

Pure Motor Hemiplegia due to Meningovascular Neurosyphilis

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● **Two young male homosexuals developed prodromal syndrome followed by penicillin-responsive meningitis and the acute onset of pure motor hemiplegia. The clinical and laboratory features are consistent with meningovascular neurosyphilis. Basis pontis infarctions were subsequently demonstrated on magnetic resonance imaging scans. To our knowledge, this is the first description of syphilitic arteritis as a pathophysiologic basis for pure motor hemiplegia.**

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Pure motor hemiplegia (PMH) was defined by Fisher and Curry¹ as unilateral complete or incomplete paralysis of the face, arm, and leg unaccompanied by sensory signs, visual field defect, dysphasia, apraxia, agnosia, or brain-stem signs. The original pathologic lesions were lacunar infarctions of the internal capsule and basis pontis, but a wide variety of causes have subsequently been described along the full extent of the pyramidal motor pathway.^{2,7} To our knowledge, PMH has not been described in the setting of meningovascular neurosyphilis (MVNS). This report documents the occurrence of PMH due to ischemic infarctions of the basis pontis caused by MVNS in two homosexual men who subsequently developed the acquired immunodeficiency syndrome (AIDS).

REPORT OF CASES

CASE 1.—A 35-year-old right-handed man was admitted to another hospital with

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flaccid right hemiplegia of one day's duration. He had a two-month history of mild fatigue, malaise, and a 5-lb weight loss. He had daily severe throbbing periorbital headaches that were present on awakening for two weeks, and that were accompanied by nausea and anorexia for three days. On the day prior to admission his right side "gave out" and he collapsed on the floor. Over the next three hours the weakness progressed in a stepwise fashion to a complete paralysis of the right arm and leg.

On admission, he was noted to have a flaccid right hemiplegia that remained unchanged prior to transfer to Massachusetts General Hospital, Boston, four days later. He denied sensory symptoms, visual symptoms, hearing deficit, dysphagia, dysarthria, dysphasia, fever, lymphadenopathy, rash, drug abuse, and tick bite. He was bisexual and had been promiscuously sexually active in the past, but had been abstinent for six months. He had been treated for two episodes of gonorrhea but denied a history of chancre or previous cases of syphilis. There was neither a personal history of migraine nor a family history of neurologic disease.

On physical examination the patient was thin, chronically ill-appearing, afebrile, and normotensive, with shotty cervical and axillary adenopathy. The heart sounds were normal without murmur or click, and the carotid pulses were full and without bruit. Neurologic examination revealed a depressed affect, minimal neck pain and stiffness at extreme flexion, mild right central facial palsy, a complete flaccid hemiplegia of the right arm and leg, hyperactive deep tendon reflexes, extensor plantar response, Hoffman's sign, and triple flexion response on the right. Results of detailed examination of sensation, pupillary responses, and extraocular movements were normal.

Significant laboratory findings included mild transient elevation of serum transaminase levels, antinuclear antibody titer of +1:8, cutaneous anergy to mumps and purified protein derivative, negative serum antibody to human immunodeficiency virus (HIV), a T-cell helper to suppressor ratio of 0.07:1, IgG antibody to *Borrelia burgdorferi*, acute 1:160 and convalescent 1:80, and minimal prolapse of the anterior

mitral valve leaflet shown on echocardiogram. Results of the following tests were normal or negative: serum immunoelectrophoresis, coagulation parameters, blood cultures, bacterial, fungal, mycobacterial, and viral (including HIV) cultures of the cerebrospinal fluid (CSF), and cryptococcal antigen in the CSF.

Initially, the rapid plasma reagin (RPR) titer was +1:256 with a fluorescent treponemal antibody absorption (FTA-ABS) of 4+, and five months later the RPR was negative. The Table shows the results of serial lumbar punctures, all of which had normal opening and closing pressures. Results of contrast cranial computed tomographic (CT) scans performed one and 11 days after the initial event were normal. A magnetic resonance imaging (MRI) scan three weeks after the initial event revealed a lesion in the basis pontis region of the left upper pons with prolonged T1 and T2 (Figure, left), consistent with an infarction.

There was a marked rise in the CSF pleocytosis, with a leukocyte count of 63 to 234 $\times 10^6/L$ (63 to 234/mm³), prior to the initiation of antibiotic therapy. The patient was started on intravenous penicillin G therapy (20 million U/d) on admission to Massachusetts General Hospital and completed a three-week course without the occurrence of a Jarisch-Herxheimer reaction. Results of serial CSF examinations showed improvement and eventual normalization of the CSF (Table). The flaccid right hemiplegia gradually became spastic and the patient regained a significant degree of strength. On discharge to a rehabilitation facility two months after admission he could ambulate with a walker but had impairment of fine movements of the right hand.

Results of neurologic examination five months after the event revealed minimal right spastic hemiparesis, hyperreflexia, extensor plantar response, and mild impairment of fine finger movements of the right hand. The follow-up CSF examination result was normal (Table). A contrast CT scan result clearly demonstrated the left basis pontis infarction (Figure, right) without atrophy or other lesions. Serum HIV antibody was now reactive, he developed *Pneumocystis carinii* pneumo-

Results of Serial Cerebrospinal Fluid Examinations*

	Case 1					Case 2		
	Day 3	Day 5	Day 10	Day 24	Day 42	Day 1	Day 6	Day 26
Leukocytes, No. $\times 10^6$ /L (No./mm ³)	63 (63)	234 (234)	154 (154)	2 (2)	6 (6)	111 (111)	18 (18)	0
Lymphocytes, %	84 (0.84)	89 (0.89)	92 (0.92)	60 (0.60)	83 (0.83)	100 (1.0)	100 (1.0)	...
Protein, g/L (mg/dL)	0.94 (94)	0.69 (69)	0.51 (51)†	0.34 (34)	0.24 (24)	1.30 (130)	0.80 (80)	0.58 (58)
Glucose, mmol/L (mg/dL)	1.8 (33)	1.8 (33)	2.3 (41)	2.7 (49)	12.6 (227)	1.6 (28)	2.1 (38)	2.7 (48)
RPR	...	—	+	...	—	1:8	1:4	...
FTA-ABS	2+
Oligoclonal bands, No.	1

* Day designations indicate number of days following onset of pure motor hemiplegia; RPR, rapid plasma reagin; FTA-ABS, fluorescent treponemal antibody absorption; minus sign, absence of substance; plus sign, presence of substance.

†IgG, 0.136 g/L (13.6 mg/dL); albumin, 0.38 g/L (38 mg/dL); ratio of IgG to albumin, 0.36:1.



Left, Inversion recovery sequence transverse magnetic resonance images showing lesion in left basis pontis region of upper pons with prolonged T1, consistent with infarction. Right, Contrast computed tomographic scan, performed four months after magnetic resonance imaging shown at left, now clearly reveals left basis pontis infarction. No atrophy or other pathological lesions were evident.

nia, and was treated with two courses of intravenous sulfamethoxazole and trimethoprim therapy.

CASE 2.—A 38-year-old right-handed homosexual man presented four months prior to admission because of penile chancres. He was treated with a single dose of intramuscular penicillin. At that time he also noted a “red” right eye, mild photophobia, and blurry vision in the right eye. Over the ensuing months his visual complaints gradually worsened after an initial period of improvement, he lost approximately 9 kg and he noticed decreased hearing in his left ear. For three weeks prior to

admission he noted occipital headache, mild stiff neck, and mental dullness, without fever or rash. He denied recent travel, exposure to pets, and intravenous drug use. He denied a history of previous syphilis but had been treated for several episodes of gonorrhea.

