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Status epilepticus revealing syphilitic meningoencephalitis

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Abstract

The incidence of seizures in neurosyphilis ranges from 14 to 60%, however, neurosyphillis 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 value of syphilitic serology in blood then in CSF, especially within any atypical presentation of encephalitis, meningoencephalitis; or encephalitis and vasculitis. We highlight 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/mm³ 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 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

Authors	Sexe	Age (year)	Type of SE	Mental disorders	Neuroimaging	EEG	Evolution
Lovecchio (1995)	F	52	Generalized tonic clonic seizures	Dementia over the past 8 months	Cerebral and cerebellar atrophy	Focal spikes and sharp waves and PLEDS	No seizures; cognitive and CSF improvement
Heald (1996) (in Primavera 1998)	M	43	CPSE	A change in personality, strange behavior and depression	Cerebral atrophy	Temporal lobe epileptiform focus with spread of activity to the parietal and occipital regions was found	Improved
Suarez (1996)	M	47	Prolonged, focal motor SE	None	Left frontal focal gumma	Slow waves	Clinical, CSF, and MRI improvement
Primavera (1998)	M	44	CPSE	Minimal changes in personality over 3 months	Multiple ischemic lesions	PLED	Clinical and CSF improvement. Residual amnesic syndrome
Lauria (2001)	M	62	Complex partial nonconvulsive SE	None	Increased signal intensity in the gyrus cinguli, inferior frontal lobe, temporal lobe, insula, amygdala, hippocampus, and head of the caudate nucleus	-	Mild anomia and left-sided deep tendon hyperreflexia. Temporal lobe atrophy in MRI
Camacho-Salas (2002)	M	45	Tonic clonic epileptic seizures	Confusion	Small left temporal infarction	PLED	Satisfactory improvement. Seizures controlled. EEG: a slowing in the known injured area
Vojvodic (2003)	M	45	CPSE	None	Lesion in temporal regions with no compressive effects	Irregular waves with discontinuous arrhythmic delta activity over both frontotemporal regions	Improved
Ance (2004)	M	41	Generalized tonic-clonic SE	None	Bilateral volume loss in medial/anterior temporal lobes	PLED	Substantial improvement. Keep emotional lability, memory loss, and leg spasticity
Marano (2004)	M	48	CPSE	A selective reduction of short term spatial memory	Cortical lesion in the right temporal and basal frontal lobes	Unreported	Unreported
Gurses (2005)	M	42	Focal-onset, generalized seizures	Progressive memory impairment and speech difficulty	Cerebral atrophy. High signal abnormality, involving bilateral medial and anterior temporal regions	PLED	Mild difficulties in perseverance and free recall of verbal memory
	M	44	Focal motor attacks secondarily generalized	None	Large left sylvian arachnoid cyst without mass effect	PLED	Some episodes of a sensation of heat and some stiffening of the right arm and brief episodes of slurred speech Chang (2006)
Chang (2006)	M	51	SE	General malaise and subtle cognitive impairment	Normal	Generalized slow background and sharp waves, with phase reversal over the right fronto-temporal area	Mild amnesia
Li (2006)	M	41	Generalized tonic-clonic	None	Edematous change in the left cingulate gyrus, left temporal lobe, and peri-Rolandic area, which suggested an inflammatory process	Slowing activities without active epileptiform discharges	Mild neurologic sequela of retrograde amnesia
Otto (2007)	M	29	Generalized tonic-clonic	None	Right mesial temporal hypersignal	Left temporal Spike	-
Sesar (2008)	M	57	Generalized tonic-clonic	None	Hyperintense signals in both mesial temporal regions	Left temporal paroxysmal activity	Memory impairment
Our case	M	46	Generalized tonic-clonic SE	None	Disappearance of cortical sulci with collapse of ventricles	Right frontal sporadic abnormalities as bi and triphasic spikes	No seizures Normal CSF

