Delirium as the first manifestation of Progressive Multifocal Leucoencephalopathy

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ABSTRACT

Progressive Multifocal Leucoencephalopathy (PML) is a demyelinating disorder caused by the reactivation of a latent virus in immunosuppressed individuals (usually as a result of Human Immune Deficiency virus infection [HIV] or Acquired Immune Deficiency Syndrome [AIDS]). This report highlights the case of a young man with PML who initially presented with psychosis but was, in fact, in a state of delirium. This was followed by a rapid global cognitive decline and eventually a terminal state. The case is interesting as an unusual diagnosis underlying a common clinical presentation.

Keywords: Human immune deficiency virus, AIDS, delirium, psychiatry

INTRODUCTION

Progressive Multifocal Leukoencephalopathy (PML) was first described in the late 1950s in immunocompromised patients. It remained uncommon until the era of Acquired Immunodeficiency Deficiency Syndrome (AIDS) caused by the Human Immunodeficiency Virus (HIV) in the 1980s. [1] PML is a demyelinating disease caused by widespread viral infection of oligodendrocytes. The virus implicated is the John Cunningham Virus (JCV) which is normally found latent in most people. PML is caused by reactivation of the virus in immunosuppressed individuals. [2] The overwhelming majority of cases are linked to HIV/AIDS. PML has also been linked to the use of immunosuppressive drugs such as fludarabine and, increasingly, in patients treated with monoclonal antibodies such as natalizumab. [3] In the case of the latter, the presenting symptoms are often neuropsychiatric in nature. [4]

Clinically, PML causes a rapidly progressive neurological deterioration leading to death within weeks or months. [5] PML can present with a range of psychiatric symptoms such as delirium, cognitive deficits, psychosis or emotional lability. [6] Diagnostic investigations include: computed tomography (CT) which usually shows multiple bilateral, asym-

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metrical hypo-attenuating foci of various sizes without mass effect or enhancement [7]; Magnetic resonance imaging (MRI) characteristically shows such findings as unifocal or multifocal areas of hyperintensity on T2-weighted images [3]; viral detection from cerebrospinal fluid; definitive diagnosis is made histologically by brain biopsy which usually shows three key findings: demyelination, enlarged nuclei of oligodendrocytes, and bizarre astrocytes. [7] The mainstay of treatment for HIV-associated PML is antiretroviral therapy. [8]

CASE REPORT

A 36-year-old Singaporean Indian was brought to the Emergency Department by his distraught wife. She gave a two week history of sexually disinhibited behaviour, diminished self-care and irrelevant speech. He had no previous history of psychiatric or medical problems. On examination, he had no neurological deficits and the rest of his physical examination was also unremarkable.

Mental state examination revealed a disheveled and distracted man with poor eye contact and rapport. He also had some psychomotor retardation. He was unable to answer questions relevantly; therefore, the history was taken from his wife. His affect was blunted, he denied suicidal thoughts and there was marked thought disorder. He denied perceptual abnormalities and was not oriented in time, place or person. His concentration, registration and long-term memory were impaired. He had no insight into his condition.

He was admitted to the psychiatric ward, the admitting doctor with suspicion of an acute psychotic disorder, possibility of drug-induced. However, there was no known history of drug or alcohol abuse. In the psychiatric ward, an in-depth assessment revealed a different picture. The history and mental state examination were thought strongly to suggest delirium. Hence, a series of diagnostic investigations was undertaken. Whilst awaiting the investigations results, the patient continued to exhibit the behaviours which prompted his family to bring him to hospital. Blood tests (full blood count, liver, renal and thyroid function tests, calcium/ phosphate, B12, folate) revealed no abnormalities.

A CT scan of the brain showed extensive vasogenic oedema crossing the midline, raising the possibility of gliomatosis cerebri (a rare primary brain tumour), astrocytoma or lymphoma. Other differentials provided were that of a demyelinating disorder or an infection. Further evaluation with Diffusion-Weighted Magnetic Resonance Imaging, a particularly sensitive MRI technique, was suggested. The MRI showed an infiltrative lesion with perilesional vasogenic and surrounding cytotoxic oedema involving both frontal lobes and the corpus callosum.

The patient was transferred to the care of the neurosurgical team. He later developed a fever and was then referred to an infectious diseases specialist. Blood culture, cerebrospinal fluid analysis and culture were all negative. Finally, a stereotactic brain biopsy of the brain lesion was undertaken and the histology interestingly reported findings consistent with a diagnosis of PML secondary to infection with JC Virus. HIV tests were also positive.

Antiretroviral therapy was commenced but sadly, the patient's continued to deteriorate. Finally, the family decided to take him home. He was then taken to a palliative care home in Malaysia (which is not uncommon for terminally ill Singaporeans) and was lost to follow up.

DISCUSSION

This case demonstrates many important facts. Firstly, it is important to reassess and exclude the possibility of an organic brain disorder in patients who present with an apparent acute psychotic disorder. Diagnoses such as delirium (with its multitude of underlying causes), substance-induced psychosis and alcohol withdrawal syndrome should always be considered. In this case, despite the high index of suspicion that the patient was experiencing a non-psychiatric organic brain disorder, initial screening failed to reveal the cause, resulting in admission to the psychiatric ward for observation and investigations due to the anticipated difficulty in managing the patient's behaviour on a general medical ward.

Secondly, we have highlighted the increasingly important role of advanced brain imaging technology in the field of psychiatry. In this case, it was fortunate that there was little difficulty in arranging the brain scans for this patient. In the twenty-first century, CT and MRI should be considered an essential part of a psychiatrist's toolkit. However, around the world, especially in the less developed and well-resourced countries, psychiatrists often do not have the use of such investigations as readily. In many services, even in the developed countries, a request for brain imaging from a psychiatrist has to be vetted by a neurologist. The request may be refused or there may be unnecessary diagnostic delay. In the long-term, reluctance to utilise this essential diagnostic tool might develop on the part of the psychiatrist.

Thirdly, despite the great strides made in the treatment of HIV/AIDS, here is a stark reminder of its potentially devastating consequences. PML and other HIV-related disorders are disease entities which psychiatrists are not generally familiar with despite HIV/AIDS being prevalent throughout the world. In traditional psychiatric teaching and practice, testing for syphilis was considered routine but syphilis with psychiatric manifestations has now become a rarity. This case raises the question of whether HIV screening should also now be considered part of our routine investigations.

In conclusion, this case stressed the importance of always considering delirium in a patient who presents in an emergency situation with psychotic symptoms. HIV testing should be considered in cases where the patient is clinically in a state of delirium but routine investigations are normal. Finally, health services which restrict the use of brain imaging technology by psychiatrists should reconsider this situation in the light of this case.

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