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Electrodiagnosis in Cancer Rehabilitation

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Abstract

With numerous advancements in early detection and multi-modal therapy, cancer has become a chronic disease. As the number of cancer survivors continue to increase, physiatrists and other neuromuscular disease specialists are more likely to encounter individuals with residual impairments, disabilities, and/or handicaps resulting from cancer or related treatments. The cancer patient is especially prone to injury directed at the peripheral nervous system at multiple anatomic levels. Tumors can directly compress or infiltrate vital nervous system structures, or can cause severe neuromuscular disorders through a paraneoplastic process. Immunocompromised cancer patients are susceptible to indirect neurologic insult through secondary mechanisms such as infection or metabolic disorders. Cancer treatments themselves; including surgery, chemotherapy, radiation therapy, and hematopoietic stem cell transplant; can result in a wide variety of neuromuscular complications with a wide range of symptom and functional severity. Electrodiagnosis is an invaluable tool in the evaluation of neuromuscular disorders in this patient population.

Keywords

Electrodiagnosis; radiculopathy; plexopathy; neuropathy; paraneoplastic syndrome; cancer rehabilitation

Introduction

Neuromuscular complications related to cancer are common. Cancer can directly affect the peripheral nervous system at any level via numerous mechanisms, including direct nerve compression or infiltration, hematogenous or lymphatic spread, meningeal dissemination, or perineural spread. Paraneoplastic syndromes often manifest with neuromuscular dysfunction, as can cancer-associated medical complications such as infections, weight loss,

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or malnutrition. Acquired neuropathies can result from effects of cancer treatment itself; be it surgery, chemotherapy, radiation therapy, hematopoietic stem cell transplantation, or immunologic therapy. Patients may also have pre-existing neurologic conditions, such as diabetic or hereditary neuropathies, that can be exacerbated by cancer or its related treatments. Often, a combination of processes can be present.

Electrodiagnostic studies, including nerve conduction studies (NCS) and needle electromyography (EMG), are invaluable tools for assessing neuromuscular function in cancer patients. Electrodiagnosis can confirm a suspected neuropathic or myopathic process as well as rule out other possibilities. It can detect subclinical neuropathies, which can inform clinical decision making regarding use of neurotoxic chemotherapeutic agents. They can help with localizing lesions and determining pathophysiology, chronicity, and severity; which in turn can aid the cancer physiatrist in determining prognosis for recovery and the utility of future rehabilitation interventions. Finally, the information obtained with electrodiagnostic testing can help guide the oncology team with regards to surgery, chemotherapy, or radiation therapy planning.

Electrodiagnosis should be thought of as an extension of the history and physical examination, with the expected clinical and NCS/EMG findings dependent on the location, distribution, and pathophysiology of the neurologic lesion. Any and all levels of the peripheral nervous system can be affected by cancer and its treatments; including spinal roots, brachial or lumbosacral plexus, peripheral axons and/or myelin sheaths, the neuromuscular junction, and muscle fibers. Because of the variety of mechanisms of injury and wide scope of clinical presentation, the true incidence and prevalence of neuromuscular disorders in cancer patients are unknown. However it is estimated that approximately one-third of adult chronic cancer pain patients, across all tumor types and stages, are felt to have cancer-related neuropathic pain [1]

Radiculopathy

After disc disease and spinal stenosis, tumors involving the spine and spinal cord are the most common causes of radiculopathy [2]. All tumor types can metastasize to the spine, although the most common primary malignancies that do so include breast, lung, prostate, colon, thyroid, and kidney. Common primary malignant spinal tumors include multiple myeloma, plasmacytoma, and Ewing's and osteogenic sarcoma. Single or multilevel radiculopathies due to malignancy can result from primary or epidural metastatic tumor extension into the neural foramina. Leptomeningeal disease is due to metastatic involvement of the leptomeninges from infiltrating cancer cells, and involvement of the cauda equina can be thought of as a lumbosacral polyradiculopathy. The most common primary cancers associated with leptomeningeal disease are breast, lung, gastric, melanoma, lymphomas, and leukemias [3]. Of the leukemias, leptomeningeal disease is most commonly seen in acute lymphocytic leukemia [4, 5].