On the day of admission he noted acute deterioration of the vision in his right eye. The right eye showed evidence of posterior uveitis with nearly complete retinal detachment. There was no evidence of optic neuritis and the left eye was normal. There was moderately severe sensorineural hearing loss in the left ear with a mild loss in

the right ear. Results of physical examination were otherwise notable for lack of fever, a 3 × 3-cm pigmented plaque in the right axilla, and five 1 × 0.5-cm reddish-purple macules on both ankles. The neck was supple, and there was cervical, axillary, and inguinal lymphadenopathy. There were no heart murmurs or carotid bruits. Results of neurologic examination revealed intact cortical function, and no focal motor or sensory deficits.

A scleral buckle procedure was performed on the night of admission. A lumbar puncture revealed a mononuclear pleocytosis, hypoglycorrhachia, and an ele-

vated CSF protein level (Table). Gram's stain, acid-fast bacillus smear, and cryptococcal antigen and toxoplasmosis antibody stains were all negative. Serum HIV antibody test result was reactive, and the HIV culture from the CSF was positive.

Intravenous penicillin G therapy (20 million U/d) was started for presumptive syphilitic meningitis. Serum RPR titer was +1:256 with an FTA-ABS of 4+, and CSF RPR titer was +1:8. Just prior to receiving the first dose of penicillin, the patient noted weakness of his left arm and leg, dysarthria, and "twitching" of his left upper extremity. The involuntary movement of the left upper extremity recurred two additional times on day 1 and once on day 2 of therapy. The weakness progressed in a stepwise fashion over 36 hours. At its most severe, the neurologic deficit was 3/5 strength in the left arm and leg, with a left Babinski's sign, mild left central facial palsy, and minimal dysarthria. Sensation, extraocular movements, and pupillary reactions were normal. An electroencephalogram was normal and a cranial CT scan revealed only mild cortical atrophy. An MRI scan revealed a small infarction in the right basis pontis.

An audiogram showed bilateral moderately severe high-frequency sensorineural hearing loss, more severe in the right ear, and brain-stem auditory evoked responses were consistent with a cochlear defect. A skin biopsy specimen of the right axillary lesion revealed a plasma cell infiltrate with a negative Dieterle stain for treponemes. A biopsy specimen of the ankle lesions showed early vascular proliferation, which was suspicious but not diagnostic of Kaposi's sarcoma.

The patient became febrile to 38.9°C (102°F) approximately six hours after penicillin therapy was started. The fever persisted for 24 hours and prednisone therapy (50 mg/d) was administered for two days for a presumed Jarisch-Herxheimer reaction. Results of repeated CSF examination six days after the initiation of penicillin therapy showed an improvement in the CSF formula, with a leukocyte count of $18 \times 10^6/L$ ($18/mm^3$); glucose, 1.9 mmol/L (34 mg/dL); and protein, 0.8 g/L (80 mg/dL). On discharge after 14 days of penicillin treatment, the motor deficit had resolved but the left Babinski's sign persisted. Results of follow-up CSF examination four weeks after the initial event were normal (Table).

COMMENT

The pathologic basis of PMH was originally described as a lacunar infarction of the internal capsule or basis pontis.¹ Subsequently, a wide variety of pathologic processes have been shown to cause PMH, including ischemic infarction,^{2,3} intracerebral hemorrhage,^{3,5,6} occluded internal carotid artery,⁵ subdural hematoma,⁵ metastatic tumor,⁵ nocardial abscess,⁷ and multiple sclerosis.⁵ These varied pathologic causes have occurred throughout the extent of the pyrami-

dal motor pathway: the motor cortex,^{5,7} corona radiata and internal capsule,^{3,5,6} mesencephalic cerebral peduncle,² basis pontis,^{1,3} and medullary pyramid.⁴ Neurosyphilis has not been previously associated with PMH, possibly because the PMH syndrome was formulated some 20 years after the peak incidence of neurosyphilis.

