Difficult-to-diagnose psychosis?
Comorbid neurological symptoms?

Have you considered Niemann-Pick type C disease?

A guide to recognizing the clinical features of Niemann-Pick type C disease (NP-C) for psychiatrists
What is Niemann-Pick type C disease?

Niemann-Pick type C disease (NP-C) is a rare, progressive, autosomal recessive neurodegenerative disorder. In two thirds of cases presentation occurs in infancy or childhood, but in up to a third of cases symptoms may not present until adolescence or adulthood.

In adolescents and young adults, the disorder is often associated with psychiatric illness, specifically schizophrenia-like psychosis. In adults, NP-C is associated with a progressive cognitive disorder characterized by executive impairment and memory disturbance.

In addition to its psychiatric and cognitive features, NP-C is marked by the development of ataxia, dysarthria, dystonia and characteristic vertical gaze palsy. As the disease progresses, seizures, dysphagia and pyramidal signs may appear.1

The diagnosis of NP-C is often delayed as initial symptoms in adults tend to be psychiatric, and the development of motor disturbance may be attributed to the effects of medication. Increased awareness of how the disease presents may help psychiatrists recognize NP-C and ensure that patients receive the support and the appropriate therapy they require.

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How to use this guide

The aim of this guide is to help psychiatrists increase their awareness of how NP-C might present in adolescence or adulthood, when to suspect NP-C, which symptoms and features should prompt further investigation and when referral is recommended.

For more information

Please visit www.npc-info.com for further information on NP-C.
### Patients present with the following psychiatric symptoms

#### Early-onset psychosis
Patients may experience paranoid delusions, visual or auditory hallucinations, delusional ideation, disturbance with aggression, self-mutilation or social isolation;\(^2\) with onset in adolescence or early adulthood.

#### Prominent visual hallucinations
Patients may experience prominent visual hallucinations in addition to other psychotic symptoms.\(^2,3\)

#### Incomplete response to treatment
Despite treatment for psychiatric symptoms e.g. with neuroleptics and mood stabilizers, patients may still experience significant residual positive psychotic symptoms, which are resistant to treatment.\(^2\)

### Patients present with the following associated neurological features

#### Vertical gaze palsy
Patients may have impaired vertical eye movement, experiencing difficulties in reading or going downstairs. Often their downward gaze is affected more than their upward gaze.\(^2\)

#### Ataxia
Patients may present with poorly co-ordinated movements affecting walking, manipulation, speech and swallowing.\(^2,3\)

#### Dystonia
Patients may demonstrate increased tone in the upper or lower limbs and face, or dystonic posturing particularly in the hands.\(^2,3\)
Consider the following visceral signs and/or neuro-imaging findings

Visceral signs:

**Unexplained splenomegaly**
Patients may present with an enlargement of the spleen, which may be asymptomatic so only discovered upon abdominal imaging such as ultrasound.²

**History of neonatal jaundice**
Patients may have experienced neonatal jaundice, frequent in classic NP-C, but uncommon in the adult form.² The neonatal period may have been overlooked, as evidence is rarely available.²

Visceral signs commonly precede neurological symptoms, so signs involving the liver/spleen could have been present for decades prior to diagnosis.²

MRI findings:

**Cortical/hippocampal atrophy**
Patients presenting with mainly psychiatric/cognitive symptoms may display frontal cortical atrophy, and may have a thin corpus callosum and small hippocampi.² At late stages of the disease, atrophy can be found to be less centralized, affecting the cortical and subcortical grey matter, and the cerebellum.²

**Cerebellar and brainstem atrophy**
Patients with predominant gait and movement disorders had more pronounced brainstem and cerebellar atrophy with relatively less cortical/subcortical atrophy.² Significant cerebellar atrophy may contribute to the hypofrontality that occurs in adult NP-C.

Early diagnosis is important as treatment can help reduce the progression of NP-C. Patients presenting with a combination of the features outlined within this guide should be considered for referral to a specialist centre. Patients presenting with vertical gaze palsy and psychosis should always be referred.

Please note that treatment information is very country-specific and you are responsible for obtaining and adhering to your country-specific product information. Only to be used in countries where specific treatment has an approved indication for Niemann-Pick type C disease.

References: