Report

Clinical and imaging findings in patients with neurosyphilis: a study of a cohort and review of the literature

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Abstract

Background Most patients with neurosyphilis are considered asymptomatic. The diagnosis is challenging and the role of neuroimaging is not yet well established. The present study was conducted to focus on the clinical findings and further characterize the imaging features of the disease, along with a review of the pertinent literature.

Methods Six male patients with neurosyphilis based on abnormal cerebrospinal fluid findings, five of whom were asymptomatic at presentation, underwent cranial computerized tomography (CT) and magnetic resonance imaging (MRI). They also underwent a complete physical, neurological, and ophthalmological examination, with special attention paid to atherosclerotic vascular risk factors. In addition, all were examined for cardiac involvement using electrocardiography and cardiac ultrasound.

Results The meticulous neurological and ophthalmological examination revealed abnormalities in five patients, most commonly cranial nerve involvement (three patients) and hemiparesis (two patients). The CT and MRI studies revealed abnormalities in five of the six patients, and in all six patients, respectively. The most common findings were brain infarcts, which were demonstrated in four of the six patients. MRI was found to be more sensitive than CT in detecting these brain infarcts, as expected.

Conclusions Vascular insult was the most common neuroimaging finding in our patients with neurosyphilis, probably due to meningovascular endarteritis. Neurosyphilis should always be considered in young patients with unexplained brain infarcts.

The use of penicillin therapy has significantly reduced the incidence of syphilis over time.^{1,2} However, the emergence of acquired immunodeficiency syndrome (AIDS) has dramatically increased the incidence of syphilis throughout the Western world during the last decade.¹⁻⁴ A high rate of syphilis coinfection has been reported in HIV-positive patients residing in northern Israel.⁵ Similarly, a syphilis outbreak among men who have sex with men has been reported in Tel-Aviv, Israel, during 2008–2009.⁶

Invasion of the central nervous system by spirochetes may occur in up to 40% of untreated patients.^{7,8} The central nervous system may be involved in four major syndrome forms: syphilitic meningitis, meningovascular syphilis, parenchymatous neurosyphilis, and gummatous neurosyphilis. Syphilitic meningitis appears mostly within two years following acquisition of the disease. Acute basilar syphilitic meningitis is characterized primarily by the presence of cranial nerve involvement, most commonly the 8th (42%), 7th (41%), 2nd (27%), and 3rd (24%) cranial nerves.⁹ General paresis and tabes dorsalis are usually progressive and largely irreversible.

The diagnosis of neurosyphilis relies on clinical and serological findings, as well as on the examination of cerebrospinal fluid (CSF). There are still only limited data available on the diagnostic value of neuroimaging in neurosyphilis.⁹⁻¹² The present study was conducted to explore further the role of neuroimaging in the diagnosis of this disease, as well as a review of the pertinent literature.

Patients and Methods

All patients referred to our clinic in northern Israel with a positive serology for syphilis, but without a known date of previous infection and/or proper therapy, undergo CSF analysis. The cohort for this study consisted of six consecutive patients who were diagnosed between 2003 and 2010 with neurosyphilis, based on abnormal CSF findings. All were men, ranging in age from 33 to 49 years old (mean 39).

Of the six patients in our cohort, five were asymptomatic at presentation. All six patients underwent cranial computerized tomography (CT) and magnetic resonance imaging (MRI). Detailed histories were taken, atherosclerotic vascular disease risk factors were investigated, and each patient underwent a physical examination with a thorough neurological assessment, including an ophthalmological examination. Baseline routine blood counts and chemistries were also performed. In addition, all six patients were examined for cardiac involvement, including electrocardiography and cardiac ultrasound (US), as part of the work-up for tertiary syphilis.

The Venereal Disease Research Laboratory (VDRL) test or the Rapid Plasma Reagin (RPR) test and the Treponema Pallidum Hemagglutination (TPHA) test were performed on the sera. (In 2007, our medical center's laboratory switched from VDRL to RPR serological testing.) Each patient underwent lumbar puncture for CSF analysis that included protein concentrations, glucose levels, and cell counts. Cerebrospinal fluid, VDRL or RPR, and TPHA tests were performed in all six cases. HIV serology was performed in all six patients using enzyme-linked immunosorbent assay test. The CSF findings were considered compatible with neurosyphilis according to the criteria currently recommended by the Centers for Disease Control (www.cdc.gov).

