Case of Neurosyphilis Presented as Recurrent Stroke

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Abstract

A 46 year old male patient was presented with a history of hypertension, diabetes mellitus and coronary artery disease was reported to have had a cerebrovascular accident of which features were suggestive of a new and rapidly progressive stroke. Upon investigation for recurrent stroke, the patient was found to have a positive serology for Syphilis. The possibility of neurosyphilis was considered, which was later confirmed by positive serology in the cerebrospinal fluid. The case is lenghly discussed in this report to emphasize the presence of syphilis in the 21st century, and to ascertain its importance as an etiological agent in cases of recurrent stroke.

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Introduction

The name Syphilis is derived from the Greek word "Syphilos" meaning crippled or maimed. Syphilis is usually a sexually transmitted infection characterized by episodes of active disease interrupted by latency periods. There are three characteristic stages of Syphilis namely; Primary, Secondary and Tertiary. The tertiary stage occurs in around one third of cases and is manifested by progressive musculoskeletal lesions, aortic involvement or symptomatic central nervous system disease. The causative organism for Syphilis is a spirochete named; *Treponema Pallidum* which is a helically coiled organism measuring some 5-20 micrometers (μm) in length. Syphilitic infection of the nervous system results in one of the most chronic and insidious meningeal processes known. Central nervous system invasion occurs early in the course of untreated syphilis.[1] Therefore, patients not treated for persistent cerebrospinal fluid abnormalities are at risk of developing clinically apparent diseases.

Case Report

A 46 year old Omani male patient was presented in hospital with a history of weakness of lower left limb and tingling sensation in the upper left limbs for 3 days duration. The patient had a very significant medical history of hypertension, diabetes, Ischemic heart disease and stroke for 5 years causing a right sided hemiplegia which partially recovered. Clinical evaluation upon presentation revealed normal mental functions and no evidence of cranial nerve involvement. Motor examination showed bilateral weakness of both lower limbs with bilateral Babinski sign. There were no cerebellar signs and cardiac examination revealed a faint diastolic murmur. However, there were no peripheral signs of aortic regurgitation.

The patient developed a Broca's type of aphasia the next day and was found to be choking on feeds. He was found to have developed palatal weakness on his right side with bilaterally reduced gag reflexes. The patient was also found to have a progression of weakness on his left side suggesting a development of crossed hemiplegia with a progressing stroke indicative of a brain stem involvement.

In view of recurrent progressive stroke and the relatively young age of the patient, it was apparent that further investigations were required. A Computerized Tomographic (CT) scan of the brain arranged at the time of admission was reported to be normal. A detailed stroke assessment was conducted and other tests including carotid and vertebral artery Doppler study, echocardiogram, connective tissue tests, thrombophilia screening, retroviral screening and Syphilis serology were performed. An MRI of the brain could not be performed due to logistical reasons.

The syphilis serology of the patient was reported to be positive. This was further confirmed with *Treponema Pallidum* Heam Agglutination test (TPHA) which was also reported to be positive. The retroviral screening was negative and the other tests did not detect any abnormality. Echocardiogram showed dilatation of the left ventricle with mild aortic regurgitation. A lumbar puncture was performed and the fluid was found to be clear with pleocytosis with a cell count of 56cells/ml and a high protein content of 101 mg/dl. Cerebrospinal fluid Veneral Disease Research Laboratory (VDRL) test and TPHA were reported to be positive suggesting the possibility of neurosyphilis as a cause for the recurrent

stroke. The patient was started on Crystalline Penicillin at a dose of 3 million units every four hours with careful observation for any evidence of Jarisch- Herx heimer reaction. Intravenous Penicillin was administrated for the next 14 days. A repeat lumbar puncture was planned but the patient refused. The patient was referred for rehabilitation and discharged on antiplatelets and antihypertensives regimen. A repeated cerebrospinal fluid analysis was planned after 6 months.

