations of SSPE and that it can masquerade as a dystonia Parkinsonism syndrome. Movement disorders, though uncommon, can be an important clinical feature of patients with SSPE and neurologists should keep a possibility of this devastating disorder in patients presenting with movement disorders, especially in developing and underdeveloped countries.

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Conflicts of interest
There are no conflicts of interest.

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Pemetrexed‑Induced Pseudotumor Cerebri Syndrome: A Rare Complication

Sir,
Intracranial hypertension results from intracranial mass lesions, cerebrovascular disorders, obstructed cerebrospinal fluid circulation, cerebral venous thrombosis, craniocerebral trauma, infections, and infiltrations.[1‑3] Intracranial hypertension without structural causes initially termed as pseudotumor cerebri syndrome (PTCS) and subsequently as idiopathic intracranial hypertension is an uncommon disorder associated with hematological, endocrine, and systemic disorders.[3] Drugs known to cause PTCS include tetracyclines, quinolones, indomethacin, vitamin A, hormonal preparations, lithium, cyclosporin, anticancer drugs, etc.[1,2,4] We present a woman who had PTCS associated with pemetrexed therapy which is a novel chemotherapeutic agent used for pleuropulmonary malignancies.

A 60‑year‑old woman presented with progressively increasing diffuse throbbing headache and asymmetric impairment of vision in both eyes for 3 months associated with nonprojectile vomiting for 2 months. She had no seizures, diplopia, imbalance, motor, sensory or cognitive symptoms.

One year ago, she had lumbar pain radiating to right lower limb without motor, sensory or sphincter impairment. Magnetic resonance imaging (MRI) revealed third lumbar vertebral fracture with heterogeneous gadolinium enhancement. Further evaluation revealed adenocarcinoma of right lung.

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A 60‑year‑old woman presented with progressively increasing diffuse throbbing headache and asymmetric impairment of vision in both eyes for 3 months associated with nonprojectile vomiting for 2 months. She had no seizures, diplopia, imbalance, motor, sensory or cognitive symptoms.

One year ago, she had lumbar pain radiating to right lower limb without motor, sensory or sphincter impairment. Magnetic resonance imaging (MRI) revealed third lumbar vertebral fracture with heterogeneous gadolinium enhancement. Further evaluation revealed adenocarcinoma of right lung.
Genetic testing for epidermal growth factor receptor (EGFR), anaplastic lymphoma kinase (ALK), and programmed death ligand-1 (PDL-1) mutations were negative. She was initiated on intensive combined therapy with carboplatin and pemetrexed along with zoledronic acid. Whole-body positron emission tomography study after completion of the intensive chemotherapy with pemetrexed revealed stable disease. Maintenance therapy with monthly cycles of pemetrexed was started 4 months before admission. She had well-controlled hypertension for 1 year.

On examination, she was apparently healthy looking and moderately built. Her blood pressure was 130/80 mmHg with heart rate of 84 per min and respiratory rate of 18 per min. There was no organomegaly, lymphadenopathy, or spinal tenderness. She had bilateral posterior subcapsular cataract with normal intraocular pressure. She was conscious, alert, and oriented with normal mental status examination. Visual acuity was reduced in both eyes (finger counting at 1 m with right eye and hand movement perception with left eye). She had bilateral grade IV papilledema with early optic atrophy [Figure 1] and bilateral abducent palsy. Other cranial nerves, motor and sensory examinations were normal. There were no signs of meningeal irritation.

