Ophelia syndrome

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Alexandre Cabanel's Ophelia

Alexandre Cabanel (French; 28 September 1823 – 23 January 1889) was a French painter. He painted historical, classical and religious subjects in the academic style. Cabanel shows Ophelia slipping very gracefully from the broken limb of a crooked willow. She doesn't seem too perturbed by the fact that she is about to land in the water. Cabanel has given his Ophelia the look of a medieval princess. She is very blonde and pretty, and her flowers have already dropped into the brook.

Ophelia syndrome is the association of Hodgkin lymphoma (HL) with an autoimmune limbic encephalitis. This syndrome is named after Ophelia, the tragic heroine of Shakespeare's play Hamlet. In contrast to Gertrude (Hamlet's mother), who is a psychologically nuanced and fleshed out character, Ophelia is considered by many to be rather one dimensional. She is, more or less, a tool to be exploited by her father (Polonius), brother (Laertes), and lover (Hamlet). As the play progresses, she transforms from a dutiful daughter to a bawdy seducer until finally, she can no longer tolerate the cognitive dissonance within her and descends into madness and ultimately dies as a result of drowning. It was first described by Dr. Ian Carr whose daughter, at the age of 15, developed progressive loss of memory, depression, hallucinations, and bizarre behaviour (*Lancet* 1982). These symptoms aptly describe Ophelia's deluded and obsessional attraction to the equally deluded and murderous Hamlet. Ophelia syndrome is a relatively mild disease without the Shakespearean tragic ending because it has a good outcome if recognised and treated.

Ophelia syndrome is the association of Hodgkin lymphoma (HL) with an autoimmune limbic encephalitis (LE), as a result of anti-metabotropic glutamate receptor 5 antibodies (mGluR5), which are found on post-

synaptic terminals of neurons and microglia and is expressed primarily in the hippocampus and amygdala. The syndrome frequently resolves following treatment of the underlying lymphoma. It is supposed that mGluR5 antibodies are pathogenic and that reduction in tumor burden leads to reduction in their circulating level.

The fairly well-recognised 'conventional' antibodies are those against VGKC (Caspr 2 and LGI1), NMDA, and AMPA. There is however an almost endless list of less familiar antibodies such as those against glycine, adenylate kinase 5, thyroid, GABA-A receptors, α-enolase, neurexin-3α, dipeptidyl-peptidase-like protein 6 (DPPX), and myelin oligodendrocyte glycoprotein (MOG). The group of disorders caused by antibodies to metabotropic receptors are another exciting area in autoimmune encephalopathies. The main antibody in this group targets the metabotropic glutamate receptor 5 (mGluR5) and at least five autoantibodies have been reported in patients with Ophelia's syndrome: anti-mGluR56-8; anti-Hu9, 10; anti-NMDAr11; anti-SOX1 and anti-PCA212, however in many other reports autoantibodies have been absent.

There is another constellation of signs and symptoms named after Ophelia, known as the Ophelia complex (and not Ophelia syndrome), in psychiatry. It is characterized by low self esteem, anxiety, inability to take decisions and increased risk for depression – especially in young females in the peripubertal period.