Discussion

Tertiary syphilis has become a rarity in the 21st century. However, after a decade of decline, incidences of syphilis have increased significantly. The pathology of tertiary syphilis involving the central nervous system in obiliterative small vessel endarteritis which usually involves the vasovasorum. The clinical spectrum of tertiary syphilis includes the neuro syphilis, cardiovascular syphilis and the late gummatous syphilis.[2] Quaternary syphilis, characterized by fulminant anergic necrotizing encephalitis is seen mostly in patients with coexistent retroviral infections. A patient with neurosyphilis may be totally asymptomatic or present an acute syphilitic meningitis, meningovascular syphilis, tabes dorsalis, optic atrophy or generalised paresis of insanity. Asymptomatic neurosyphilis is characterized by reactive serology in the cerebrospinal fluid along with other features such as elevated protein and pleocytosis.[3] Acute syphilitic meningitis usually presents features of meningeal irritation. Fever is rarely observed. Involvement of cranial nerves especially of 7th, 8th, 6th and 2nd in order of decreasing frequency is common. Meningitis can be self limiting but can present more severe in later forms. The most common clinical syndrome of meningovascular syphilis is stroke; in a relatively young adult it involves the middle cerebral or basilar arteries. Tabes dorsalis is a slowly progressive disorder involving the posterior columns and posterior roots of the spinal cord. Patients may experience with severe lancinating pains of the legs, ataxia and posterior column sensory impairment. Bladder incontinence and sexual dysfunction can occur. The rare delayed manifestation of neurosyphilis is general paresis of insanity which usually occurs 20 to 30 years after the initial exposure. It represents a chronic progressive frontotemporal meningoencephalitis with ongoing loss of cortical function. Ocular involvement in neurosyphilis can lead to posterior placoid chorioretinitis.[4] It is not clear whether the clinical spectrum of syphilis differs in an immunocompromised individual. However, recent data suggests that individuals who are immunocompromised have higher chances of developing neurosyphilis.[5]

The diagnosis of Syphilis is performed by serological and non serological tests. The serological tests can be further sub classified into treponemal and nontreponemal tests. The non serological tests include; dark filed microscopy, direct immunoflouroscence and demonstration of *Treponema Pallidum* in tissues.[6] Current recommendations for evaluation of neurosyphilis in any patient with positive serology for syphilis include those with focal neurological signs, patients with other late syphilis and cases of suspected treatment failure.

In patients with concurrent Human Immunodeficiency Virus (HIV) infection and syphilis, the need for lumbar puncture to rule out asymptomatic neurosyphilis is controversial. Centre for Disease Control (CDC) recommends a criterion of high plasma regain titre and CD4 cell count of equal to or less than 350cells /ml in these patients to consider lumbar puncture to rule out asymptomatic neurosyphilis.[7]

Penicillin has remained the drug of choice for all stages of Syphilis.[8] A single dose of Benzathine penicillin in a dose of 2.4 million units resulted in cure for more than 95% cases of primary Syphilis.[9] Late latent syphilis and late syphilis without evidence of involvement of central nervous system has to be treated with 3 weekly doses of 2.4 million units of Benzathine penicillin. In contrast, neurosyphilis requires treatment with crystalline penicillin with a dosage regimen of 2 to 6 million units every 4 hours for a total of 10 to 14 days. An alternative is to use aqueous Penicillin G procaine at a daily dosage of 2.4 million units intramuscularly, along with 500 mg of oral Probenecid every 6 hours for a course of 14 days.[10] Recommendations for treatment remain the same for HIV coinfected patients with syphilis. There is no data supporting the use of other antibiotics for the treatment of neurosyphilis, however the use of certain 3rd generation Cephalosporins and Azithromycin may merit further evaluation. In a recent study by Bai et al, published in the international journal of STD/AIDS, Azithromycin achieved a higher cure rate than Benzathine penicillin for early syphilis.[11]

The activity of neurosyphilis correlates best with cerebrospinal fluid abnormalities, notably the pleocytosis. The elevated protein levels slowly decrease after treatment and the serological tests show a progressive decline in titre. A patient treated for neurosyphilis should have their cerebrospinal fluid reevaluated every 6 months for 3 years or until the findings return back to normal.

Conclusion

Neurosyphilis is thought to be rare in the 21st century, however, the possibility should be considered in all cases of recurrent

strokes, and particularly in cases of stroke amongst young people. It is important to be aware of the therapy for neurosyphilis since it differs from the treatment of primary and late syphilis, due to the fact that adequate treatment can retard further progression of the neurological disease.

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