Voltage-gated Potassium Channel-complex Antibody-associated Limbic Encephalitis

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Our immune system works to clear our bodies of foreign invaders such as infections. It does this, in part, by producing antibodies which attach to and help destroy the invaders. Instead of attaching to the invaders, occasionally the antibodies can mistake parts of the body as foreign and attach to these regions. If the brain is the mistaken region, the antibody attack produces an Autoimmune Encephalitis. When the antibodies target the voltage-gated potassium channel complex in the brain, they cause ‘Voltage-gated Potassium Channel-complex Antibody-associated Limbic Encephalitis’ (VGKC-LE).

**Presentation**
Men are roughly affected twice as often as women. Initially, family members usually notice that their relative becomes forgetful, drowsy and withdrawn. Patients can also develop mood disorders (like depression) or bizarre thoughts and behaviours.

In addition, seizures frequently occur. These may take the form of brief ‘absences’ when patients glaze over for a few seconds (also called ‘temporal lobe epilepsy’), or full blown arm and leg jerking which can be very disturbing for observers (also known as generalised seizures). Finally, patients may develop brief jerks of the face and arm (so-called faciobrachial seizures) – this is an important feature and highly suggestive of VGKC antibodies.
Investigations

VGKC-LE can be mistaken for many other diseases, including Viral Encephalitis or other autoimmune conditions. Most patients are investigated with

- blood tests (patients can have a low salt level with VGKC-LE)
- lumbar puncture (LP) to help exclude infection
- electrical recordings of the brain (EEG) to look for seizure activity
- Magnetic Resonance Imaging (MRI) scans which often show swelling and inflammation of the brain.

To obtain a definitive diagnosis with the above clinical features, the VGKC-antibodies can be measured in blood and sometimes spinal fluid.

It has recently been discovered that the VGKC-antibodies do not actually target the potassium channel. They target proteins called LGI1, and less frequently CASPR2, which are tightly associated with the potassium channels in the brain. Therefore, various reports, diagnostic tests and doctors now use the terms VGKC, VGKC-complex, LGI1 and/or CASPR2 antibodies. In practice, there is usually little difference between these antibodies but this is an area currently under active research which may change the way we diagnose this disease in the future.

Treatments for VGKC-LE

VGKC-LE is a serious disease and patients often spend some weeks in hospital receiving specialist treatment and assessment. If the antibodies are found in a patient with the recognised clinical features, VGKC-LE can be treated by dampening down the immune reaction that is causing the inflammation using immunosuppression.

However, no single set of medications is proven to be superior to others and research into new or optimal treatments is ongoing. Nevertheless, most clinicians opt to use immunosuppression with steroids (either taken as tablets or into a vein), intravenous immunoglobulin (a blood product given into the vein in a drip) and/or plasma exchange (when some of a person’s blood is taken out from a vein, washed of various components including antibodies, and then put back into the vein in a drip). All these treatments have known side-effects and their benefits need to be weighed against possible side-effects in individual patients.
Treatment often results in fewer seizures and some improvement in confusion and memory problems. Improvements may be seen within a few days of treatment or in some cases only noticed after several months. Treatment may be continued for 1-2 years.

**Relapses**

In 95% of cases (although the exact figures are not yet known) VGKC-LE will occur only once and then never recur. Unfortunately, in the remaining 5% of cases it may recur and in so doing causes many of the same symptoms as before (such as seizures, confusion or forgetfulness). It is not yet known what leads to this recurrence but it usually warrants aggressive inpatient treatment that might range from steroids into the vein (intravenous methylprednisolone) through to plasma exchange.

**Outcomes and future challenges**

As this disease was only relatively recently described, there is still much to learn about what happens to patients in the long-term.

Very few patients describe having no residual problems. Some people are left with significant problems in memory, seizures and behaviour which require medical and psychological input and may need long-term placement in a home or other care facility. Other patients may return to their previous functioning, including getting back to work, some months or years after treatment.

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