The six patients diagnosed with neurosyphilis were treated with intravenous (IV) penicillin and scheduled six months later for a repeat CSF examination to evaluate the response to treatment. They all had a cranial CT performed with a 16 or 64 multidetector row CT (MX 8000 IDT & Brilliance, Philips, Netherlands), with or without contrast, and by a 1.5T MRI system (Signa HDX14, GE Healthcare, Milwaukee, WI, USA). The MRI studies included T1-weighted spin echo or fast spin echo sequences, T2-weighted imaging (fast spin echo), T2 fluid attenuated inversion recovery, and diffusion weighted imaging sequences in different planes before and after IV injection of contrast material, which was gadolinium based.

Case 1

A 40-year-old man underwent serological screening for syphilis during withdrawal therapy from alcoholism. The blood work-up indicated a positive VDRL test with a titer of 1 : 16 and a positive TPHA test. The patient did not report any clinical history of syphilis or neurological complaints. The neurological examination was normal, and HIV serology results were negative.

To rule out asymptomatic neurosyphilis, the patient underwent lumbar puncture. The CSF examination demonstrated normal protein levels; lymphocytic pleocytosis (17/mm³); neutrophils 2/mm³; a positive VDRL test with a titer of 1 : 2; and a negative TPHA test. Consequently, the patient was diagnosed with asymptomatic neurosyphilis and was treated with IV crystalline penicillin, 24 million units/day, for 14 days.

Six months later, a persistent positive serum VDRL test was found on two consecutive occasions, with titers of 1 : 32 and

1 : 64. He underwent a repeated CSF examination, which showed normal protein levels and lymphocyte counts, a positive VDRL test with a titer of 1 : 2, and a positive TPHA test with a titer of 1 : 2560. A repeated neurological examination revealed a decreased vibratory sense and absence of the Achilles reflex response.

Electromyographic test results were normal, and the brain CT disclosed mild generalized atrophy above and below the tentorium (mild dilatation of the third and fourth ventricles). The left lateral ventricle was found to be somewhat wider than the right one. A mild to moderate dilatation of the frontal and temporal sulci and prominent dilatation of the sylvian fissures were noted. Mild dilatation of the cerebellar and parietal sulci was also observed.

MRI demonstrated the same atrophic changes and revealed two small lesions not seen on the CT. A small ill-defined left parietal lesion of high intensity on both T2WI and fluid attenuated inversion recovery was found adjacent to the roof of the left ventricle. The other lesion abutted the lower lateral wall of the fourth ventricle, compatible with an old infarct.

The patient was again treated with IV crystalline penicillin, 24 million units/day, for 14 days. Unfortunately, he did not return for his follow-up examination and died two years later from an unknown cause.

Case 2

A 40-year-old man with positive HIV (CD4 count 190/ μ l) and hepatitis C virus (HCV) serologies underwent routine serological screening for syphilis. The work-up indicated a positive RPR test with a titer of 1 : 128 and a positive TPHA test. Three months later, he was hospitalized because of seizures, loss of consciousness, and fever. The repeated serological RPR test was positive with a titer of 1 : 64.

The CSF examination revealed normal protein levels; slight lymphocytic pleocytosis (5 cells/mm³); a positive VDRL test with a titer of 1 : 8; and a positive TPHA test. The patient did not report any clinical history of syphilis or neurological complaints. The neurological examination was normal. The brain CT disclosed mild general cerebral atrophy, more prominent in the frontal lobes, and somewhat dilated superior ophthalmic veins on both sides. MRI demonstrated the same findings and showed mild atrophy of the parietal convexity as well.

Based on the CSF findings, the patient was diagnosed with neurosyphilis and was treated with IV crystalline penicillin, 24 million units/day, for 14 days. He did not return for his follow-up examination and died four years later from an unknown cause.

Case 3

A 33-year-old patient with a history of drug abuse and positive HCV serology underwent serological screening for syphilis. The work-up indicated a positive RPR test with a titer of 1 : 2 and a positive TPHA test. The patient did not report any clinical

history of syphilis or neurological complaints. The HIV serology results were negative.

The CSF examination demonstrated normal protein and glucose levels without pleocytosis. The VDRL test was positive with a titer of 1 : 2, and the TPHA test was negative. The neurological examination revealed anisocoria and bilateral Adie's tonic pupil syndrome. The brain CT and MRI findings were normal except for mild atrophy in the convexity of the cerebral hemispheres.

The patient was diagnosed with neurosyphilis and treated with IV crystalline penicillin, 24 million units/day, for 14 days. He did not return for further follow-up examination.

Case 4

A 49-year-old healthy man, who came to Israel from an endemic region for syphilis, underwent routine serological testing for syphilis. The work-up indicated a positive VDRL test with a titer of 1 : 2 and a positive TPHA test. The HIV serology results were negative. The patient recalled noticing a small ulcer on his penis 1.5 years earlier, which had healed spontaneously without leaving a scar and without ensuing skin eruptions. Five years earlier, he had also been treated with antibiotics for gonorrhea.

The CSF examination demonstrated: elevated protein levels (55 mg/dL); normal glucose levels; lymphocytosis (20 cells/ mm³); a positive VDRL test with a titer of 1 : 8; and a positive TPHA test with a titer of 1 : 160. The neurological examination revealed right hemiparesis, increased muscular tonus, hyperreflexia, and tongue deviation. In addition, an Argyle Robertson pupil was found. Concerning atherosclerotic vascular risk factors, the patient had both hypertension and hyperlipidemia.

The brain CT disclosed an old left cerebellar infarct. The MRI demonstrated mild to moderate cerebral atrophy, mainly in the parietal lobes; the same old left infarct in the anterior inferior cerebellar artery territory; an old partially hemorrhagic left frontoparietal infarct, affecting both white matter and gray matter in the convexity of the left hemisphere (Fig. 1); and another old left upper paramedian parietal infarct. There was a tiny vascular insult noted within the body of the left caudate nucleus, adjacent to the ventricular wall. Multiple small and tiny lesions of high intensity were observed on T2-weighted sequences in the periventricular and deep white matter, compatible with ischemic lesions and lacunar infarcts due to small vessel disease. In addition, numerous prominent Virchow– Robin spaces were depicted. Carotid Doppler ultrasound (US) demonstrated normal hemodynamics without pathological changes in the carotid arteries on both sides.

The patient was treated with IV crystalline penicillin, 24 million units/day, for 14 days. Six months later, the patient underwent a repeated CSF examination, which revealed close to normal protein levels (42 mg/dL); normal glucose levels; mild lymphocytosis (6 cells/mm³); a positive VDRL test with a titer of 1 : 4; and a positive TPHA test with a titer of 1 : 80. There was no change in the results of the neurological examination. A repeated brain MRI showed all of the lesions detected in the previous MRI, with no new findings.

Case 5

A 33-year-old patient was admitted to the neurology department because of vision disturbances in his right eye. The neurological examination revealed left abducens paresis. The right eye visus was 6/6. As part of the routine laboratory workup, the patient underwent a serological examination for syphilis, which indicated a positive VDRL test and a positive TPHA test. The HIV serology results were negative. The CSF examination showed elevated protein and glucose levels, lymphocytosis (12 cells/mm³), and negative VDRL and TPHA tests. The patient reported no clinical history of syphilis.

The brain CT disclosed a hypodense lesion within the genu of the corpus callosum, representing an old encephalomalacic focus. An MRI performed two days later (Fig. 2) revealed two

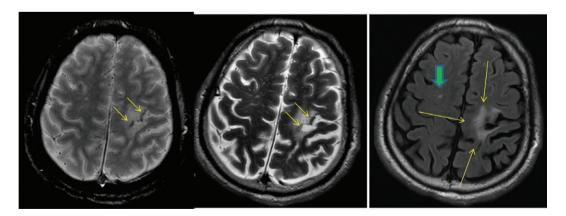


Figure 1 Case 4. Partially hemorrhagic (small arrows) chronic encephalopathy surrounded with gliosis (long arrows), possibly due to an old vascular event. Note the small high-intensity white matter lesion in the right frontal lobe (arrowhead)

