PARANEOPLASTIC CHANNELOPATHIES

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Autoimmune channelopathies are caused by antibodies to various voltage-gated or ligand-gated neuronal and muscle ion channels. In paraneoplastic channelopathies, the autoimmune response is elicited by a distant tumour expressing antigens in common with a specific channel. The same antibodies are responsible for idiopathic disorders and are to be considered more disease specific than tumour markers.
Most of these disorders affect ion channels at the neuromuscular junction, even though dysfunction of the C.N.S. can also occur. Clinical symptoms are secondary to "loss-of-function", as pathogenic IgG cause internalization and down-regulation of channel number.
Lambert-Eaton myasthenic syndrome (LEMS) and neuromyotonia (NMT) are pre-synaptic disorders in which the autoimmune attack is directed to the voltage-gated calcium and voltage-gated potassium channel, respectively. These diseases are characterized by muscle and autonomic symptoms and both can be associated with C.N.S. involvement: cerebellar ataxia in LEMS and different forms of encephalitis in NMT. Paraneoplastic LEMS is typically related to small-cell lung carcinoma (SCLC), while 50% of NMT patients have a thymoma or, less commonly, SCLC.
Myasthenia gravis (MG) with antibodies to the muscle acetylcholine receptor is the prototypic autoimmune channelopathy and is associated with thymoma in 15-20% of cases. In this disease entity, there is a high frequency of serum antibodies against the ryanodine receptor, that are generally found in patients with severe disease, sometimes with heart dysfunction.
Antibodies against ganglionic $(\alpha 3)_2(\beta 4)_3$ acetylcholine receptor are responsible for an autonomic neuropathy, which in its paraneoplastic form is generally associated with thymoma.
A rare cerebellar ataxia with antibodies to a glutamate receptor (mGluR1) has been described in patients with Hodgkin's disease; however, its relation with the associated tumour is still unclear.
Autoimmune channelopathies are treatable diseases and have a better prognosis than other paraneoplastic neurological disorders. Treatment of the associated tumour significantly ameliorates LEMS, while its impact on thymoma-associated diseases is less evident. Specific symptomatic drugs are generally effective and immunomodulatory therapy is recommended for severely affected patients.