ATYPICAL CSF PICTURE IN VIRAL MENINGITIS HSV- TYPE-2

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ABSTRACT

INTRODUCTION

Acute infections of nervous system are among the most important problems in medicine because early recognition, efficient decision making and rapid institution of therapy can be lifesaving. Making a clinical diagnosis of acute meningitis depends on the cornerstone of cerebrospinal fluid (CSF) examination. We present a case with the above-mentioned difficulty and the approach involved in establishing the exact diagnosis and institution of appropriate treatment.

CONCLUSION

About findings in viral meningitis one should be careful while evaluating a CSF report so as to not make a mistaken diagnosis and delay treatment. The most important analysis in patients whose symptoms are consistent with herpes simplex meningitis is the detection of Herpes simplex Virus deoxy-ribo-nucleic acid (HSV-DNA) in CSF with Polymerase Chain Reaction (PCR).

KEYWORDS

Cerebrospinal fluid (CSF), Herpes simplex Virus deoxy-ribo-nucleic acid (HSV-DNA), Polymerase Chain Reaction (PCR).

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INTRODUCTION: Acute infections of nervous system are[1] among the most important problems in medicine because early recognition, efficient decision making and rapid institution of therapy can be life-saving. The distinct clinical syndrome include acute bacterial meningitis, viral meningitis, encephalitis, focal infections such as brain abscess. Each may present with a nonspecific prodrome of fever, headache, altered consciousness, focal neurological signs, or seizures. Key goals of early management are to urgently distinguish between these conditions, identify the pathogens and initiate appropriate anti-microbial therapy. Making a clinical diagnosis of acute meningitis depends on the cornerstone of CSF examination. The classical description of three frequently encountered infective cause of meningitis i.e. bacterial, viral, tubercular depends largely on the classical CSF picture. However, the classical description of CSF in three types of meningitis at times is difficult to interpret because of a CSF picture which usually varies with one described and show overlapping feature of other aetiology. Another difficulty arises when the radiological entity for diagnosis i.e. MRI and CT scan are not contributory to the diagnosis.

We present a case with the above-mentioned difficulty and the approach involved in establishing the exact diagnosis and institution of appropriate treatment.

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CASE REPORT: We report a case of a 53-year-old male, a known case of T2DM who was brought to hospital with a history of high grade fever; headache and altered sensorium 5 hours prior to admission. Patient was in his usual state of health when he suddenly started with high grade fever and within few hours developed vomiting, headache, and altered sensorium. A detailed neurological examination at time of admission revealed patient drowsy and agitated. On motor system examination, he was moving all the 4 limbs and was localising painful stimulus, though verbal response was confused. His Glasgow coma scale (GCS score) at the time of admission was 12/15. Neck stiffness was present. Pupils were normal in size and reacting to light. Plantar left was downgoing and right was equivocal. Few hours later, patient's sensorium deteriorated further and the patient became stuporous and started throwing GTC seizures. The patient was shifted to ICU and was intubated and put on ventilator support. His routine lab parameters were as follows: Random blood sugar 280 mg/dL, blood urea 40 mg/dL, serum creatinine 1.3 mg/dL, TLC – 14,000 cells/cu. mm, DLC – neutrophils 76%, lymphocytes 20%, monocyte 03%. Haemoglobin 10 g%, platelets 1.5 lakh, ESR 5 mm/hr., PTI 88%. Serum total protein 7.6 g/dL, serum albumin 3.5 g/dL, serum bilirubin 0.8 mg%, conjugated 0.2 mg%. Urine routine examination: Albumin nil, glucose 3+, pus cells 2-3/hpf. X-ray chest was within normal limits. ECG normal sinus rhythm. A neuroimaging study was carried out. CT scan showed bilateral lateral ventricles to be prominent, rest to be normal. MRI Imaging of brain was performed and T1 and T2 weighted images were obtained. No significant abnormality was detected on MR imaging of the brain. A lumbar puncture was done which was reported as follows: - Total CSF protein 285 mg/dL, CSF glucose 70 mg/dL, chloride 126 mEq.

CSF cytology was as follows: TLC -800 cells/µL. DLC: Neutrophil 80%, lymphocytes 16%. RBC 10 -12/hpf. CSF culture did not show evidence of any growth. CSF Gram-staining was also negative. KoH preparation and India ink staining of CSF was also negative.

A CSF PCR for HSV1 and HSV2 was sent. It was positive for HSV2. Patient was initially started on empirical treatment regimen of meningitis. However, after receiving the PCR report for HSV2, the treatment was tailored to viral meningitis. Patient was put on IV acyclovir for 10 days. The patient showed clinical improvement, his sensorium improved. He did not throw any fresh seizure and was off ventilator on 4th day. A subsequent check lumbar puncture was done on 10th day. The report was as follows: CSF protein 43 mg/dL, sugar 76 mg/dL. TLC: 5 cells/hpf. DLC: All lymphocytes. The patient made a complete recovery and was discharged from the hospital on 14th day of admission.