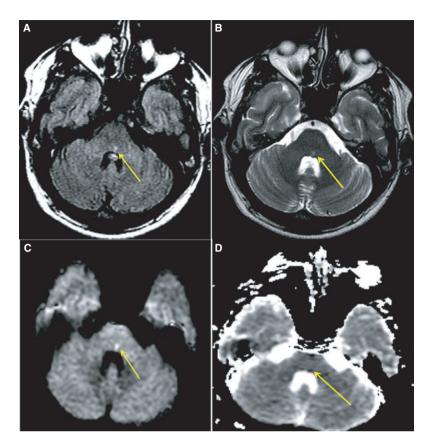


Figure 2 Case 5. A tiny acute infarct in the pons, adjacent to the anterior wall of the 4th ventricle. Demonstrated as a bright spot on T2 and FLAIR sequences and proved by restricted diffusion, as shown with high intensity on DWI and a black tiny spot on ADC maps. ADC, apparent diffusion coefficient; DWI, diffusion weighted imaging; FLAIR, fluid attenuated inversion recovery; FSE, fast spin echo

more lesions in the genu of the corpus callosum, with isotropic diffusion and intensity equal to that of CSF, raising the possibility of cysts, lacunae, or Virchow–Robin spaces. A tiny acute infarct with restricted diffusion was depicted in the posterior aspect of the pons adjacent to the anterior wall of the fourth ventricle. In addition, a small lacunar infarct was observed anterior to the right temporal horn. Carotid Doppler US demonstrated normal hemodynamics without pathological changes in the carotid arteries on both sides. Electrocardiogram and cardiac US results were also normal, with no indication of any changes due to ischemic events.

As neurosyphilis was the likely diagnosis, the patient was treated with IV crystalline penicillin, 24 million units/day, for 10 days. His condition improved within several days after initiation of therapy, with fading of his neurological complaints. Eighteen months later, he was hospitalized again because of diplopia and weakness of his right extremities. The neurological examination revealed left abducens paresis and mild weakness of his right arm and leg. He declined a repeated CSF examination.

A repeated cranial CT did not point to any changes when compared with the previous one (Fig. 3). A second MRI demonstrated resolution of the tiny pontine infarction noted in the first one, with a new acute, more extensive infarct appearing in the mesencephalon with restricted diffusion weighted imaging. There were no other significant changes when compared to the previous MRI study. A third MRI (Fig. 4) performed 14 months later again showed the left mesencephalic infarct, which was now chronic, with newly appearing subacute ischemic lesions/infarcts in the medulla oblongata that were more prominent on the left side. Three years later, the patient's neurological condition remained unchanged.

Case 6

A 40-year-old patient with a positive serology for HCV underwent routine serological testing for syphilis, which indicated a positive RPR test with a titer of 1 : 64 and a positive TPHA test. The HIV serology results were negative. The patient recalled a small ulcer on his penis that had appeared seven years earlier and had healed spontaneously without leaving a scar. He did not report any history of eruptions or neurological complaints.

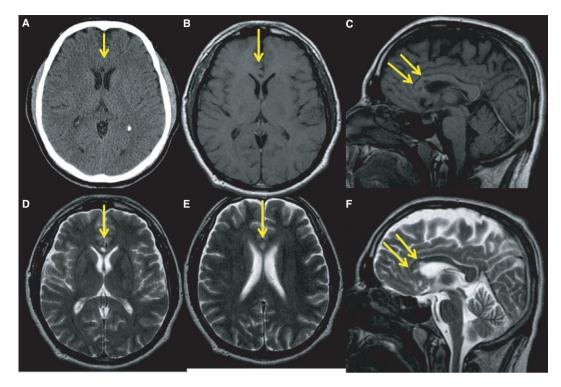


Figure 3 Case 5. Axial computed tomography and magnetic resonance imaging (T1) showing an encephalomalacic small lesion in the genu of the corpus callosum. T2 (fast spin echo) and T1 sagittal images and two axial images on different planes depicting two different lesions

The CSF examination demonstrated: elevated protein levels; normal glucose levels; lymphocytosis (10 cells/mm³); neutrophils 37/mm³; a positive VDRL test with a titer of 1 : 2; and a positive TPHA test. The neurological examination and brain CT were interpreted to be normal. The MRI showed multiple old lacunar infarcts in the basal ganglia on both sides, including the internal and external capsules. The patient did not have atherosclerotic vascular risk factors except for untreated mild hypertension. He was treated with IV crystalline penicillin, 24 million units/day, for 14 days. The patient did not return for further follow-up examination.

