The Autonomic Neuropathies: Some Recent Insights

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The autonomic neuropathies are peripheral neuropathies with a selective or disproportionate involvement of autonomic fibers. Recent insights into diabetic and autoimmune autonomic neuropathies are of particular interest. There is a spectrum of diabetic neuropathies. Autonomic involvement is prominent in the great majority of diabetic neuropathies and may critically impact clinical presentation and prognosis. The diabetic state causes pathological damage to the micro- and macrovessels, Schwann cell, axon and neurons, beginning in the metabolic syndrome. An inflammatory perivascular response can be present and oxidative injury appears to be present. Phenotypes include distal small fiber neuropathy, diabetic autonomic neuropathy and diabetic radiculoplexus neuropathy. The earliest autonomic involvement is the distal ends of the longest fibers, with cardiovagal and distal postganglionic impairment. The splanchnic mesenteric bed can also be affected resulting in enteric neuropathy. Some forms of diabetic neuropathy are highly treatable. Cardiac autonomic neuropathy occurs early and can be mutifocal with areas of hyperinnervation. Cardiac involvement seems to be associated with increased mortality.

Autoimmune autonomic neuropathy can be due to A3 AChR antibody. This AAN is characterized by orthostatic hypotension and a cholinergic neuropathy comprising gastroparesis, neurogenic bladder, Adies pupils and widespread anhidrosis. There is a linear relationship between severity of autonomic failure and antibody titer. Several recent advances include the following. It is possible to generated experimental AAN by immunization with AChR in the rabbit, resulting in an AAN that mimics all essential aspects of human AAN. It has also been possible to passively transfer experimental AAN by injection of A3 AChR IgG to mouse. There is some preliminary studies that suggest that removal of the antibody, or blocking it binding to receptor will improve AAN in humans with severe AAN. There are a number of additional phenotypes that have been recently recognized. One in 7 patients with the postural tachycardia syndrome (POTS) have low antibody titers. Patient with the phenotype of pure autonomic failure (Bradbury Eggleston syndrome) can also have low titers, suggesting that this might be a very chronic AAN. Another form of AAN is paraneoplastic autonomic neuropathy. There are a series of antibodies associated with neoplasms of the lung, breast, ovary and thyroid. Neural targets include autonomic neuron, dorsal root ganglion cells, peripheral nerve, cerebellum, spinal cord and brain in various combinations.

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