

Exploring Hypertrophic Pachymeningitis: A Report of Two Cases

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ABSTRACT

Hypertrophic pachymeningitis is a rare and complex disease with various aetiologies characterized by inflammation and thickening of the cranial or spinal duramater or both. The diagnosis is to be suspected on clinical, laboratory, radiological examination and can be confirmed on Dural biopsy. For the management, early diagnosis through relevant clinical history and radiological investigation is required. This case series highlight hypertrophic meningitis as a rare cause of altered mental status and the importance of a comprehensive medical history and examination for the diagnosis of such disease as early diagnosis of such cases and early initiation of the therapy can lead to better outcome. Steroid therapy is given as the first line of management but if patient does not respond to steroid therapy, it may progress to permanent neurological deterioration.

KEYWORDS: Pulse Steroid Therapy, Dural Biopsy, Dural Thickening

CASE 1

A 26-year-old female presented with complains of altered mental status for 15 days in form of aggressive behavior, unable to recognize family members and irrelevant talking along with fever for 2 days (up to 101 F), not associated with chills and rigor and relieved on medication. There was no history of drug abuse, trauma, ear discharge, loss of consciousness, abnormal body movement, weakness, or abnormal sensation, and she had normal bladder and bowel function. On Examination: GCS- E4V4M5, patient was conscious, not cooperative, not oriented to time, place, and person. Blood pressure was 130/60 mm Hg, pulse rate -110/min, regular, SPO2: 99% under room air, with RBS of 103 mg/dl and the patient was morbidly obese. CNS examination – Bilateral pupil was normal size and reactive to light, bilateral planters were extensor, deep tendon reflexes on knee jerk, ankle jerk, biceps reflex and triceps reflex were normal, and patient was spontaneously moving all four limbs, Neck rigidity was terminal, with no spinal deformity and tenderness, no neurocutaneous markers were seen. Other systemic examination was within normal limits. On Investigation: Hemoglobin was 10.4 gm/dl Total leucocyte count was 9850/microL, Differential leucocyte count was- Neutrophils: 70 % Lymphocytes: 20% Monocytes: 8 % Eosinophils: 2 %. Urea: 45.2 mg/dl, Creatinine :0.65 mg/dl, AST: 26, ALT: 26, Total bilirubin: 1.7 mg/dl, Sodium: 149 mmol/l, Potassium: 3.5 mmol/l, Arterial Blood gas analysis showed pH: 7.48, Pco2:38 mmHg, HCo2:21 mEq/l, Po2:78 mmHg, So2-98%, Urine routine microscopy was normal. Cerebrospinal fluid Cytology: 5 cells all lymphocytic, Total protein: 13, Glucose: 67, Adenosine Deaminase: 0.01, CBNAAT: Negative, Gram stain and Cultures including ZN stain: negative , viral panel (Herpes Simplex Virus 1 and 2, Japanese Encephalitis virus): Negative, CSF TBPCR: negative, Hepatitis B: negative, Hepatitis C: negative, HIV:

negative, Urine cultures and blood cultures: Negative, Serum ACE levels were within normal limits. Autoimmune panel: ANA by Immunofluorescence – 1:3600 titer with nuclear homogenous pattern (Fig. 1), CRP >10 mg/dl, IgG-3450 mg/dl (650-1600 mg/dl), C3/C4 were normal, P-ANCA was 1:80 (2+). Chest X-Ray: normal, ECG: normal sinus rhythm, fundus examination was within normal limits, NCCT Head revealed sub centimetric calcified granuloma in left temporal lobe. Patient underwent contrast enhanced MRI (Fig.2) which revealed Diffuse smooth Dural thickening with enhancement along bilateral cerebral hemisphere, no obvious leptomeningeal enhancement or enhancing brain parenchymal lesion, no acute infarct or FLAIR sulcal hyperintensity seen suggestive of Pachymeningitis. Based on above findings patients was diagnosed as a case of hypertrophic pachymeningitis with autoimmune encephalitis and treated with intravenous pulse steroid therapy. Following the steroid therapy patient completely improved with no residual neurological deficit. On follow up after 6 weeks, patient was found to be completely normal without any neurological deficit.