Results

The clinical, laboratory, and neuroimaging data are summarized in Table 1. Five asymptomatic, mostly high-risk patients were diagnosed following routine serological testing for syphilis, and the sixth patient was diagnosed because of neurological complaints. Of the six patients, only one tested positive for HIV but without clinical signs of AIDS. Two patients recalled untreated penile lesions in the past, which healed spontaneously.

The neurological examination revealed abnormalities in five of the six patients. The most common neurological findings were cranial nerve involvement, observed in three of the six (50%) patients. Hemiparesis was the second most common finding, occurring in two of the six (33%) patients. The other neurological findings, which were found in one patient each, included seizures, loss of vibration, hyperreflexion, increased muscular tone, and tongue deviation.

The CSF findings (Table 1) included lymphocytic pleocytosis in five patients, positive VDRL test in five patients, and positive TPHA test in three. Two patients had atherosclerotic vascular risk factors, namely, hypertension and hyperlipidemia in one patient (case 4) and mild untreated hypertension in a second patient (case 6). The former patient had a Doppler US examination of his carotid arteries, which showed normal hemodynamics. All six patients had normal results on cardiac US examination.

The brain CT indicated abnormal findings in five of the six patients, whereas the MRI demonstrated pathological findings in all six patients. The MRI detected cerebral infarcts in four of the six patients and was more sensitive than the CT, which detected infarcts in only one case.

All six patients underwent IV therapy with crystalline penicillin, 24 million units/day, for 14 consecutive days, as recommended by the Centers for Disease Control. Of the three patients who were followed up, only one

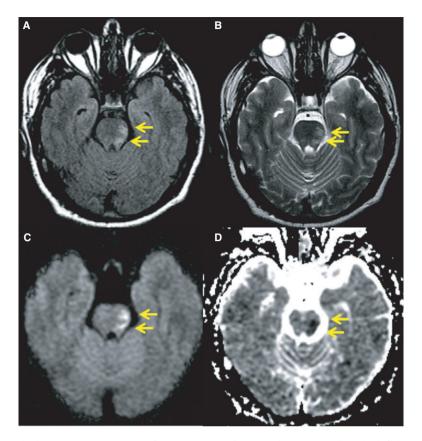


Figure 4 Case 5. 14 months later – an appearance of a new acute infarct, as demonstrated in the left lower aspect of the mesencephalon as a bright lesion on both T2 (FSE) and FLAIR sequences, with restricted diffusion on DWI and ADC maps (red arrows). ADC, apparent diffusion coefficient; DWI, diffusion weighted imaging; FLAIR, fluid attenuated inversion recovery; FSE, fast spin echo

improved neurologically. The two patients who underwent a repeated CSF examination following therapy demonstrated improvement in some of the CSF parameters.

Discussion

Neurosyphilis is often asymptomatic. Most of our patients were diagnosed by routine serological tests in asymptomatic high-risk patients. Although the majority of our patients, with the exception of one, had no initial neurological complaints, the neurological examination revealed abnormal findings in three patients. Upon meticulous history taking, two patients admitted having untreated penile ulcers in the past. These findings underscore the value of serological testing for syphilis in asymptomatic high-risk patients.

There have been only a few reports of neuroradiological findings in a relatively small series of patients with neurosyphilis.^{10–12} Peng *et al.*¹¹ described 14 patients

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with neurosyphilis whose CT results were similar to their MRI findings, though MRI seemed to be more useful in the diagnosis of general paresis. Using CT and MRI with 14 HIV-negative neurosyphilis patients, Peng *et al.*¹¹ demonstrated cerebral infarction in six cases, arteritis in four, nonspecific white matter lesions in three, acute syphilitic meningitis in one, and normal neuroimaging in one. In addition, four of their patients had general paresis supported by the MRI findings.¹¹

