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FAST FACTS AND CONCEPTS #197

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Background Chemotherapy associated peripheral neuropathy (CAPN) is a common dose-limiting toxicity of many anti-cancer agents. This Fast Fact will review the clinical features and treatment of CAPN.

Etiology & Risk Factors CAPN is a common and expected part of treatment with the platins (cisplatin, oxaliplatin), vincristine, taxols (paclitaxel and docetaxel) and more recently with bortezomib. CAPN is less commonly seen with cytosine arabinoside, inteferons, procarbazine, and thalidomide. The risk of CAPN is higher in patients over 50 years old, heavy alcohol users, patients with renal or hepatic insufficiency, and those with preexisting neuropathies. The severity of CAPN is correlated with both cumulative and high single doses of the causative chemotherapeutic agent. The physiology of CAPN varies among different drugs and can involve damage to the neuron, vasa vasorum, or myelin sheath.

Clinical Features

- CAPN usually presents as a symmetric, axonal neuropathy, although focal and autonomic neuropathies can also occur. Symptoms usually begin within the first 3 cycles of chemotherapy, and may peak in severity up to 3 months after the drug is discontinued. Sensory symptoms generally improve over many months following discontinuation, but not in all patients; motor symptoms are less likely to improve.
- Symptoms include sensory (tingling, numbness, burning, peri-oral numbness), motor (foot, wrist drop, difficulty buttoning a shirt or holding a pen), autonomic (constipation), or myalgias or muscle cramps.
- Signs include loss of deep-tendon reflexes, sensory deficits (stocking glove distribution is most common), foot or wrist drop, or symmetric motor weakness.
- The most common pattern is an asymptomatic loss of deep tendon reflexes, progressing to a sensory, and finally motor neuropathy. Oxaliplatin can cause both an acute and chronic neuropathy. The acute process can begin during the drug infusion and include cold-induced paresthesias of the hands, feet, throat, and perioral area; the chronic form is a dose-dependent sensory neuropathy similar to other chemotherapy-induced neuropathies. Vincristine can cause pharyngeal myalgias (sore throat) and autonomic neuropathy manifested by constipation, in addition to a typical axonal neuropathy.
- Diagnosis is based on a history and neurological exam. Nerve conduction studies and electromyography, while confirmatory, are usually not needed.
- Differential diagnosis includes direct tumor effects, non-chemotherapy induced neuropathies (e.g. postoperative, post-radiation, diabetic), or paraneoplastic syndromes.

Prevention Early detection is key, allowing for dose reduction or drug discontinuation. Even after discontinuation, symptoms may progress for several months and then stabilize or slowly improve over a period of weeks to months. Neuroprotective agents including amifostine, vitamin E, glutamine, L-carnitine, and magnesium, have been proposed to prevent CAPN. There is currently no consensus on their use due to limited evidence and likely variable efficacy for different chemotherapies. Other protective measures advised to patients are to protect hands and feet from extremes of temperature (wearing socks, using gloves while cooking), routinely inspect for cuts or abrasions, and fall prevention education.

Treatment No specific treatment exists to reverse CAPN, however pain should be treated symptomatically. There is little research to guide analgesic therapy, but clinical experience suggests treating this as any other painful peripheral neuropathy with adjuvant analgesics including gabapentin and pregabalin (see Fast Fact #49), tricyclic

antidepressants such as amitriptyline, and serotonin-norepinephrine reuptake inhibitors such as duloxetine and venlafaxine (see Fast Fact #187). Opioids are recommended as a short-term treatment while waiting for an adjuvant to work, and for ongoing moderate to severe pain despite the use of adjuvant analgesics.

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