DPPX encephalitis

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What is DPPX encephalitis?

DPPX (dipeptidyl-peptidase-like protein-6) encephalitis, also known as anti-DPPX encephalitis, is a very rare autoimmune disorder where the body's immune system mistakenly attacks DPPX proteins found on nerve cells in the gut and brain. The proteins play an important role in regulating neuronal excitability.

The condition is a form of autoimmune encephalitis (AE). Unlike infectious encephalitis, DPPX encephalitis occurs when the immune system produces antibodies that attack these specific proteins in the brain, leading to inflammation and neurological symptoms. The trigger for this autoimmune response is often unknown but in some cases it may be associated with underlying cancers. The condition affects mainly individuals in middle to older age and men are more commonly affected than women.

Symptoms

The condition typically develops gradually over weeks to months, with patients experiencing:

- Severe diarrhoea and significant weight loss before neurological symptoms emerge (often many months before)
- Progressive cognitive decline
- Memory problems
- Sleep disorders
- Tremors, muscle twitching, spasms and stiffness
- Balance problems and difficulty walking
- Psychiatric symptoms like agitation, anxiety, confusion, depression or hallucinations
- Seizures in some cases

While the combination of gastrointestinal and neurological symptoms is particularly characteristic of DPPX encephalitis, only about half of affected individuals have gastrointestinal features.

How is it diagnosed?

Investigations which can help make a diagnosis of DPPX encephalitis include:

- Detection of DPPX antibodies in blood or cerebrospinal fluid (CSF)
- Magnetic resonance imaging (MRI) brain imaging (though results may be normal)
- Lumbar puncture to analyse CSF
- Electroencephalography (EEG) to assess brain activity patterns
- Screening for underlying cancers that may trigger the condition (though cancers are rarely detected in DPPX encephalitis compared to some other forms of autoimmune encephalitis)

Is it treatable?

Yes, DPPX encephalitis is treatable with immunotherapy. Treatment options include:

- High-dose corticosteroids
- Intravenous immunoglobulin (IVIG)

- Plasma exchange
- Rituximab
- Cyclophosphamide

Treatment often requires hospitalisation, especially in the acute phase of the illness. Some patients may need intensive care support. If a cancer is detected, treatment of the cancer is usually required to improve the neurological condition. Physical and cognitive rehabilitation are often an important component of recovery.

What is the course of the illness?

The course varies between patients. Many patients respond well to immunotherapy, though recovery can be slow. A degree of residual memory problems after DPPX encephalitis is common. It is thought that starting treatment soon after the development of neurological symptoms leads to better outcomes. Without treatment, the condition can be severe and potentially life-threatening.

For some patients DPPX encephalitis is a one-off illness, but for others relapses occur. When a relapse occurs, symptoms experienced previously may worsen or come back, requiring further treatment. In patients who relapse, longer-term treatments aimed at preventing future relapses are often used. Long-term follow up is helpful to monitor recovery from the initial illness, occurrence of relapses and any long-term medications used to prevent relapses.

Can it be prevented?

Currently there is no known way to prevent DPPX encephalitis. Research is ongoing to better understand the triggers of this condition and potential preventative strategies.

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