DISCUSSION: The rapid diagnosis of CNS infection with HSV[2] is important because of potential morbidity and mortality associated with herpes simplex virus encephalitis and the availability of antiviral therapy. Acyclovir has proven to ameliorate this disease. Without the therapy, > 70% HSV encephalitis cases are fatal. Treatment with acyclovir has been shown to reduce the mortality rate to 20% for patients of all ages.

HSV is a neuronophagic[3] virus which characteristically causes haemorrhagic necrosis in temporal lobe. This property is accepted as a distinctive finding in differential diagnosis from other encephalitis. Broad spectrum of clinical syndromes associated with HSV infection of CNS present as 1 of 3 general entities: Neonatal infection; encephalitis; meningitis. Neonatal infections are most often caused by HSV type 2, transmitted vertically during delivery. Viral meningitis caused by HSV is predominantly HSV type 2. The usual clinical manifestation of it is headache, fever plus signs of meningeal irritation, associated with inflammatory CSF. However, profound alteration of sensorium, stupor, coma, seizures are unusual for viral meningitis and suggest presence of parenchymal involvement and encephalitis. HSV encephalitis is an acute onset localised necrosis of brain parenchyma with localised CNS findings. Classically, temporal and frontal lobes are involved. It may occur in patients of any age beyond neonatal period. It is predominantly caused by HSV type 1 {>85%}. Though in our case, the patient had profound alteration of sensorium and was having recurrent GTC seizures suggestive of parenchymal involvement and encephalitis.

His PCR report was positive for HSV type 2.

HSV meningitis is reported to be a sequelae of primary genital herpes in 36% of affected females and 13% of affected males. But only 25% - 33% of patients ever report history of genital lesion. In this particular case, the patient did not report of any genital lesions. A subset of these patients possibly as many as 25% have recurrent[4] bouts of HSV meningitis separated by asymptomatic periods of months to years.

The CSF[5] analysis of our patient with HSV2 meningoencephalitis differed from the expected counts in typical viral meningitis while a CSF cell count of 25-500 cells/µL with a predominance of mononuclear cells are generally expected in viral infections. Our patient had a total CSF cell count of 800 cells/µL. Only few viral CNS infections like LCMV, mumps are known to cause counts of several thousand cells in CSF. A CSF cell picture of predominant neutrophil although known to occur in certain viral meningitis like ECHO virus, eastern equine encephalitis and mumps, it is usually not reported in HSV2 meningitis. Our case showed a CSF cytology of 80% neutrophils. Subsequent lumbar puncture 10 days post acyclovir treatment showed CSF cell count reduced to 5 cells/hpf and all to be lymphocytes. The case in study also showed a CSF RBC count of 10 -12/hpf which was consistent with known evidence of erythrocytes in CSF in herpes encephalitis. The CSF glucose was within normal limits in our case. However, the CSF proteins expected for viral meningitis is a slight elevation of up to 20 – 80 mg/dL while in our case a marked elevation of 285 mg/dL was reported. Neuroimaging in form of MRI[6] brain helps to identify or exclude alternative diagnosis and assists in the differentiation between a focal as opposed to a diffuse encephalitic process. Focal findings in a patient with encephalitis should always raise the possibility of HSV encephalitis. Focal findings include: {1} Areas of increased signal intensity in the frontotemporal, cingulate, or insular regions on T2 weighted MRI imaging. {2} Focal areas of low absorption, mass effect, and contrast enhancement on CT. {3} Periodic focal temporal lobe spikes on a background of slow or low amplitude activity on EEG. It is; however, to be kept in mind that though MRI is very sensitive and specific in detecting lesions mentioned above; approximately 10% of patients with PCR[7] documented HSV encephalitis will have a normal MRI. CT scan is less sensitive than MRI and is normal in up to 33% of patients. The case reported by us had both MRI and CT scan findings to be normal and noncontributory. Nowadays, detection of HSV–DNA in CSF with PCR method has become gold standard for diagnosis of HSV meningitis. HSV-DNA in CSF can be found positive from 24 hours on after the initiation of disease symptoms to one week later after the beginning of treatment. The sensitivity and specificity of detection of HSV–DNA has been found to be 98% and 99% respectively in studies performed. It has been shown that the diagnostic value of the detection of HSV-DNA is same as temporal lobe biopsy. In studies, it has been shown that antiviral therapy has very little effect on sensitivity and specificity of HSV-DNA in CSF PCR. HSV –DNA is found positive in all samples taken before treatment and in 98% of samples taken one week after treatment. The positive predictive value decreased to around 50% in second week of treatment. In the present case, the CSF HSV-DNA PCR sample was sent on the next day of admission and it was reported as HSV-2 PCR positive. Akran ogus et al have reported two cases of entirely normal CSF findings which were diagnosed with HSV encephalitis by means of HSV-DNA.

CONCLUSION: Thus, taking into account the variations in CSF findings in viral meningitis, one should be careful while evaluating CSF report and not make a misdiagnosis and delay treatment.[7]

The most important analysis in patients whose symptoms are consistent with herpes simplex meningitis is the detection of HSV –DNA in CSF with PCR.

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