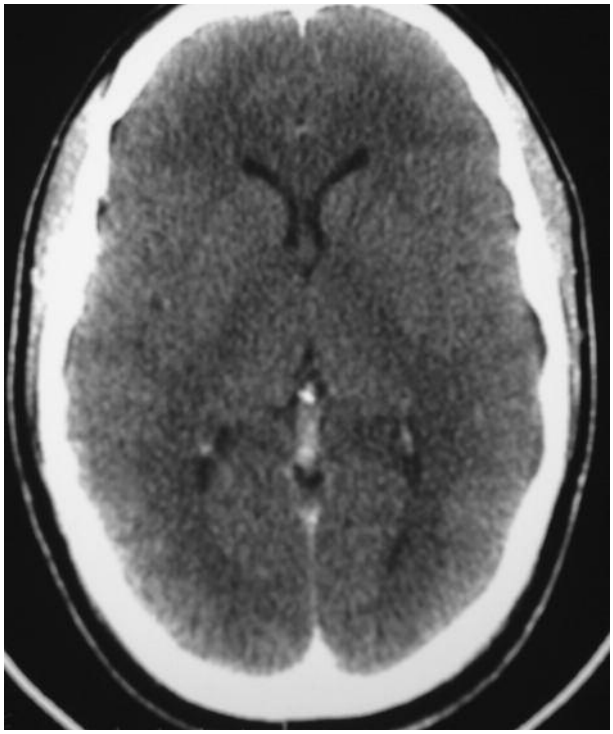

FIG. 1. — Cerebral CT scan showing disappearance of cortical sulci with collapse of ventricles.

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

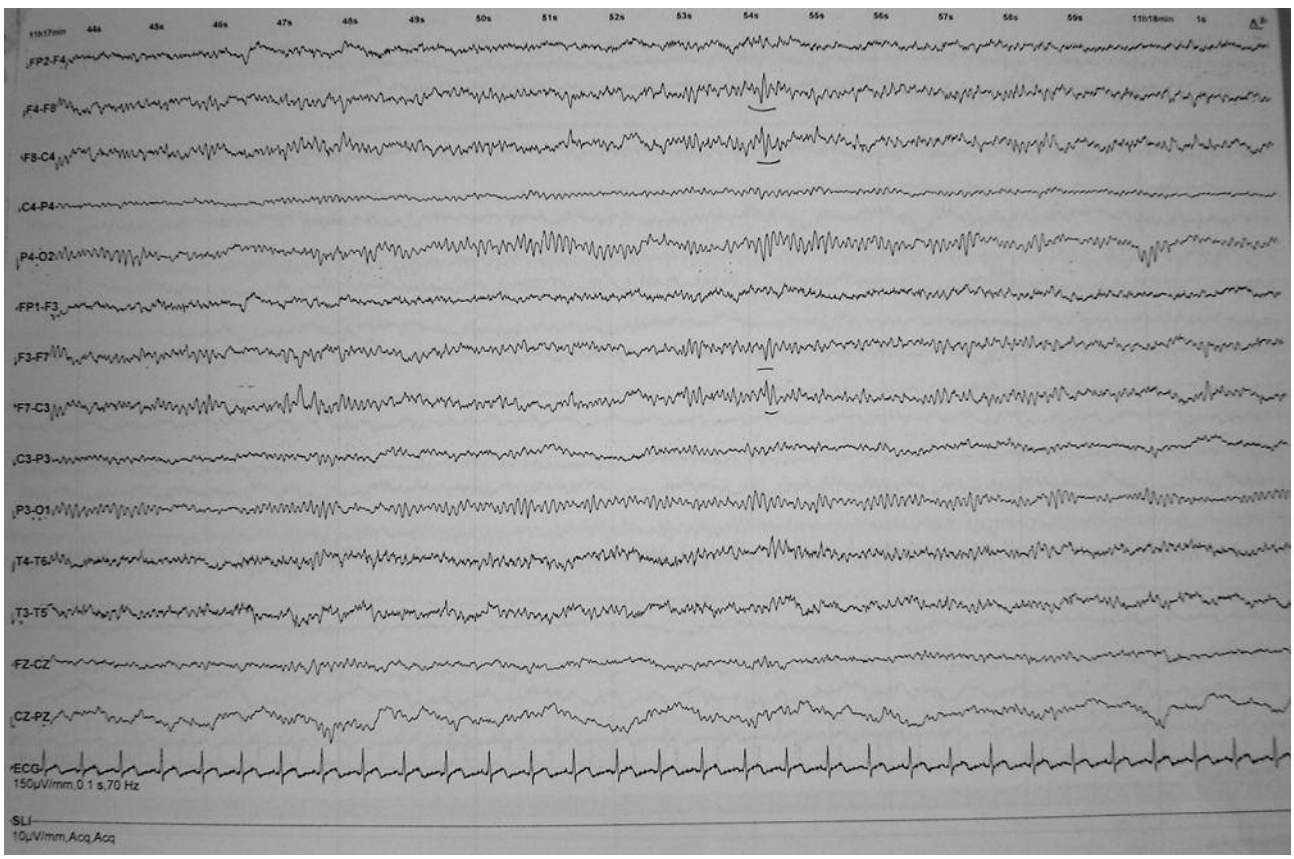

FIG. 2. — EEG showing post ictal bi frontal epileptic abnormalities

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) (Ances *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 à 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 azithromycine 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.

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