Acta Neurol. Belg., 2011, **111**, 69-71

General paresis of the insane: a case with MR imaging

Gregory HELSEN
Department of Neurology, Antwerp University Hospital, Edegem, Belgium

Abstract

We describe the case of a 36-year-old man presenting with cognitive impairment and personality change. General paresis of the insane, the chronic cerebral parenchymatous form of neurosyphilis, was diagnosed. MRI showed the typical severe frontotemporal atrophy. Despite antibiotic treatment his mental state further declined. General paresis is rare and diagnosis is difficult because of the non-specific neuropsychiatric symptoms. Early diagnosis and treatment are important.

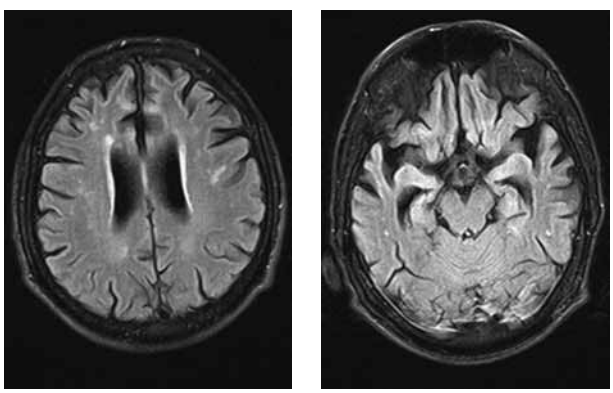
Key words: General paresis of the insane; neurosyphilis; dementia.

Introduction

Neurosyphilis has traditionally been divided into 4 main groups: syphilitic meningitis, meningovascular syphilis, general paresis of the insane and tabes dorsalis (Carr, 2003). General paresis of the insane (GPI), the chronic encephalitic form of neurosyphilis, typically presents as progressive dementia beginning 15-20 years after the original infection (Luo *et al*., 2008). We report a patient with GPI who was at the time of diagnosis already in an advanced stage of this disease and failed to improve after antibiotic treatment.

Case report

A 36-year-old Georgian bus driver consulted because of failing memory and character change. These symptoms were gradually progressive and were first noticed about 1 year before. According to his wife, he was often irritable and aggressive. Cognitive screening was virtually impossible because he was very hostile and not cooperative. He had a bilateral Babinski sign; somatic clinical examination was otherwise unremarkable. A brain CT showed important global atrophy. At first, a hypothesis of alcoholic dementia was made on account of a story of alcoholism although the patient had stopped drinking 2 years earlier and his mental problems seemed to be progressive. Because of this hypothesis, no further investigations were done and neurological follow-up was provided to determine if the problem was progressive after stopping alcohol abuse. About 6 months later neurosyphilis with GPI was diagnosed. Treponema pallidum RPR (rapid plasma reagin test) titer in blood was 1:32 positive and TPHA (Treponema pallidum hemagglutination assay) > 1:20480 positive. HIV serology was negative. Examination of cerebrospinal fluid (CSF) showed a normal cytosis of 4 leukocytes/μl and > 3 oligoclonal IgG-bands. Treponema pallidum RPR in CSF was 1:2 positive and TPHA in CSF was > 1:20480 positive. Due to the significant cognitive deficit, a history of a primary syphilitic infection could not be reliably traced. On clinical re-examination we found Argyll Robertson pupils. Brain MRI at that time showed severe atrophy of the frontal and medial temporal lobes and multiple small hyperintense le-



FIGS. 1A + B. — Axial FLAIR brain MRI demonstrates severe frontotemporal atrophy and small hyperintense lesions mainly in frontal lobes.

sions (Fig. 1). He was treated with intravenous penicilline. RPR in blood 6 months after antibiotic treatment was decreased to a titer of 1:16. Repeat lumbar puncture was refused by the patient. His mental state didn't improve and he needed to be treated with a combination of clotiapine, pipamperon, clorazepate and trazodone. A few years later, clotiapine and pipamperon were replaced by high dosed quetiapine. He had a convulsive epileptic seizure and treatment with valproate was started. About 5 years after the first consultation, he was forcibly admitted in a psychiatric hospital at the request of his family because of progressive misbehaviour. At the time of writing this report, the patient requires a lot of nursing care and attention.

Discussion

GPI (dementia paralytica) is the clinical syndrome of cerebral parenchymatous neurosyphilis displaying neuropsychiatric disturbances with progressive mental and physical decline. GPI is rare nowadays because of treatment of early syphilis. However, considering the diagnosis is important since treatment at an early stage can prevent further progression. Diagnosis is difficult because presenting symptoms (e.g. memory impairment, personality change; Table 1) are non-specific (Carr, 2003; Kodama *et al*., 2000). Merritt, Adams and Solomon, in their classic work of the 20th century on neurosyphilis, stated that the clinical manifestations of GPI mimic "every type of mental disorder" (Merritt, 1946). The only specific clinical clues to the diagnosis are Argyll Robertson pupils or an associated tabes dorsalis but these signs are not always associated (Carr, 2003; Kodama *et al*., 2000). True Argyll Robertson pupils are seen in only 8.7% of GPI but as much as 44.3% display other pupillary abnormalities (Merritt, 1946). Other possible somatic findings are dysarthria, tremor of facial, ligual and hand muscles, aphasia, ataxia, epileptic seizures, paralysis and rarely eye muscle palsies and optic atrophy (Southard, 1928; Merritt, 1946).

