Cancer-related Neuropathic Pain

Neuropathic pain is a common pain syndrome for patients with cancer. As I mentioned in my introductory pain post, neuropathic pain is one of the three main types of pain (somatic, visceral, and neuropathic). It is nerve-related and is typically described as an electrical or burning sensation; it can occur both due to damaged peripheral nerves (outside of the spinal cord and the brain) or damage within the central nervous system (CNS, which includes the spinal cord and brain). Because of associated nerve injury, some patients can develop decreased sensation or actual muscle weakness. While there are certainly isolated instances of pure neuropathic pain, often neuropathic pain is part of a “mixed” syndrome in which a patient can have neuropathic pain in conjunction with the other types of pain as well.

Why does this pain develop when a nerve is damaged, even after the injury has occurred? Nerves that are damaged can begin to have abnormal sensing—the pain fibers in the nerves can become more sensitive due to damage and can also trigger pain spontaneously. In the spinal cord, the signals from pain can be amplified by nerve damage—this causes the pain response to be much higher than expected to minor stimuli (a bedsheet touching the feet or something cold hitting the skin).

In hearing about neuropathic pain, we often think of the hands and feet being affected and feeling paresthesias (pins and needles) there, but neuropathic pain can occur anywhere there are nerves. In cancer, the mechanism of nerve injury can occur through three main ways:

1) direct pressing on the nerve by tumor
2) cancer treatments toxic to nerves
3) paraneoplastic syndromes where the cancer causes an abnormal reaction from the body’s autoimmune system against the nerves. Paraneoplastic syndromes are much less common, so I won’t be discussing this.

Multiple chemotherapeutic agents can cause neuropathic pain. The big culprits include the platinum agents (cisplatin), the taxanes (taxol), the vinca alkaloids (vincristine), and thalidomide. Cisplatin is probably one of the most common chemotherapies that causes neuropathic pain. As an example, cisplatin will damage peripheral sensory nerves including those in the hands and feet; it can also cause a syndrome of neuropathic pain that feel like electrical shocks from the back down to the feet due to cisplatin’s effects on nerves in the spinal cord. Unfortunately, it can take months for the neuropathies from cisplatin to resolve, and there may not be complete recovery.

Certain cancer-related surgeries can cause neuropathic pain as well, including mastectomy, neck surgeries, and thoracotomy. Sometimes this pain can become chronic, though the pain can resolve or at least improve with time. For patients who undergo amputation, phantom limb pain (pain perceived where an amputated limb had been) and “stump” pain (at the site of the amputation) are other neuropathic pain syndromes that can occur.
Treatment

In terms of medications, anti-seizure medications have been very beneficial in the treatment of neuropathic pain and are considered first-line. Neurontin, or gabapentin, is the big player here, and there is growing evidence for the use of neurontin in cancer-related pain, after gabapentin was studied for diabetic neuropathy and neuropathic pain from shingles. Lyrica, or pregabalin, is also being used which is an analog of neurontin and has the same mechanism of action. Both neurontin and lyrica have become more widely used compared to other medications for neuropathic pain; neurontin has been recommended by the WHO and the NIH as first-line therapies for neuropathic pain. They have fewer side effects and drug interactions compared to other meds for neuropathic pain; however, they should be used cautiously in patients with kidney dysfunction. The primary side effects are somnolence and dizziness. Neurontin is generally started at a low dose and titrated up, which helps with the initial somnolence; often I will start neurontin first at bedtime and then titrate up over the course of several days to 3 times a day.

Other anti-seizure medications are also used but less commonly, such as tegretol (carbamazepine), lamictal (lamotrigine), or trileptal (oxcarbazepine).

Antidepressants have also been used and studied for treating neuropathic pain even prior to neurontin. The most common anti-depressants used are the tricyclic anti-depressants (named so for their chemical structure) such as nortryptiline and amitriptyline; however, their side effects can be a problem, as they can cause anti-cholinergic side effects, like dry mouth, urinary retention, and constipation, as well as drowsiness and heart arrhythmias.

Other types of anti-depressants are being used more and more. Both effexor (venlafaxine) and cymbalta (duloxetine) are newer agents that have had benefit for patients with neuropathy, though not specifically cancer-related.

Opioids are still considered a good therapy for neuropathic pain, often in combination with other medications. Clinicians don’t often use these as first line treatments, but they have been studied in combination with medications like gabapentin and have shown improved pain control overall. See my prior post on opioids for more about this class of pain medications.

Anesthetics are another class of medications for neuropathic pain. This includes lidoderm patches, or transdermal lidocaine, used in the treatment of pain from shingles but also in pain after mastectomy or thoracotomy. Notably, capsaicin cream is also considered a topical anesthetic treatment for neuropathic pain. In general, these topical agents have fewer systemic side effects than oral medications. Other anesthetic medications include intravenous lidocaine and mexiletine—these are generally reserved for severe neuropathic pain and used under the supervision of pain specialists.

Pain specialists are a great resource in the treatment of neuropathic pain, particularly when the standard treatments are not working. Some of the adjunct medications they use include ketamine (an anesthetic) as well as clonidine (a type of blood pressure medication and used in opioid withdrawal); these can be paired with standard therapies to improve pain control. There are also interventional strategies such as nerve blocks and the use of intrathecal (into the
spinal fluid) medications.

There are some non-medication-based treatments for neuropathic pain, including radiation therapy, i.e. targeting a tumor that is pressing on a nerve, and surgical decompression of the spinal cord when there is tumor pressing on the cord. With regards to complementary therapies, there has been some study of acupuncture in diabetic neuropathy but not in cancer-related neuropathic pain.

Thankfully, there is a growing body of research looking at neuropathic pain in cancer, as well as a growing armamentarium for controlling this type of pain. I’m optimistic that we will be seeing more treatments coming down the pipeline!