In our cohort, the MRI was more sensitive than the CT in detecting brain infarcts, as expected due to its superiority in detecting small infratentorial lesions. The most common MRI findings were brain lacunar infarcts detected in four of the six patients. In two of these patients, there were risk factors for atherosclerotic vascular disease, namely hyperlipidemia and/or hypertension. In one of them (case 4) with both hyperlipidemia and hypertension, the carotid Doppler US was normal, and the patient was found to have an Argyle Robertson pupil. In another patient (case 6) with mild untreated

Cranial MRI	Cranial CT	Neurological complaints and findings	CSF findings	Abnormal serological findings	Patient no./ sex/age (years)
Two small infarcts adjacent to left ventricle and 4th ventricle	Generalized atrophy above and below the tentorium. Mild dilatation	1st: none 2nd: diminished vibratory	1st: lymph: 17/mm ⁹ VDRL: 1 : 2	1st: VDRL: 1 : 16 TPHA: +ve	1/M/40
	of 3rd and 4th ventricles	sense. Achilles tendon reflex: -ve	2nd: VDRL: 1 : 2 TPHA: 1 : 2560	2nd: VDRL: 1 : 64 TPHA 1 : 2560	
Mild enlargement of the	Mild general atrophy. Slightly dilated	Seizures, loss of consciousness, fever,	Lymph: 5/mm ³	RPR: 1:128	2/M/40
cerebral sulci	superior ophthalmic veins, bilaterally	neurological examination – normal	VDRL: 1 : 8TPHA: +ve	TPHA: +ve	
				HIV: +ve HCV: +ve	
Mild atrophy in the convexity of	Mild atrophy in the convexity of	Anisocoria,	VDRL: 1 : 2	RPR: 1 : 2	3/M/33
the cerebral hemisphere	the cerebral hemisphere	bilateral Adie's tonic pupils	TPHA: -ve	TPHA: +ve	
				HCV: +ve	
Several infarcts in the cerebellum, fronto-	Old left cerebellar infarct	Right hemiparesis, increased tonus,	Proteins: 55 mg/dL	VDRL: 1 : 2	4/M/49
parietal region, caudate nucleus,		hyperreflexia, tongue deviation,	Lymph: 20/mm ³	TPHA: +ve	
periventricular and deep white matter		Argyle Robertson pupil	VDRL: 1:8		
			TPHA: 1 : 160		
1st: lesions in the genu of the corpus	1st and 2nd: hypodense lesion within	1st: vision disturbances.	Proteins: 67 mg/dL	VDRL: 1 : 2	5/M/33
callosum + infarcts in the pons and	the ingenue of the corpus	Right visus 6/60	Lymph: 12/mm ³	TPHA: +ve	
temporal horn	callosum = old	Left abducens	VDRL: -ve		
2nd: resolution of the pontine infarction	encephalomalacic focus	2nd: left abducens paresis. Mild	TPHA: -ve		
 + new infarct in the mesencephalon 3rd: new infarct in the medulla oblongata 		weakness of right arm and leg			
Multiple lacunar infarcts in the basal ganglia on both sides	Normal	Normal	Proteins: 128 mg/dL Lymph: 10/mm ³ Neutrophils: 37/mm ³	RPR: 1 : 64 TPHA: +ve HCV: +ve	6/M/40
			VDRL: 1 : 2 TPHA: +ve		

Table 1 Summary of major findings

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resonance imaging; N, normal; -ve, negative; +ve, positive; RPR, Rapid Plasma Regain; TPHA, Treponema Pallidum Hemagglutination; VDRL, Veneral Disease

hypertension, the relatively young age (40 years old) and serological and CSF findings of active untreated syphilis made asymptomatic atherosclerotic vascular disease unlikely as the cause of his brain infarcts. Furthermore, all six patients had normal cardiac US, which ruled out patent foramen ovale as a possible conduit for emboli. Clotting disorders were not a likely cause because of the involvement of small blood vessels in the brain without any evidence of thrombotic episodes elsewhere.