She had normocytic normochromic anemia (8.4 gm/dL) and elevated serum creatinine (1.94 mg/dL). Cranial MRI revealed empty sella with bilateral optic nerve head swelling, distended perioptic subarachnoid space, and dilated superior ophthalmic veins without parenchymal lesions, ventriculomegaly, or abnormal enhancement [Figures 2 and 3]. Lumbar cerebrospinal fluid (CSF) was colorless, clear, and acellular with markedly elevated opening pressure (420 mm of water). CSF protein was 25 mg/dL and sugar 64 mg/dL. Lumbar puncture 2 days later revealed CSF pressure of 340 mm of water. CSF cytology was negative for abnormal cells and sterile on both occasions. She was treated with acetazolamide and prednisolone. She did not consent for thecoperitoneal shunt or optic nerve fenestration and was continued on medical therapy for intracranial hypertension. At 6-week follow-up, her visual acuity was unchanged and repeat lumbar puncture revealed opening pressure of 290 mm of water with normal analysis. On telephonic interview at 4 months, she reported that her vision was unchanged and that there were no other neurological or systemic symptoms.

We report the development of intracranial hypertension resulting in blindness in a middle-aged woman while on the maintenance regimen of pemetrexed for pulmonary adenocarcinoma. Intracranial hypertension in patients with systemic malignancy can occur due to intracranial metastasis, meningeal infiltration, venous thrombosis, and neoplastic meningitis. Our patient had clinical features of raised intracranial pressure in the absence of structural intracranial pathologies. Radiological features of PTCS include empty sella turcica, tortuosity of optic nerves with enlarged perioptic CSF space, flattening of the posterior globe, and optic nerve head swelling which were present in our patient. With these clinical and radiological features along with normal CSF analysis including cytology, we made a diagnosis of pseudotumor cerebri syndrome in our patient. In addition, the diameter of the superior ophthalmic veins was increased on both sides in our patient. Increased diameter of the superior ophthalmic veins correlated with degree of intracranial hypertension from diverse causes and can be considered as a feature of intracranial hypertension. Pseudotumor cerebri syndrome is a preferred term over primary and secondary idiopathic intracranial hypertension.

Cancer chemotherapy can lead to peripheral and cranial neuropathy, encephalopathy, seizures, cerebellar dysfunction, myelopathy, posterior reversible encephalopathy, etc. The occurrence of chemotherapy-induced raised intracranial hypertension in patients with systemic malignancy is rare. The management of such patients can be challenging.

Figure 1: Showing right optic fundus with papilledema and early optic atrophy

Figure 2: Showing the MRI findings in the patient. Axial T2 weighted images (a and b), axial FLAIR image (c), and oblique orbital T2 weighed image (d). The optic nerve is tortuous with dilated perioptic cerebrospinal space (long white arrows), flattening of posterior globe with optic nerve head swelling (short white arrow) and superior ophthalmic veins are dilated (black arrow)
pressure is rare and is reported with methotrexate and 5-fluorouracil.\(^6\) The mechanisms of chemotherapy-induced raised intracranial pressure are not well understood. PTCS is also reported with severe renal dysfunction.\(^2\) However, renal dysfunction in our patient was mild which could have been related to hypertension or secondary to pemetrexed therapy.\(^7\)

Papilledema with normal CSF pressure and analysis occurred in a patient receiving carboplatin.\(^6\) Posterior reversible encephalopathy syndrome (PRES) with impaired vision occurred with regimens using carboplatin\(^6\) and pemetrexed.\(^10\) A patient receiving pemetrexed for adenocarcinoma of the lung developed raised intracranial pressure secondary to communicating hydrocephalus and underwent ventriculoperitoneal shunt.\(^11\) Our patient did not have features of PRES or hydrocephalus. She received carboplatin and pemetrexed in the intensive chemotherapy phase with carboplatin stopped 3 months before the onset of intracranial hypertension. She was on pemetrexed monotherapy when intracranial hypertension leading to blindness occurred. Clinical profile of PTCS in our patient was supported by the cranial MRI findings, elevated CSF pressure, and normal CSF analysis.\(^1\)\(^-\)\(^3\)

To the best of our knowledge, this is the first report showing pemetrexed-induced pseudotumor cerebri syndrome. As our patient did not have hydrocephalus, underlying mechanism may be different. Patients on pemetrexed therapy may need to be monitored for raised intracranial pressure which can prevent visual impairment.

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