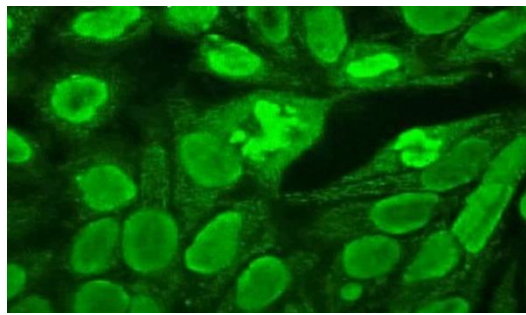


Figure 1: showing homogenous immunofluorescence staining pattern of nucleus on Hep 2 cell lines.

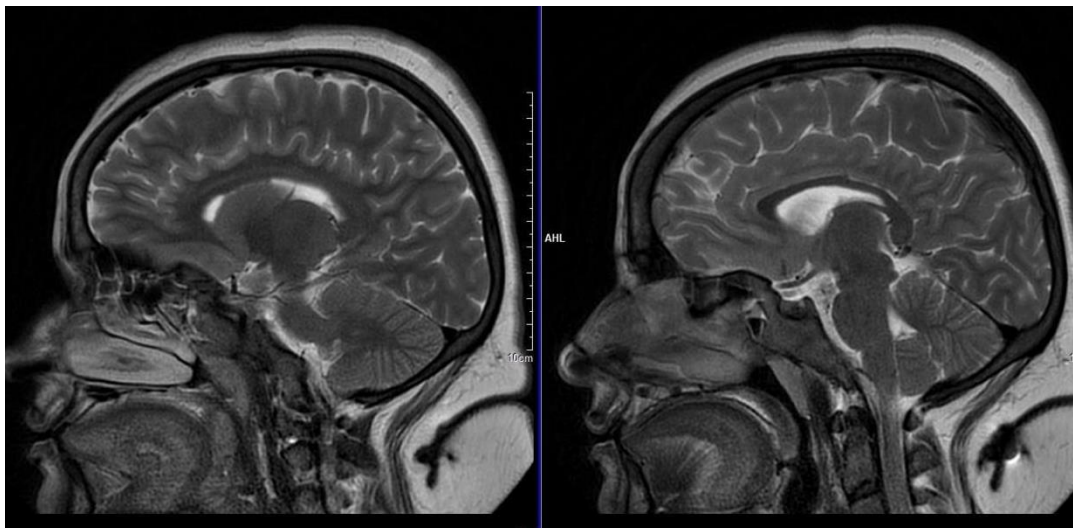


Figure 2: CEMRI Brain showing diffuse smooth Dural thickening with enhancement along bilateral cerebral hemisphere.

CASE 2

A 69 year old male presented with complaint of left lower limb weakness for 5 month in form of difficulty in wearing slippers, fever for 20 days which was 99 F, undocumented not associated with chills or rigors, altered sensorium for one day in form of irrelevant talk , No history of drug abuse, trauma, Ear discharge,

