Neuropsychiatric manifestations in General Paralysis of Insane (GPI)
Upadhyaya S, Pant SB, Dhungana S, Tulachan P, Chapagai M, Ojha SP

Department of Psychiatry and Mental Health, Institute of Medicine, Tribhuvan University Teaching Hospital, Marajgunj, Kathmandu, Nepal.

ABSTRACT
General paralysis of insane is a form of neurosyphilis which brings parenchymatous changes in the central nervous system. Its manifestations include a variety of neuropsychiatric symptoms ranging from cognitive impairment to overt psychosis. Clinicians face difficulties in proper diagnosis as variety of symptoms changes from one form to other within a short period of time. Rarity of the disease at this modern era of penicillin is also another factor in timely diagnosis and management of such cases. Here we present a case of general paralysis of insane who presented with variety of neuropsychiatric symptoms and have had great difficulties to reach into the diagnosis.

KEY WORDS
Cognitive impairment, General paralysis of insane, Neuropsychiatric symptoms, Syphilis

INTRODUCTION
Neurosyphilis is clinically classified into asymptomatic, meningeal, meningoovascular and parenchymatous type. Parenchymatous neurosyphilis, in turn is divided into tabes dorsalis and general paralysis of insane (GPI). GPI is also known as dementia paralytica or general paresis.

We never know which stage of syphilis may turn into neurosyphilis. Its common manifestation is asymptomatic pupillary afferent defect also known as Argyll Robertson pupil but may not be present in significant number of cases. Progressive dementia begins 15-20 years after primary syphilis which is the typical presentation of GPI. The clinical features include cognitive impairment, delusional or apathetic states, dysarthria, myoclonus, intention tremors, seizures, hyperreflexia, and Argyll Robertson pupils.

In this modern antibiotic era, neurosyphilis is rare but due to Human immuno-deficiency virus (HIV) co-infection, inadequate antibiotic treatment, and the rise of high risk sexual behaviour among youth, frequency of subtle and atypical symptomatic presentations of neurosyphilis have increased. GPI was one of the most deadly disease of the psychiatry which progresses into mental and physical deterioration carrying a grave prognosis ultimately leading to death.

CASE REPORT
A 40 years female was sbrought to our centre with irritability, physical and verbal aggression, inappropriate eating behaviour, abnormal behaviour, impaired memory and decrease sleep for 5 months. As per her husband, before these symptoms were apparent, there was a history of multiple physical complaints like tingling sensation whole body, headache, pain over multiple sites, palpitation and shortness of breath for 2 months, 2 years back. She underwent multiple consultation but no any physical basis for the complaints were found and was referred to psychiatrist for evaluation and was diagnosed somatoform disorder for which Escitalopram 10 mg/day was prescribed. She left medication after one month following multiple episodes of nonprojectile vomiting.
After about 3 months of onset of illness, her family members noticed her being very much excited without any obvious reason. She seemed very happy keeping out of the situation and excessively talkative with her family members only. Though being very happy, she complained of easy fatiguability. She would not talk much with her neighbor and friends and spent most of the time doing her household activities only. Such symptoms last for about 6 months. During this period psychiatrist evaluated where she was diagnosed Mania and prescribed Sodium valproate which was increased to 1200 mg/day. Though no any improvement was noticed. With sodium valproate patient became very drowsy due to which her relatives stopped the medication without consulting the psychiatrist.

Following which she displayed self-smiling behaviour, irrelevant talk, gesturing, disrobing episodes, fearfulness without any apparent reason and not able to maintain basic activities of daily living like dressing, bathing and eating. She could not voluntarily control her bladder and bowel movement. She was then taken to local hospital, later referred to tertiary level hospital. In tertiary hospital, she was diagnosed with Psychosis Not otherwise specified (NOS) and prescribed Quetiapine 400 mg/day. With that medication too, she showed no any improvement thus stopped the medication and was brought to our centre for further evaluation and management.

Patient was afebrile and her vitals were stable. General physical examination did not reveal any abnormalities. On neurological examination there was no any abnormality except bilateral positive Babinski sign. Her psychomotor activity was increased, speech was slurred, attention was aroused but concentration was not sustained and was oriented to time, place and person. Her recent memory was impaired with relatively intact remote memory.

