Abstract

The incidence of seizures in neurosyphilis ranges from 14 to 60%, however, neurosyphilis presenting with status epilepticus (SE) is rare. We report the case of a 49 year old man with no history of epilepsy and with a 9-year history of untreated syphilitic chancre. He presented in October 2005 with four stereotyped epileptic seizures lasting less than 2 minutes followed by a prolonged seizure lasting 20 minutes without recovery of consciousness. He regained consciousness after admission in intensive care unit for SE management. Brain CT scan showed disappearance of cortical sulci with collapse of ventricles. Ophthalmological examination revealed papillary hyperemia. Interictal EEG showed bi-frontal bi- and triphasic spikes. Syphilitic serology in blood then in cerebrospinal fluid (CSF) confirmed the diagnosis of neurosyphilis. The clinical course was favorable after early administration of penicillin and carbamazepine with total remission of seizures. We underline the rarity of neurosyphilis vasculitis as possible etiology of SE and underline the crucial diagnostic value of syphilis serologies in blood and CSF, and highlighting the very good prognosis if treated precociously.

Key words: Status epilepticus, Neurosyphilis, Meningoencephalitis, Seizures, Epilepsy.

Introduction

The incidence of seizures in neurosyphilis ranges from 14 to 60%, however, the revelation of neurosyphilis by status epilepticus (SE) is rare (Primavera et al., 1998). Status epilepticus inaugurates neurosyphilis has been previously reported in the literature (Table). We report an observation of vasculitis neurosyphilis revealed by status epilepticus, focusing on the crucial diagnostic value of syphilis serologies in blood and CSF, and highlighting the very good prognosis if treated promptly.