A comparison of the usual clinical features of PMH with those in the present cases reveal that they followed a fairly typical course. Lacunar infarcts generally occur in the setting of risk factors for atherosclerosis, such as hypertension,^{1,3} but these are not prerequisite for the development of a severe arteropathy in the setting of neurosyphilis. The onset of PMH occurs usually in an intermittent, stepwise manner over several hours.^{1,3}

The hallmark of PMH is a unilateral motor deficit unaccompanied by other persistent neurologic abnormalities.¹ However, subjective sensory phenomena at the onset of the deficit are relatively common.¹ Additional evanescent neurologic signs and symptoms occur in the initial phases of pontine PMH, including dizziness, dysphagia,³ dysarthria, conjugate gaze palsy, nystagmus, and forced deviation of eyes.¹ Headache is a rare occurrence in PMH¹ and in our patients was probably secondary to the concomitant meningitis.

Meningovascular neurosyphilis occurs predominantly in young males who had primary syphilis a few months to 12 years earlier (mean, seven years), although many patients do not recall previous syphilis infection.⁸ There has been a recent increase in the incidence of primary syphilis and an increase in neurosyphilis incidence is therefore anticipated.⁹ This increase is seen in those forms of neurosyphilis with the shortest latency periods, such as acute syphilitic meningitis and MVNS.^{9,13} Incidence of MVNS has been noted to be more frequent among the forms of neurosyphilis in the antibiotic^{10,12} vs pre-antibiotic eras.⁸

Meningovascular neurosyphilis characteristically consists of a prodromal syndrome for weeks to months followed by a superimposed vascular event and an abnormal CSF formula.⁸ The prodromal symptoms include intermittent headaches, dizziness, paresthesias, insomnia, emotional lability, personality change, irritability, apathy, decreased memory, and giddiness.^{8,9,12} This constellation of symptoms has been characterized as a form of "subacute encephalitis."⁹ The vas-

cular events are usually of acute apoplectic onset but can be subacute.^{8,9} The neurologic deficits occur most commonly in the middle cerebral artery territory,^{8,12} with deficits in the basilar artery or its branches next highest in frequency.⁸ A number of midline brain-stem syndromes are known to be caused by MVNS, including the Millard-Gubler syndrome, which consists of contralateral PMH plus abducens or facial cranial nerve palsies.⁸

The CSF abnormalities, in conjunction with the clinical state and blood syphilis serology, are crucial to the diagnosis of MVNS. The CSF shows a mononuclear pleocytosis with most patients having leukocyte counts of 11 to $100 \times 10^6/L$ (11 to $100/mm^3$),⁸ although cell counts of greater than $200 \times 10^6/L$ ($200/mm^3$) have been reported.^{9,10} There is a mild increase of total protein and discrete elevations of γ -globulin and IgG levels.^{9,10,14} The marked elevations of total IgG and more specific measures of central nervous system IgG levels (eg, CSF IgG index) seen in neurosyphilis are present in relatively few other conditions, such as some viral meningoencephalitis¹⁵ and in Lyme disease.¹⁶ Oligoclonal bands are present in the CSF in neurosyphilis^{10,14} and have been shown to be intrathecally produced IgG antibodies to *Treponema pallidum*.¹⁴ Low CSF glucose levels occur in acute syphilitic meningitis⁸ and may be secondary to glycolytic activity of the treponemes. Alternatively, these patients may have had acute syphilitic meningitis with a localized arteritis leading to vascular occlusion. The CSF reactivity serves as an index of adequacy of therapy and examination of the CSF six months after treatment should show a normal cell count and falling protein content.^{11,12}

The CSF nontreponemal tests (eg, VDRL and RPR) are highly specific but rather insensitive for the diagnosis of neurosyphilis, with a false-negative rate that ranges from 19%⁸ to approximately 50%.^{9,11} A nonreactive CSF VDRL titer does not preclude neurosyphilis, and therefore it must remain a diagnosis of exclusion when there are positive serum serologic test results, an active CSF, and the appropriate clinical setting. The CSF VDRL tends to be of very low titer, typically less than or equal to 1:4.¹¹ A negative FTA-ABS in the blood excludes the diagnosis of neurosyphilis and thus renders CSF examination unnecessary.¹²

The pathologic lesion of MVNS is an

endarteritis of the medium and large arteries (Heubner's) and of the small arteries and arterioles (Nissl-Alzheimer's). Hyperplasia of the subintimal fibrous tissue results in a pathologically narrowed lumen, which becomes thrombotically occluded and causes an ischemic infarction.⁸ The basis pontis infarcts demonstrated on MRI (Figure, left) and subsequently on CT scan in case 1 (Figure, right) closely resemble those pathologically proven to be responsible for PMH.¹ These lesions are most likely due to thrombosis of small paramedian branches of the basilar artery,¹ due to the Nissl-Alzheimer type of syphilitic arteritis.

