Teaching Case Report

The re-emergence in Canada of meningeovascular syphilis: 2 patients with headache and stroke

Case 1: A previously healthy 51-year-old man came to hospital complaining of headache of 3 weeks’ duration and several days of nausea, vomiting and confusion. He had some difficulty recalling the events of the preceding 3 weeks, but the results of his general and neurologic examinations were otherwise normal. A CT scan of the brain showed bilateral, symmetric infarcts in the heads of the caudate nuclei, with hyperdensity surrounding the anterior communicating artery. The infarcts were confirmed via MRI; conventional angiography showed a 4-mm saccular aneurysm of the anterior communicating artery (Fig. 1). To treat the aneurysm, we successfully inserted detachable coils endovascularly. Afterward, the patient remained medically stable and was discharged home 2 weeks later.

One month after discharge, he returned to hospital with a sudden onset of slurred speech, left-sided facial weakness and unsteady gait. Another CT scan revealed a new left thalamic hypodensity; MRI showed an acute infarct in the left thalamus and recent strokes in the pons and midbrain (Fig. 2). A cerebral angiograph showed bilateral narrowing of the M1 segments of the middle cerebral arteries. Results of transesophageal echocardiography were normal. Given the prominent headache, strokes in several vascular territories and arterial narrowing, we considered vasculitis of the central nervous system (CNS).

Results of cerebrospinal fluid (CSF) analysis showed a predominant lymphocytic pleocytosis (leukocytes $2.44 \times 10^9/L$, 71% lymph), low glucose (2.0 mmol/L) and markedly elevated protein levels (1.55 g/L). Results of a Venereal Disease Research Laboratory test of CSF were positive. Further serum testing provided a positive response to a rapid plasmin reagin test at a 1:64 dilution, confirmed by a Treponema pallidum hemagglutination assay and fluorescent treponemal antibody–absorption staining.

The patient was treated for meningo-vascular syphilis with penicillin G delivered intravenously at a dosage of 4 million units every 4 hours for 2 weeks. On further examination of the patient’s medical history, he did remember a painless penile ulcer that appeared about 1 year earlier. He denied any symptoms of systemic syphilis.

Case 2: A 54-year-old man arrived with a worsening headache of 2 weeks’ duration and unsteady gait. Four months before, he had had an episode of complete right facial weakness and gait ataxia, which improved. Two months before presentation, he had experienced an infarct to his posterior cerebral artery distribution. This caused right hemisensory loss and right inferior visual-field loss associated with a severe headache that persisted for weeks.

A neurologic exam found right inferior quadrantanopia, residual from his recent stroke. His motor and cerebellar results were normal; reflexes were easily elicited. He displayed impaired vibration sense and joint position sense bilaterally at the toes, his gait was broad-based and he exhibited Romberg’s sign.

Given the prominent headache with stroke and new signs and symptoms of posterior column proprioceptive loss, we considered a diagnosis of syphilis.

Results of a rapid plasmin reagin test of serum were positive to a 1:16 dilution. Confirmatory tests also returned positive results, including a Venereal Disease Research Laboratory test of CSF, a serum T. pallidum hemagglutination assay and fluorescent treponemal antibody–absorption staining. CSF fluid analysis revealed a predominant lymphocytic pleocytosis (55 cells, 98% lymphocytes), with elevated protein (0.70 g/L) concentration, a normal glucose level and positive results of a Venereal Disease Research Laboratory test to 1:4 dilution.

Gadolinium MRI scans of the brain and spine showed only the previous stroke in the left posterior cerebral artery. A conventional angiograph appeared normal, with no evidence of arterial narrowing. He was treated with penicillin G for 2 weeks (4 million units every 4 h, delivered intravenously).
On further questioning, the patient reported unprotected heterosexual encounters 10 years earlier, followed by the appearance of 2 painless penile ulcers. These resolved with antibiotic treatment.

Syphilis, a chronic multisystem infection by Treponema pallidum, can be spread venereally or vertically. The disease passes through a series of frequently overlapping stages. The incidence of infectious syphilis has recently increased in Canada from 0.6 cases per 100 000 population (174 patients) in the year 2000, to 3.5 per 100 000 (1127 patients) in 2004. Neurosyphilis occurs with CNS invasion, typically in secondary and later stages of syphilis. Incidence data for neurosyphilis, unfortunately, are unavailable.

In the pre-antibiotic era, symptomatic neurosyphilis developed in about one-third of patients; parenchymal forms involving the brain and spinal cord (syphilitic encephalitis, tabes dorsalis) were seen the most often. With the advent of penicillin therapy, the typical clinical presentation has shifted away from chronic forms of neurosyphilis, which involve CNS parenchyma, to earlier forms that involve CNS meninges and blood vessels (e.g., syphilitic meningitis, meningovascular syphilis with associated ischemic stroke). Persistent and prominent headache in a patient with stroke may suggest meningovascular syphilis even in the absence of meningism. Physicians who manage stroke patients should be aware of early systemic features of syphilis, such as previous chancre, regional lymphadenopathy, alopecia, uveitis, retinitis and rash. They should inquire into risk factors for and history of sexually transmitted infections. Nontreponemal syphilis screening tests such as the rapid plasmin reagin test should be reincorporated into the diagnostic workup of any young patient with stroke and all patients with stroke who have the historical or clinical features outlined.

Syphilis has been described as “the great imitator.” Its recurrence within Canada will challenge clinicians to reeducate themselves about the varied manifestations of this timeless disease.

REFERENCES
1. Garnett GP, Aral SO, Hoyle DV, et al. The natural history of syphilis. Implications for the transmission dynamics and control of infection. Sex Transm Dis 1997;24:185-200.
2. Public Health Agency of Canada. 2004 Canadian sexually transmitted infections (STI) surveillance report: pre-release. Reported infectious syphilis cases and rates in Canada by province/territory and sex, 1993-2004. Available: www.phac-aspc.gc.ca/std-nts/stddata_pre06_04/tab3-2_e.html (accessed 2007 Mar 26).
3. Burke JM, Schuberg DR. Neurosyphilis in the antibiotic era. Neurology 1985;35:1588-71.
4. Holland BA, Perrett LV, Mills CM. Meningovascular syphilis: CT and MR findings. Radiology 1986; 158:439-42.
5. de Villiers WJ, Mitchell PJ. Posterior communicating artery aneurysm caused by meningovascular syphilis. S Afr Med J 1985;67:1039.