HIV-related psychosis

Introduction

This article describes the presentation of acute psychosis in a human immunodeficiency virus (HIV)-positive man and discuss the differential diagnosis, clinical features and aetiology. It also summarizes research findings which suggest that HIV-related psychosis may be a clinically and neuropathologically distinct condition.

HIV and psychosis

There is a recognized association between HIV infection and psychosis. HIV-positive individuals have a higher incidence of new-onset psychosis. Conversely, patients with psychotic disorders have an increased risk of contracting HIV (Dolder et al, 2004).

Common aetiological factors, such as substance misuse, may predispose to both psychosis and HIV (Dolder et al, 2004). Also HIV may predispose an individual to psychosis, either because of the psychological stress of having a stigmatized chronic disease, or through HIV-related neuropathological mechanisms.

While HIV-related psychotic episodes used to be more common, their frequency has reduced as a result of effective antiretroviral treatments.

Clinical features

Dolder et al (2004) and De Ronchi et al (2006) suggest that HIV-related psychosis may be clinically distinct from functional psychotic conditions, particularly schizophrenia and bipolar affective disorder. Their findings are summarized in *Table 1*.

Differential diagnosis

The differential diagnosis of psychosis in HIV-positive individuals includes a comorbid functional psychosis, HIV-related psychosis, and organic psychosis as a result of immunosuppression, such as opportunistic infections or malignancies of the CNS.

Neurochemical hypothesis

Neurochemical research suggests that HIV-related psychosis may occur via the glutamate–N-methyl-D-aspartic-acid (NMDA)–calcium pathway. Normally NMDA receptors respond to glutamate by opening channels which allow calcium into the cell. Substances that block this receptor can cause psychosis.

Quinolinic acid is an NMDA agonist, released from macrophages when induced by HIV proteins. It is found in increased concentrations in the CNS of HIV-positive patients. High levels of quinolinic acid are neurotoxic (Smith et al, 2001).

Kynurenic acid is an endogenous NMDA antagonist. It is present in raised concentrations in the CSF of HIV-positive patients, and in even higher levels in those who are also psychotic (Atlas et al, 2007). Kynurenic acid levels are also increased in the CSF of patients with schizophrenia (Nilsson et al, 2005).

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Case Report

A 35-year-old Ugandan man was escorted to the emergency department by his family following 2 days of uncharacteristic behaviour. He had presented himself to a police station believing that he was guilty of terrorist acts. He had no psychiatric history and no history of illicit drug use. The patient was responding to auditory hallucinations and lacked insight into his symptoms.

Preliminary blood investigations and a computed tomography brain scan were normal. The patient was able to give informed consent for an HIV test, which was positive. He was admitted to a psychiatric ward and was successfully treated with antipsychotic medication.

Table 1. Comparison of HIV-related psychosis with that in HIV-negative patients

	New-onset psychosis in HIV-positive individuals	Psychosis in HIV-negative individuals
Prevalence	Up to 15%	1%
Paranoid delusions	More common	Less common
Nature of delusions	Simple	More structured and complex
Affective symptoms	Usually absent, but may have prominent manic symptoms	Often prominent
Attention-concentration impairment	More common	Less common
Common form of hallucinations	Auditory or visual	Auditory
Schneiderian first rank symptoms	Less common	Frequent
Active suicidal ideation	Uncommon	Common
Eventual remission of psychosis	More common	Less common
Need for long-term antipsychotic agents	Less common	Very common
Antipsychotic doses required	Lower	Higher

From Dolder et al (2004); De Ronchi et al (2006)

The mechanisms that trigger psychosis in HIV-positive patients are unclear. One possibility is that the brain may compensate for quinolinic acid-mediated neurotoxicity by upregulating kynurenic acid. Overcompensation may cause hypofunction of the NMDA receptor, resulting in psychosis (Atlas et al, 2007).

Conclusions

In cases such as this, after ruling out organic causes of psychosis in HIV-positive individuals there may still be diagnostic uncertainty over whether this is a functional or organic disorder. Although HIV is one of many neurological disorders that are associated with an increased risk of psychosis, clinical features and neurochemical findings suggest that HIV-related psychosis is a distinct condition. **BJHM**

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Nilsson LK, Linderholm KR, Engberg G et al (2005) Elevated levels of kynurenic acid in the cerebrospinal fluid of male patients with schizophrenia. *Schizophr Res* **80**(2-3): 315–22

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