loss of consciousness, abnormal body movement, abnormal sensation was there. Normal bladder and bowel function was present. Patient was known case of benign prostatic hyperplasia planned for surgery but deferred in view of hyponatremia(118meq/l) and altered sensorium. Patient has history of TB contact. On examination patient was conscious oriented to person,,not to time and place with intermittent decreased responsiveness, GCS-E4V4M5. Blood pressure was 128/70 mm Hg, pulse rate -90/min, regular with SPO2: 99% under room air, with RBS of 108 mg/dl. CNS examination - b/l pupil-Normal size and reactive to light, tone increased in b/l upper and lower limb, right planter extensor and left planter flexor, deep tendon reflexes on knee jerk and biceps reflex and triceps reflex were exaggerated, Neck rigidity was terminal, with no Spinal deformity and tenderness, no neurocutaneous markers. Other systemic examination revealed no abnormality. Hemoglobin: 12.9 gm/dl Total leucocyte count was 10050/ microL, Differential leucocyte count was- Neutrophils: 66 % Lymphocytes: 24% Monocytes: 10 % Eosinophils: 0 %. Urea: 34.2 mg/dl, Creatinine :0.8 mg/dl, AST: 42, ALT: 34, Total bilirubin: 0.8 mg/dl, Sodium: 118 mEq/l, Potassium: 3.5 mEq/l, Arterial Blood gas showed pH: 7.36, PCo2: 34 mmHg, HCo3: 20 mEq/l, Po2: 72 mmHg, So2-99%, Urine routine microscopy was normal. Urinary Na- 45 mEq/l ,serum osmolarity 260 mOsm/kg ,urine osmolality-292mOsm/kg. Patient was diagnosed with syndrome of inappropriate antidiuretic hormone secretion and was further evaluated for the cause of the same. Cerebrospinal fluid findings showed glucose of 71 mg/dl, protein of 284 mg/dl, ADA-2.3 with 10cells in cytology in which 60% were lymphocytic and 40% were polymorph. Cerebrospinal fluid CBNAAT: Negative, Cerebrospinal fluid Gram stain and Cultures including ZN stain: Negatives, viral panel (HSV 1 AND 2, JE virus): Negative, Cerebrospinal fluid TBPCR: Negative, Hepatitis B: negative, Hepatitis C: negative, HIV: negative, Urine cultures and blood cultures: Negative. During ultrasound of abdomen patient was found to have bilateral suprarenal mass of approximately 6.2x3 cm. Further evaluation of same was done by CECT abdomen (Fig. 3) of the patient suggestive of bilateral adrenal mass (6.8x3.6x6.5 cm) can be either malignancy or tuberculosis. NCCT Head suggestive of small vessel ischaemic changes and age related cerebral atrophy. Urine metanephrines were 28 mcg/24hours (normal range- 24-96 mcg /24 hour) CEMRI Brain (Fig. 4) was suggestive of pachymeningitis with smooth Dural wall thickening with enhancement along bilateral cerebral hemisphere, interhemispheric region and along the tentorium. PET SCAN (Fig. 5) showed increased metabolic activity in bilateral adrenal glands with necrosis and also increased uptake in meninges.As patient was diagnosed with hypertrophic pachymeningitis secondary to possible tubercular etiology, Anti-tubercular therapy with steroid was initiated. In course during hospital stay patient condition worsened and patient was shifted to intensive care unit where he got intubated in view of poor GCS and shock and later expired.

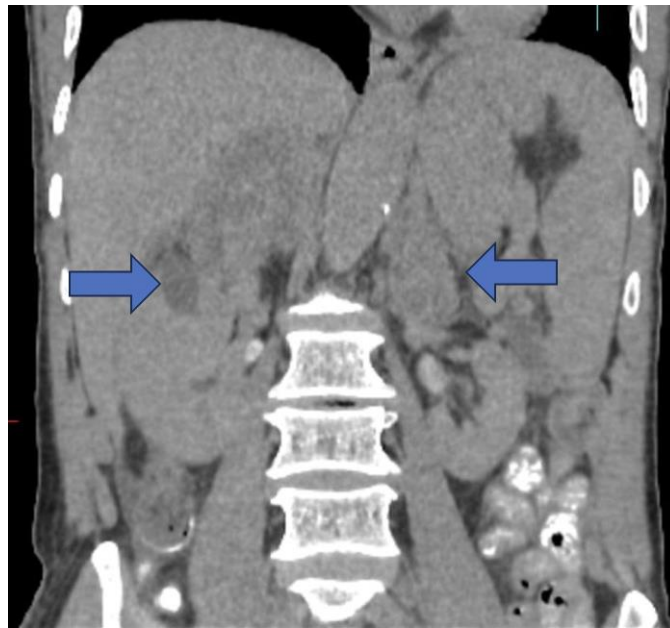


Figure 1.CECT Whole Abdomen showing bilateral adrenal mass of approx. 6.5X3.4(SI) cm on coronal mage.