Case report

A 46 year old man presented with status epilepticus (SE). He had no previous history of epilepsy, no head injury, and no cognitive or psychiatric disorders; but had untreated syphilitic chancre in 2002, was chronic smoker and alcoholic in last 3 months. He presented in October 2005 a stereotypical ictal phenomena described by his wife as 5 generalized tonico-clonic seizures, lasting 2 to 3 minutes associated with tongue-biting, urinary incontinence and loss of consciousness. On presentation, the seizure lasted 20 minutes without recovery. The patient was admitted few hours later with SE, and admitted to the intensive care unit. He was unconscious (GCS: 8/15), apyrexic and ophthalmological examination revealed papillary hyperemia. There were no focal signs on neurological examination. Haematologic investigations (glycemia, fluid and electrolyte balance, blood cell count and inflammatory markers) were normal. CT-brain on admission with and without contrast revealed disappearance of cortical sulci with collapse of ventricles (Fig. 1). Interictal EEG showed alpha activity mixed with a rate of beta activity at 14 to 17 cycles per second, with paroxysmal bi- and triphasic spikes in bi-frontal (Fig. 2). Syphilitic serologies were positive in blood (VDRL 1/4 and TPHA 1/10 240). Analysis of CSF showed a clear fluid, white blood cell (WBC) count of 8 cells/mmc² with lymphocytic predominance, normal glucose (0.60 g/l), and normal protein (0.31 g/l). Direct examination was negative and culture was sterile. In CSF, TPHA was positive at 1/320 and VDRL was negative. After treatment of SE by antiepileptic drugs, the patient received 30 millions of penicillin therapy preceded by 100 mg of hydrocortisone hemisuccinate daily for 10 days, followed by 4 more cycles every 3 months. (Serragui et al., 1999). CSF
<table>
<thead>
<tr>
<th>Authors</th>
<th>Sexe</th>
<th>Age (year)</th>
<th>Type of SE</th>
<th>Mental disorders</th>
<th>Neuroimaging</th>
<th>EEG</th>
<th>Evolution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lovecchio (1995)</td>
<td>F</td>
<td>52</td>
<td>Generalized tonic clonic seizures</td>
<td>Dementia over the past 8 months</td>
<td>Cerebral and cerebellar atrophy</td>
<td>Focal spikes and sharp waves and PLEDs</td>
<td>No seizures; cognitive and CSF improvement</td>
</tr>
<tr>
<td>Heal (1996) (in Primavera 1998)</td>
<td>M</td>
<td>43</td>
<td>CPSE</td>
<td>A change in personality, strange behavior and depression</td>
<td>Cerebral atrophy</td>
<td>Temporal lobe epileptiform focus with spread of activity to the parietal and occipital regions was found</td>
<td>Improved</td>
</tr>
<tr>
<td>Suarez (1996)</td>
<td>M</td>
<td>47</td>
<td>Prolonged, focal motor SE</td>
<td>None</td>
<td>Left frontal focal gumma</td>
<td>Slow waves</td>
<td>Clinical, CSF, and MRI improvement</td>
</tr>
<tr>
<td>Primavera (1998)</td>
<td>M</td>
<td>44</td>
<td>CPSE</td>
<td>Minimal changes in personality over 3 months</td>
<td>Multiple ischemic lesions</td>
<td>PLED</td>
<td>Clinical and CSF improvement. Residual amnesic syndrome</td>
</tr>
<tr>
<td>Lauria (2001)</td>
<td>M</td>
<td>62</td>
<td>Complex partial nonconvulsive SE</td>
<td>None</td>
<td>Increased signal intensity in the gyrus cinguli, inferior frontal lobe, temporal lobe, insula, amygdala, hippocampus, and head of the caudate nucleus</td>
<td>-</td>
<td>Mild anemia and left-sided deep tendon hyperreflexia. Temporal lobe atrophy in MRI</td>
</tr>
<tr>
<td>Vojvodic (2003)</td>
<td>M</td>
<td>45</td>
<td>CPSE</td>
<td>None</td>
<td>Lesion in temporal regions with no compressive effects</td>
<td>Irregular waves with discontinuous arrhythmic delta activity over both frontotemporal regions</td>
<td>Improved</td>
</tr>
<tr>
<td>Marano (2004)</td>
<td>M</td>
<td>48</td>
<td>CPSE</td>
<td>A selective reduction of short term spatial memory</td>
<td>Cortical lesion in the right temporal and basal frontal lobes</td>
<td>Unreported</td>
<td>Unreported</td>
</tr>
<tr>
<td>Gurses (2005)</td>
<td>M</td>
<td>42</td>
<td>Focal-onset, generalized seizures</td>
<td>Progressive memory impairment and speech difficulty</td>
<td>Cerebral atrophy. High signal abnormality, involving bilateral medial and anterior temporal regions</td>
<td>PLED</td>
<td>Mild difficulties in perseverance and free recall of verbal memory</td>
</tr>
<tr>
<td></td>
<td>M</td>
<td>44</td>
<td>Focal motor attacks secondarily generalized</td>
<td>None</td>
<td>Large left sylvian arachnoid cyst without mass effect</td>
<td>PLED</td>
<td>Some episodes of a sensation of heat and some stiffening of the right arm and brief episodes of slurred speech Chang (2006)</td>
</tr>
<tr>
<td>Chang (2006)</td>
<td>M</td>
<td>51</td>
<td>SE</td>
<td>General malaise and subtle cognitive impairment</td>
<td>Normal</td>
<td>Generalized slow background and sharp waves, with phase reversal over the right fronto-temporal area</td>
<td>Mild amnesia</td>
</tr>
<tr>
<td>Li (2006)</td>
<td>M</td>
<td>41</td>
<td>Generalized tonic-clonic</td>
<td>None</td>
<td>Edematous change in the left cingulate gyrus, left temporal lobe, and peri-Rolandic area, which suggested an inflammatory process</td>
<td>Slowing activities without active epileptiform discharges</td>
<td>Mild neurologic sequela of retrograde amnesia</td>
</tr>
<tr>
<td>Otio (2007)</td>
<td>M</td>
<td>29</td>
<td>Generalized tonic-clonic</td>
<td>None</td>
<td>Right mesial temporal hypersignal</td>
<td>Left temporal Spike</td>
<td>-</td>
</tr>
<tr>
<td>Sesar (2008)</td>
<td>M</td>
<td>57</td>
<td>Generalized tonic-clonic</td>
<td>None</td>
<td>Hyperintense signals in both mesial temporal regions</td>
<td>Left temporal paroxysmal activity</td>
<td>Memory impairment</td>
</tr>
<tr>
<td>Our case</td>
<td>M</td>
<td>46</td>
<td>Generalized tonic-clonic SE</td>
<td>None</td>
<td>Disappearance of cortical sulci with collapse of ventricles</td>
<td>Right frontal sporadic abnormalities as bi and triphasic spikes</td>
<td>No seizures. Normal CSF</td>
</tr>
</tbody>
</table>

**Table 1**

Review of cases of SE as first manifestation of neurosyphilis.

- **M** = male, **F** = female, **PLED** = periodic lateralized epileptiform discharges, **SE** = status epilepticus, **CPSE** = complex partial status epilepticus
was normal (WBC: 4 cells/mm³; protein: 0.40 g/l; glucose: 0.76 g/l) and syphilitic serology was negative 13 months after the beginning of penicillin therapy. His outcome was very good with total remission of seizures.

Discussion

Recently, the incidence and clinical spectrum of neurosyphilis has changed. Compared to the pre-antibiotic era, a lower frequency of late neurosyphilis is observed and atypical forms are reappearing. The most frequent clinical patterns are meningovascular, meningeal and general paresis (Conde-Sendín et al., 2004). With the increasing incidence of HIV, AIDS-related mortality, and reduced high-risk sexual behavior among gay men, syphilis has once again become a disease more prominent in the heterosexual population. (Zetola et al., 2007). In Morocco, neurosyphilis is still frequent. Its incidence was 31 cases per year in 1989. Then began to decline from 1990 to reach 10 cases per year in 1997 (Yahyaoui et al., 2005). In CHU hospital Marrakech; we have collected over 108 cases of neurosyphilis
in a period of 14 years, the majority of which were immunocompetents. Epileptic seizures are classified as a complication of neurosyphilis, and can appear at any stage of the disease (Li et al., 2006). SE as the first manifestation of neurosyphilis is very rare (Primavera et al., 1998) and it accounts for about one third of oligosymptomatic events of neurosyphilis in 1971 (Cisse et al., 2002). However, one Indian series of convulsive SE observed neurosyphilis in 1/6th of patients and hence might not be that rare (Sinha et al., 2008). SE can be partial, partial secondary generalized or generalized. It is sometimes preceded by encephalitic manifestations, such psychiatric disorders, memory disorders, confusion or dementia which can progress silently. In the literature (Table), partial SE was more often observed than the generalized SE and meanwhile they occur within cognitive and psychiatric manifestations. Two hypotheses are usually proposed to explain the occurrence of seizures in neurosyphilis (Cisse et al., 2002): All the complications of syphilis are the consequence of a persistent brain inflammation, in which the meningeal irritation is inconsistent. Or the seizures could be the consequence of the presence of small brain lesions secondary to micro-stroke without any clinical neurological sign. The EEG abnormalities have no orientation value to established neurosyphilis aetiology. Abnormalities like spikes, sharp waves, periodic lateralized epileptiform discharges (PLED) and slowing were described (Table 1) (Ance et al., 2004).

The MRI can show (Table): brain atrophy, gumma, multiple vascular lesions or temporal hyperintense signals. In the latter case, neurosyphilis can mimic herpes simplex encephalitis. These findings are probably secondary both to syphilitic inflammation and status epilepticus and usually reversible especially if the diagnosis is made early, but may result in residual atrophy (Marano et al., 2004) (Sesar et al., 2008). In our case, the CT scan found disappearance of cortical sulci with collapse of ventricles due to brain oedema. In the CSF, abnormalities observed include pleocytosis (in 30%), increased protein concentration (in 50 %); reactive VDRL (in 30%) and reactive TPHA (in 100%) (Janier et al., 2002). In Marra study, they defined neurosyphilis as a CSF white blood cell count > 20 cells/ml and also suggested the group of individuals with syphilis who must have a lumbar puncture (serum rapid plasma reagin (RPR) titer > 1/32 and a peripheral blood CD4+ T cell count > 350 cells/ml in HIV-infected subjects) (Marra et al., 2004). Treatment consists firstly, or emergency management of SE, due to its bad prognosis, including a partial one; which can potentially progress to generalized one. Antiepileptic drugs should be followed by the administration of penicillin G. The Jarisch-Herxheimer reaction can be observed during treatment. It occurs 6 to 8 hours after administration of penicillin and can be life-threatening. In this case, the disorders can be prevented by gradually increasing doses of antibiotics with concurrent administration of corticosteroids. Except in the ictal phase; the evolution remains favorable with disappearance of the seizures in most cases.

Preventive therapy is an important element of syphilis control efforts. Treatment by a single dose of penicillin G benzathine or single dose of azithromycin seems to be efficient for prevention of syphilis in persons exposed to infected sexual partners (Hook 1999). Also, male circumcision reduces risk of HIV and syphilis in 60% (Weiss, 2007). However, the awareness, education and treatment of primary and secondary syphilitic forms remain the fundamental step to prevent neurosyphilis.

**Conclusion**

Neurosyphilis has been described as “the great imitator” and with the antibiotic era its forms become more atypical, as it was demonstrated through our case and other cases of SE in the literature. Its late diagnosis and treatment trend to worsen the prognosis, with development of cerebral atrophy, responsible for severe cognitive sequels. All these arguments represent enough reasons to practice syphilitic serology in blood then in CSF in any case of encephalopathy without clear aetiology.

**REFERENCES**


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