The differential diagnosis of stroke in a young man encompasses a wide variety of causes, including atherosclerosis, embolus from a cardiac source or from an intracranial aneurysm, coagulopathy, complicated migraine, and inflammatory arteropathy (including syphilis, tuberculosis, amphetamine abuse, systemic lupus erythematosus, periarteritis nodosa, and rheumatoid arthritis).¹⁷ The patient in case 1 did have mild mitral valve prolapse detected on echocardiogram, but the stuttering onset of his deficit and the location of the infarct are more consistent with a thrombotic rather than an embolic vascular occlusion. Both patients had only minimal risk factors for atherosclerosis, normal coagulation parameters, and negative serologic test results for collagen vascular disease. Among the inflammatory arteropathies, only syphilis and tuberculosis are associated with meningitis. There were

multiple negative mycobacterial CSF cultures in our patients. Patient 1 developed a penicillin-responsive case of meningitis in an endemic area for Lyme disease with low positive titers against the Lyme spirochete, but the dramatic central nervous system involvement and lack of other manifestations of Lyme disease contradict the diagnosis.

Cerebral infarctions have been noted in patients with AIDS. Some patients have had nonbacterial thrombotic (marantic) endocarditis,^{18,19} while others had no identifiable source of embolus or atherosclerosis.¹⁸ An atypical aseptic meningitis, with a prolonged or recurrent course and prominent cranial nerve involvement, has been described as a neurologic complication of AIDS.^{18,19} Most recently, HIV has been cultured from the CSF of patients with AIDS with meningitis and other neurologic disorders.²⁰ Patient 1 had a negative CSF viral culture including specific culture for HIV. Patient 2 had a positive CSF culture for HIV. Aseptic meningitis and subacute encephalitis have been noted as an early or even the initial manifestation of AIDS.^{18,19,21} A recent case of cerebral granulomatous angiitis, which resulted in multiple cerebral infarctions, was associated with isolation of HIV from the CSF.²² This raises the possibility that HIV may directly cause a vasculitis or may have acted in synergy with *T pallidum* in patient 2 to shorten the latency to onset of MVNS. It is also possible that patient 2 had clinically occult primary syphilis months or years earlier and that the penile chancres four months

prior to admission represented reinfection. Case 2 may represent the first example of isolation of HIV in the active CSF of neurosyphilis, perhaps due to the virus having increased access to the central nervous system because of meningitic inflammation.

Gay males are at increased risk for both syphilis and AIDS.^{18,21} Repeated infection with venereal disease has been identified as a major risk factor for the subsequent development of AIDS.¹⁸ Cell-mediated immunity has an important role in the host defense against *T pallidum*,²³ and HIV-induced cell-mediated immunodeficiency may have adversely affected the course of primary syphilis in these patients and led to the development of neurosyphilis. It is also possible that dual infection with HIV and *T pallidum* synergistically contributed to the vascular occlusions. The incidence of neurosyphilis in patients with AIDS is unknown but it may be a more common cause of neurologic illness in these patients than has been previously appreciated. This is important since neurosyphilis is more readily treated than most opportunistic infections that involve the central nervous system in AIDS. The present cases illustrate the fact that patients at risk for immunocompromise are susceptible to "traditional" as well as opportunistic pathogens. Clarification of a possible interaction between AIDS and neurosyphilis awaits continued clinical observation, but we have recently encountered two other cases of neurosyphilis in young homosexual men with evidence of concurrent HIV infection.²⁴

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