With all these finding at hand and changing pattern of symptoms relatively within a short period of time, we suspected organic causes for the illness. Impaired memory with personality change pointed towards neurocognitive disorder but primary neurodegenerative disorder was probably not a cause because of rapid progression of disease and unusual age of presentation. Though possible causes of neurocognitive disorder were sought for from laboratory investigations. Haematological and biochemical reports were normal thus excluding possible hypothyroidism, hypercalcemia, hypoglycemia and any metabolic causes including hepatic and renal manifestations. In the absence of history of any psychoactive substance use, neurocognitive disorder related to substance was also excluded. Serum vitamin B12 was also within normal limit. Magnetic Resonance Imaging (MRI) head showed diffuse T2 white matter hyperintensities in bilateral cerebral hemisphere with marked atrophic changes in the brain suggestive of adult onset metabolic disease. With evidence of rapid progression of neurocognitive impairment at unusual age of onset infection of Central nervous system was considered for which serological tests for HIV, Hepatitis and syphilis were done. Test for HIV and Hepatitis were non-reactive but serum Venereal Disease Research Laboratory (VDRL) was reactive with a titer level of 1:32. Syphilis was confirmed with positive Treponema Pallidum Haemagglutination (TPHA) test. Cerebrospinal fluid (CSF) analysis was done and VDRL and TPHA was found to be positive. CSF sugar and protein levels were within normal range but all mononuclear cells were found.

Considering the history, clinical examination, serological findings and CSF analysis, General paresis of insane was diagnosed. Patient was treated with penicillin in the line of neurosyphilis. Since, quetiapine was already stopped we started olanzapine 5 mg/day which was increased to 10 mg/day over a week. With medication her behavioural symptoms were improved but cognitive symptom did not show any improvement. Before discharge she was administered Mini Mental State Examination (MMSE) which came to be 13/30. She was discharged after a month of admission. During follow-up on first and second week and one month after the discharge, her behaviour was controllable but cognitive impairment as per MMSE did not show any improvement. Penicillin and olanzapine were continued in the same dose. She was not brought for follow up after her third visit.

**DISCUSSION**

GPI is a parenchymatous neurosyphilis and presented with cognitive impairment and personality change which themselves are non-specific findings. Presenting features may imitate any of the neuropsychiatric condition so such cases should be assessed with high index of suspicion and serological test should be done.6 In our case report, patient was initially diagnosed as somatoform disorder. Later within a brief period she developed manic symptoms which was not improved with mood stabilizer. Before presenting in our centre with neurocognitive impairment, she was diagnosed with psychosis NOS. From this presentation also, we can analyse the trend of symptoms the same patient may show in this illness.

In this antibiotic period, neurosyphilis is almost a forgotten entity for present day practicing physicians. It is found to be of historical interest and due to the atypical presentation of this disease, physicians have had difficulties in prompt diagnosis of the cases.5,6 In the absence of typical presentation and serological test, diagnosis of GPI was delayed in this case. In a study done by Yanhua and colleagues, 38.2% of the patients were misdiagnosed as primary psychiatric disorder, including schizophrenia, mania, bipolar disorder, anxiety disorder and somatoform disorder. In the same study, authors found that 19 out of 37 misdiagnosed patients have severe neurocognitive impairment as measured by Mini-mental state examination (MMSE).8
In addition to proper history and serological test, structural brain imaging findings may also be helpful in the diagnosis of GPI. MRI study showed focal lesions and generalized brain atrophy in 55% of patients diagnosed with neurosyphilis. Those lesions were consisted of multiple foci of increased signal intensity on T2-weighted images, in multiple arterial distributions. MRI findings in our patient also showed similar pattern of lesion and brain atrophy. MRI findings are useful not only in the diagnosis but also in predicting the prognosis of the patient. Cerebral atrophy mostly in the temporal lobe along with severe cognitive impairment and personality changes does not favour good prognosis. Most probably because of the MRI findings, Penicillin administration did not show any improvement in her cognitive symptoms. However, this prediction could be wrong as patient was not brought after 3rd follow up. Remission of symptoms in GPI is determined by severity and duration of symptoms. Hence early diagnosis may institute early treatment and thus either improving the cognitive impairment or reducing unfavourable course of the illness.

GPI is a secondary cause of treatable neurocognitive disorder. Therefore, treating physicians should have great suspicion of this condition and institute prompt clinical examination, serological test and MRI to reduce the grave prognosis of this condition.

REFERENCES