Traditionally, screening for syphilis infection is a 2-step process that involves an initial nontreponemal test (VDRL (venereal disease research laboratory) or RPR) followed by a confirmatory treponemal test (FTA-ABS (fluorescent treponemal antibody absorbed) or TPHA) (Calonge, 2004). There is no gold standard for the diagnosis of neurosyphilis and it is usually based on a combination of reactive serologic blood tests, abnormalities of CSF cell count and protein levels or a reactive CSF VDRL (Singh *et al*., 1999). CSF RPR is slightly more sensitive and specific than CSF VDRL. The specificity for current neurosyphilis was 99% for the CSF VDRL and 99.3% for the CSF RPR and the sensitivity was 70.8% for the CSF VDRL and 75% for the CSF RPR (Castro *et al*., 2008). The presence of treponemal antibody in the CSF is not diagnostic for neurosyphilis since it may represent passive diffusion of treponemal antibody from the blood into the CSF rather than active central nervous system infection (Singh *et al*., 1999). Analysis of CSF usually reveals a lymphocytic pleocytosis. In early neurosyphilis higher cell counts are seen than in late neurosyphilis. In a series of Merritt, Adams and Solomon 27% (4/15) of GPI patients had 5 or less white blood cells/μl in CSF. The same authors found a normal cell count in as much as 50% (50/100) of patients with tabes dorsalis (Merritt, 1946). Brain imaging in GPI usually shows bilateral frontal and/or temporal atrophy in combination with T2-hyperintense focal lesions, suggesting gliosis (Zifko *et al*., 1996). One study demonstrated that the grade of cerebral atrophy (especially temporal lobe atrophy) before antibiotic treatment was inversely correlated with the possibilities of recovery of mental state following penicillin treatment (Kodama *et al*., 2000). On pathological examination of GPI one finds cerebral atrophy of the frontal and temporal lobes, a characteristic syphilitic ependymitis and diffuse infiltration of the leptomeninges and small vessels of the cortex with lymphocytes, plasma cells and macrophages. Treponemes are demonstrable in the brain in some 50% of the cases (Merritt, 1946; Storm-Mathisen, 1978).

Table 1

Mental symptoms of general paresis of the insane (Southard, 1928; Merritt, 1946)

Early
- Irritability or herbetude
- Excessive fatigability
- Amnesia
- Oversuggestibility
- Personality change
- Conduct slump
- Headaches
- Change in sleep habits
- Weight loss

Late
- Defective judgement
- Emotional lability
- Depression or elation
- Lack of insight into illness
- Confusion and disorientation
- Poorly systematized delusions
- Seizures

GPI is considered to be a "treatable" dementia but an early diagnosis and treatment is important because the longer the clinical course, the more complicated the clinical manifestation and unfavourable prognosis (Luo *et al*., 2008). Clinicians, especially psychiatrists and neurologists, should therefore remain aware of this diagnosis and serologic tests for syphilis should be routine part of the of the evaluation of patients with neuropsychiatric symptoms (Sobhan *et al*., 2004).

REFERENCES

Carr J. Neurosyphilis. Pract Neurol. 2003;3:328-341.

Luo W, Ouyang Z, Xu H, Chen J, Ding M. *et al*. The clinical analysis of general paresis with 5 cases. J Neuropsychiatry Clin Neurosci. 2008;20:490-493.

Kodama K, Okada S, Komatsu N, Yamanouchi N, Noda S. *et al*. Relationship between MRI findings and prognosis for patients with general paresis. J Neuropsychiatry Clin Neurosci. 2000;12:246-250.

Merritt HH, Adams RD, Solomon HC. Neurosyphilis. New York, Oxford; 1946.

Southard EE. The systematic diagnosis of the main forms of neurosyphilis. In: Southard EE, Solomon HC, eds. Neurosyphilis: modern systematic diagnosis and treatment. Boston, WM Leonard; 1928.

Calonge N; U.S. Preventive Services Task Force. Screening for syphilis infection: recommendation statement. Ann Fam Med. 2004;2:362-365.

Singh AE, Romanowski B. Syphilis: review with emphasis on clinical, epidemiologic, and some biologic features. Clin Microbiol Rev. 1999;12:187-209.

Castro R, Prieto ES, da Luz Martins Pereira F. Nontreponemal tests in the diagnosis of neurosyphilis: an evaluation of the Venereal Disease Research Laboratory (VDRL) and the Rapid Plasma Reagin (RPR) tests. J Clin Lab Anal. 2008;22:257-261.

Zifko U, Wimberger D, Linder K, Zier G, Grisold W. *et al*. MRI in patients with general paresis. Neuroradiology. 1996;38:120-123.

Storm-Mathisen A. Syphilis. In: Vinken PJ, Bruyn GW, eds. Handbook of clinical neurology. Volume 33: Infections of the nervous system. Part I. Amsterdam, Elsevier; 1978.

Sobhan T, Rowe HM, Ryan WG, Munoz C. Three cases of psychiatric manifestations of neurosyphilis. Psychiatr Serve. 2004;55:830-832.

Gregory Helsen, M.D.,
Department of Neurology,
Antwerp University Hospital ,
Wilrijkstraat 10,
B-2650 Edegem (Belgium).
E-mail: gregory.helsen@uza.be