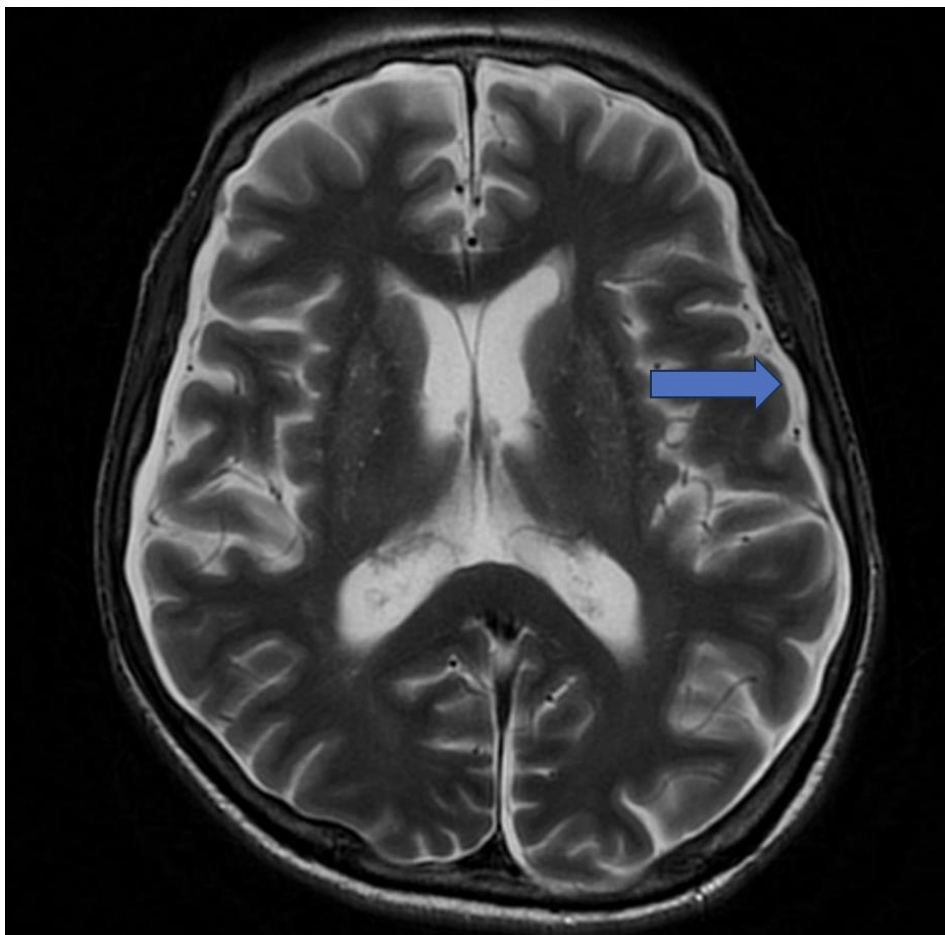


Figure 2.showing T2 weighted CEMRI Brain suggestive of diffuse smooth Dural thickening with enhancement along bilateral cerebral hemisphere, interhemispheric region and along the tentorium