Gurses et al.¹⁰ found some incongruency with the clinical findings, as two of their eight patients with neurosyphilis had normal MRI studies, though both had abnormal neurological findings. The cranial nerve neuropathy in three of our six cases was compatible with the sequelae of syphilitic meningitis. This may explain the absence of specific parallel MRI findings. Cranial nerve abnormalities are seen in 45% of patients with syphilitic meningitis.⁸ Meningovascular lesions are common in patients with neurosyphilis, and many manifest neuroradiologically as small infarcts in the basal ganglia or brain stem, as in our patients. These may result from insult to perforating arteries by endarteritis, causing cortical and subcortical infarcts, leptomeningeal enhancement, meningitis, and arteritis.7,13 Neurosyphilis resulting in cerebral infarctions was found to be common in our study, as in previous research.7,11,14

The presentation of neurosyphilis has changed over the last 40 years.¹⁵ Patients now tend to present atypically with seizures, ophthalmic symptoms such as poor vision, stroke, confusion, or personality changes.¹⁵ The present study has demonstrated that routine serological testing for syphilis, followed by CSF examination of the positive cases, may detect asymptomatic neurosyphilis. Subsequent meticulous neurological examination may detect abnormal findings even in patients who initially present without complaints. Moreover, cranial neuroimaging may detect abnormal findings not always suspected during neurological examination. Vascular lesions were the most common neuroimaging finding in our patients with neurosyphilis, probably due to meningovascular endarteritis, and MRI was found to be more sensitive than CT in detecting such lesions. In conclusion, neurosyphilis should always be considered in young patients with idiopathic brain infarcts.

References

- I Musher DM, Hamill RJ, Baughn RE. Effect of human immunodeficiency virus (HIV) infection on the course of syphillis and on the response to treatment. *Ann Intern Med* 1990; 113: 872–881.
- 2 Kinghorn G. The re-emergence of syphilis. *Br J Hosp Med* 1993; **49**: 683–685.
- 3 Hilton C. General paralysis of the insane and AIDS in old age psychiatry: epidemiology, clinical diagnosis, serology and ethics. *Int J Geriatr Psychiatry* 1998; 13: 875–885.
- 4 Tien RD, Gean Marton AD, Mark AS. Neurosyphilis in HIV carriers: MR findings in six patients. *Am J Roentgenol* 1992; 158: 1325–1328.
- 5 Joffe H, Bamberger E, Nurkin S, *et al.* Sexually transmitted diseases among patients with human immunodeficiency virus in northern Israel. *IMAJ* 2006; 8: 333–336.
- 6 Brosh-Nissimov T, Mor Z, Avramovich E, *et al.* Syphilis outbreak among men who have sex with men, Tel Aviv, Israel 2008-2009. *IMAJ* 2012; 14: 152–156.
- 7 Holland BA, Perrett LV, Mills CM. Meningovascular syphilis: CT and MR findings. *Radiology* 1986; 158: 439-442.
- 8 Workowski KA, Bergman S. Sexually transmitted diseases guidelines 2010. MMWR Recomm Rep 2010; 59: 1–110.
- 9 Storm-Mathisen A. Syphilis. In: Vinken PJ, Klawans HL, eds. *Handbook of Clinical Neurology*, Vol. 33. North-Holland Publishing Company, 1978: 337–394.
- 10 Gürses C, Bilgiç B, Topçular B, et al. Clinical and magnetic resonance imaging findings of HIV-negative patients with neurosyphilis. J Neurol 2007; 254: 368–374.
- 11 Peng F, Hu X, Zhong X, *et al.* CT and MRI finding HIV-negative neurosyphilis. *Eur J Radiol* 2008; 66: 1–6.
- 12 Zifko U, Wimberger D, Lindner K, *et al.* MRI in patients with general paresis. *Neuroradiology* 1996; **38**: 120–123.
- 13 Gallego J, Soriano G, Zubieta JL, *et al.* Magnetic resonance angiography in meningovascular syphilis. *Neuroradiology* 1994; 36: 208–209.
- 14 Aldrich MS, Burke JM, Gulati SM. Angiographic findings in a young man with recurrent stroke and positive fluorescent treponemal antibody (FTA). *Stroke* 1983; 14: 1001–1004.
- 15 Carlson JA, Dabiri G, Cribier B, et al. The immunopathobiology of syphilis: the manifestations and course of syphilis are determined by the level of delayedtype hypersensitivity. Am J Dermatopathol 2011; 33: 433-460.