Experience of Meningovascular Syphilis in Human Immunodeficiency Virus Infected Patient

Jung-Pyo Lee, M.D., Sun-Ho Koo, M.D., So-Young Jin, M.D., Ph.D., Tae-Hyong Kim, M.D., Ph.D.

Departments of Neurosurgery, Pathology, Division of Infectious Disease, Department of Internal Medicine, College of Medicine, Soochunhyung University, Seoul, Korea

Since the start of the antibiotic era, syphilis has become rare. However, in recent times, it has tended to be prevalent concomitantly with human immunodeficiency virus (HIV) infection and coinfection in North America and Europe. Now, such cases are expected to increase in elsewhere including Korea. A 40-year-old male patient visited hospital complaining of a headache for about one month. Brain computed tomography and magnetic resonance imaging, showed leptomeningeal enhancing mass with edema in the right porus Sylvian region, which was suspected to be glioma. Patient underwent a blood test and was diagnosed with syphilis and acquired immune deficiency syndrome. Partial cortical and subcortical resection were performed after small craniotomy. The dura was thick, adhered to the brain cortex, and was accompanied by hypervascular change of the cortex. The pathologic diagnosis was meningoovascular syphilis (MS) in HIV infection. After the operation, the patient was treated with aqueous penicillin G. Thereafter, he had no neurological deficit except intermittent headache. At first, this case was suspected to be glioma, but it was eventually diagnosed as MS in HIV coinfection. At this point the case was judged to be worth reporting.

KEY WORDS: HIV • AIDS • Neurosyphilis.

INTRODUCTION

Although neurosyphilis has become an uncommon disease among the general population, people who live with human immunodeficiency virus (HIV) have a greater tendency to develop it. In fact, at least one third of HIV-infected people are coinfected with syphilis.

The immunodeficiency induced by HIV results in more frequent, more rapid progression to severe neurosyphilis, which is less responsive to therapy and more prone to frequent relapse.

The frequency of neurosyphilis in the HIV-positive population is probably 3-35%2. The number of acquired immune deficiency syndrome (AIDS) patients is on the increase even in Korea, therefore the number of patients with neurosyphilis is also expected to increase. A significant problem is that radiologic findings are nonspecific in the case of neurosyphilis, and furthermore there are very few physicians experienced in the diagnosis of neurosyphilis. It is on account of this that at first the case was suspected to be glioma after the initial radiologic evaluation, although the final pathologic diagnosis was meningoovascular syphilis (MS) in HIV infection.

Following is a report of this case of meningoencephalitic type neurosyphilis with AIDS.

CASE REPORT

A 40-year-old man was referred to hospital with a one month history of progressive headache. He didn’t complain any focal weakness, visual disturbance, hearing loss, nausea, vomiting or fever. There was no past history of trauma, transfusion or surgery. He was married but had been separated from his wife for 10 years. He had traveled frequently to Southeast Asia on business.

On admission the patient did not look ill. Neurological examination revealed an awake, well-oriented patient. Other focal abnormal neurological signs were not noted.
Routine complete blood count was within normal range except an elevated erythrocyte sedimentation rate (94 mm/hr). Liver function and serum electrolytes were within the normal range. Among the serological tests, serum rapid plasma reagent was positive with a titer of 1 : 128.

The fluorescent treponemal antibody-absorption test (FTA-ABS) was positive. Laboratory test for HIV were as follows; Treponema pallidum latex agglutination increased up to 230TU, strong positive anti-HIV 1/2 antibody test (enzyme-linked immunosorbent assay, ELISA) and western immunoblot assay confirmed HIV infection. CD4 cell test was 567/mL (34.9%) with HIV ribonucleic acid 150,000 Copy/mL.

The brain computed tomography (CT) with contrast enhancement, showed a leptomeningeal enhancing lesion with edema on the right perisylvian region (Fig. 1). The magnetic resonance image of the brain, more clearly demonstrated the leptomeningeal enhancement with dural thickening and edema around right sylvian fissure (Fig. 2).

Two weeks after admission, an open biopsy was performed. The tentative diagnosis before the operation was low grade glioma or herpes encephalitis. After a small craniotomy, the dura was exposed. The dura was thick and adhered to the cortex, which showed hyperemic change (Fig. 3). Partial cortical and subcortical resection was carried out at the lesion site.

In the histopathological finding, submitted tissue disclosed a widening of meninges by proliferation of blood vessels, infiltration of many inflammatory cells, and deposition of collagen fibers. This inflammatory process extended into the brain parenchyma with obliteration of the meningeocerebral junction. Vascular lumens were partially or near totally obliterated by proliferation of endothelial cells and dense perithelial infiltration of inflammatory cells, predominantly plasma cells admixed with lymphocytes, resulting in endarteritis obliterans (Fig. 4). There was widespread reactive gliosis surrounding the inflammatory mass. However, there were no neoplastic cells. Warthin-Starry stain exhibited spirochetal organisms (Fig. 5). The pathological diagnosis was meningovascular syphilis.