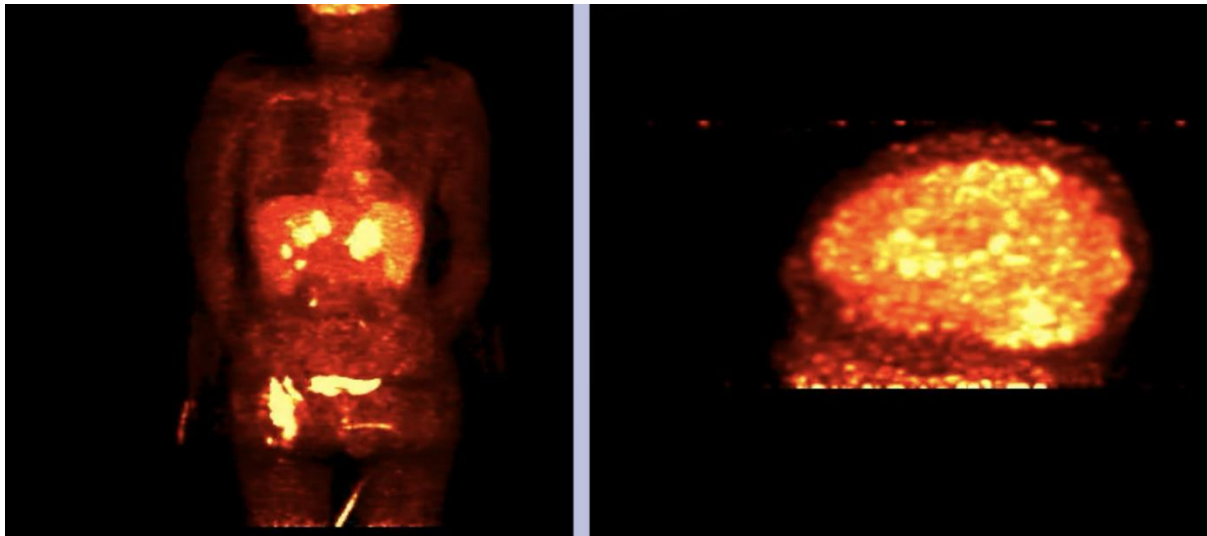


Figure 3. A 18F-FDG PET-CT Study showing (A) hypermetabolic large lobulated necrotic mass lesion in bilateral adrenal gland; (B) hypermetabolic activity among bilateral cerebral convexity

DISCUSSION

Hypertrophic pachymeningitis (HP) is a fibrosing inflammatory disorder featuring localized or diffuse thickening of the cranial or spinal dura mater. The disorder can be divided into cranial or spinal pachymeningitis by lesion location and idiopathic or secondary HP based on aetiology. Infections and autoimmune diseases are among the most identified causes of secondary HP [1]. The exact etiopathogenesis of this entity is still unknown, but it is speculated to be an autoimmune phenomenon or occur as a direct result of infectious or infiltrative pathology [2,3]. Notably, the thickening of the dura mater is present in other conditions, such as intracranial hypotension syndrome or neoplastic pachymeningitis, which should be carefully differentiated to avoid misdiagnosis. Pathophysiological mechanisms underlying parenchymal involvement include venous congestion, ischemia resulting from compression of cortical vessels, and inflammatory infiltration into the brain parenchyma.

In our first case, the patient presented with altered sensorium and was later diagnosed with pachymeningitis secondary to an autoimmune cause, which improved with pulse steroid therapy. In a study by Tomomi Yonekawa et al., among 159 cases with detailed data, antineutrophil cytoplasmic antibody (ANCA) positivity was found in 34.0% of patients [4]. In another study by Tsuda R et al., a 69-year-old female was diagnosed with hypertrophic pachymeningitis with MPO-ANCA positivity. She was treated with intravenous methylprednisolone, which drastically reduced her symptoms, normalized her MPO-ANCA titers, and improved her MRI findings [5].

Tuberculosis (TB), a great masquerader of present times, is an important cause of pachymeningitis, especially in developing countries, with peak incidence commonly seen in the sixth decade [6]. In our second case, a 69-year-old male presented with intermittent decreased responsiveness and was later found to have hypertrophic pachymeningitis secondary to tuberculosis. A case study by Cordeiro et al. described a patient complaining of chronic headache, found to have pachymeningitis secondary to tuberculosis, and responding well to antitubercular therapy (ATT) with steroids [7]. Another case study by Das and Ray showed that tuberculosis was the cause in 22.8% of cases of pachymeningitis. Patients with TB-related HP received antitubercular drugs (ATD) with steroids. Two patients had partial resolution of their

headaches, and others had complete resolution; three had residual cranial neuropathies (extraocular muscle weaknesses) [8].

Magnetic resonance imaging (MRI) is essential for diagnosis. T1-weighted images show isointense meningeal thickening with contrast enhancement, and T2-weighted images demonstrate hypointense lesions [9]. Extra-neurological or systemic manifestations of HP may help define the aetiology. For example, involvement of salivary glands, lymph nodes, the pancreas, and retroperitoneum suggests IgG4-related disease (IgG4-RD); pulmonary, renal, and paranasal sinus involvement may suggest granulomatosis with polyangiitis (GPA), formerly known as Wegener's granulomatosis; hypothalamic involvement suggests IgG4-RD, sarcoidosis, or histiocytosis; and coexistence with neoplasia may suggest meningeal carcinomatosis [10]. Administering ATD in the second case was a prudent choice, as demonstrated in previous studies, where ATD improved symptoms and radiological findings. To prevent long-term neurological sequelae, early initiation of antitubercular therapy along with steroids should be considered in countries endemic to tuberculosis.

CONCLUSION

Given the diverse aetiologies and presentations of hypertrophic pachymeningitis, a comprehensive diagnostic approach, including clinical evaluation, imaging studies, and consideration of systemic manifestations, is essential for accurate diagnosis and timely initiation of appropriate treatment to improve patient outcomes and prevent neurological sequelae.

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