The patient received an intravenous administration of 24 million units of aqueous penicillin G every day for 2 weeks. After operation and antibiotic treatment, the patient had no neurological deficits except intermittent headache, at a
DISCUSSION

Syphilis is still a major cause of morbidity in most developing countries and is endemic in some areas of North America and Europe, particularly Eastern Europe. In 1999, the overall incidence rate of primary and secondary syphilis in the U.S. was 2.5 per 100,000 population, but some cities showed incidence rates as high as 104.2 per 100,000 population. Globally, there are more than 900,000 cases of pregnant women infected with syphilis every year, resulting in 360,000 fetal or perinatal deaths and in the birth of 270,000 infants with serious or permanent impairment owing to mother-to-fetus transmission.

Coinfection of syphilis with HIV is an important issue for global HIV control strategies. A recent literature review including 30 studies on HIV prevalence among patients with primary diagnosis of syphilis showed a mean coinfection seroprevalence of 15.7%.

Such observations highlight the need to provide HIV testing for every patient diagnosed with syphilis. Several studies have demonstrated that syphilis constitutes an independent risk factor for HIV infection and the risk seems to be a result of a breakdown in the mucocutaneous barrier due to genital ulceration. Treatment of syphilis in HIV-positive people can be an important means of preventing HIV transmission. The incidence of syphilis among HIV-positive individuals is difficult to estimate, but seroprevalence studies have shown evidence of previous exposure to Treponema pallidum in 3% to 35% of HIV-positive patients.

Concurrent HIV infection may alter the progression of syphilis by increasing the propensity of the disease to progress to neurosyphilis, decreasing the latency period before the onset of neurosyphilis, increasing the severity of the manifestations of neurosyphilis, or rendering standard therapy for primary and secondary syphilis inadequate. Asymptomatic neurosyphilis is common during untreated primary and secondary syphilis and during latent syphilis in HIV patients.

While symptomatic neurosyphilis usually manifests after 2 years of untreated infection, syphilitic meningitis, the earliest manifestation, usually occurs during the first two years following infection.

The most common clinical manifestations of meningeal involvement are headache, nausea, vomiting, stiff neck, delirium, cerebral and cranial nerve dysfunction (mainly of cranial nerves VII and VIII), and, less frequently, polyradiculopathy.

Radiologic findings in neurosyphilis are nonspecific and include multifocal infarction and multiple white matter lucencies. The increase in meningeal and parenchymal enhancement observed on brain CTs in HIV-infected patients with neurosyphilis most likely reflects the increased incidence of syphilitic meningitis in this group.

Establishing a definitive diagnosis of neurosyphilis is difficult because there is no "gold standard" criterion. Cerebrospinal fluid (CSF) examination is indispensable for the initial diagnosis and for following the patient's response to treatment. The CSF opening pressure may be increased in cases of acute syphilitic meningitis. The traditional hallmarks for the diagnosis of neurosyphilis are the CSF-venereal disease research laboratory test (VDRL), the CSF white blood cell (WBC) count and CSF protein levels. Classical abnormalities are a reactive CSF-VDRL test, pleocytosis and elevated CSF protein levels. However, normal values of these three parameters have been found in neurosyphilis. The CSF WBC count is generally abnormal in early meningoovascular neurosyphilis, but it is not necessarily abnormal in late parenchymatous neurosyphilis.

The CSF immunoglobulin G index appears to have higher sensitivity than the CSF protein level. CSF glucose is normal but occasionally it may be slightly decreased, especially in HIV-coinfected patients.

CSF VDRL, despite its high specificity, has limited application due to its low sensitivity, especially in asymptomatic neurosyphilis.

False-positive CSF VDRL results can occur occasionally, although rarely, due to blood contamination. During lumbar puncture the CSF-FTA-ABS test is more sensitive than the CSF-VDRL test for the diagnosis of neurosyphilis, but it also has limitations when there is blood contamination or diffusion of serum immunoglobulin into the CSF.

The therapy of choice is intravenous penicillin G 12 to 24 million U per day for 10 to 14 days. In special cases requiring use of an alternative therapy, oral doxycycline,
200 mg every 12 hours for 4 weeks or intravenous doxycycline are indicated. Ceftriaxone (1 g to 2 g IM daily, for 10 to 14 days) has been used\textsuperscript{18}, but treatment failures have been reported, especially in HIV-infected patients.\textsuperscript{7}

Parameters for the results of the treatment of neurosyphilis are clinical improvement (which generally does not improve in parenchymatous neurosyphilis and may sometimes progress relentlessly despite treatment) and laboratory findings. CSF WBC count should have decreased at 6 months and CSF should be normalized by 2 years. If not, retreatment should be considered. Cases of persistence of CSF pleocytosis recurrence and treatment failures of symptomatic neurosyphilis after treatment with IV penicillin have been reported in HIV coinfected patients.\textsuperscript{9,15,19} In fact, it is recommended that treatment continue until the CSF WBC count is normalized, so CSF examination can be performed every 6 months.\textsuperscript{11}

CONCLUSION

This report is of a case of MS in an HIV positive patient, mimicking glioma at brain CT and brain MRI.

References