Patients can present with an asymmetric array of symptoms resulting from radicular or polyradicular involvement; including focal and radicular pain, areflexia, paresthesias, and lower motor neuron weakness. In leptomeningeal disease, there may be associated findings

of nuchal rigidity, as well as upper motor neuron signs, especially if there is concomitant brain involvement. Cranial nerves can be involved as well, with the oculomotor, facial, and auditory nerves most commonly affected.

In radiculopathies, sensory responses should be normal on NCS, as the location of involvement is proximal to the dorsal root ganglion, thereby making the segment of sensory nerve fibers tested metabolically and histologically intact. Motor responses within the affected myotomes may be normal or reduced in amplitude, depending on severity. Needle EMG is the most sensitive electrodiagnostic test for evaluation of a radiculopathy. One should record neuropathic abnormalities in at least two muscles innervated by different peripheral nerves but sharing the same root innervation, including increased insertional activity, fibrillation potentials, reduced recruitment, and large, polyphasic motor unit potentials (MUPs). Because paraspinal muscles are innervated by the dorsal primary rami, branching directly off of the nerve root, abnormal neuropathic EMG findings noted in the paraspinals further support the diagnosis of radiculopathy. Electrodiagnostic studies in leptomeningeal disease can sometimes be consistent with a polyradiculopathy, with preserved sensory nerve action potentials and abnormal paraspinal needle EMG findings. Absent F-waves or prolonged F-wave latencies on NCS are felt to be an early indicator of nerve root involvement, but are not specific for either radiculopathy or leptomeningeal disease [6].

Plexopathy

Brachial plexopathies from neoplasms are usually the result of metastatic disease, with breast and lung being the most common primary sources [7]. Symptoms include pain, paresthesias, numbness, and weakness in the distribution of plexus involvement. Metastases can involve any portion of the brachial plexus, but usually involve the lower trunk preferentially, due to its proximity to axillary lymph nodes and the superior sulcus of the lung. Neoplastic lumbosacral plexopathies can also stem from metastatic disease, but are much more likely to be caused by direct extension of local tumor or perineural spread [8]. Common tumors involved in lumbosacral plexus injury include colon, gynecologic tumors, lymphomas, and sarcomas.

The primary differential diagnostic concern in a cancer patient with a plexus injury is distinguishing between a neoplastic and radiation-induced etiology. Occasionally, the two conditions can coexist. Classically, radiation-induced plexopathy is delayed in onset, pain is less common than in neoplastic plexopathy, and symptoms of weakness and paresthesias are usually progressive [33, 34]. There is also more likely to be associated lymphedema in the involved limb. It has been reported that neoplastic brachial plexopathy tends to preferentially affect the lower trunk, and radiation plexopathy the upper portion of the plexus; however further studies suggest that plexus involvement may be more diffuse and with more overlap in both etiologies than previously suspected [35].

The distribution of motor and sensory nerve conduction abnormalities is important in the localization of both brachial and lumbosacral plexopathies. For instance, upper extremity NCS in a lower trunk brachial plexopathy will demonstrate a characteristic pattern of normal

median sensory nerve action potential (SNAP) amplitudes, reduced ulnar SNAP amplitudes, and reduced median and ulnar compound muscle action potential (CMAP) amplitudes. Abnormalities will also be noted in the medial antebrachial cutaneous SNAP. Findings on needle EMG will demonstrate fibrillation potentials, reduced recruitment, and large, polyphasic motor unit potentials within the distribution of involvement. Needle EMG of the paraspinal muscles is normal in a pure plexopathy, however one often sees both root and plexus involvement in a given patient, depending on the extent of disease. Documenting asymmetric findings on NCS and needle EMG can sometimes help distinguish a newer onset radiculopathy or plexopathy in the setting of an underlying chemotherapy-induced polyneuropathy.

Approximately 50% of all cancer patients will undergo radiation therapy at some point during the course of their disease, and radiation therapy is involved in approximately one quarter of all cancer cures [31]. As patients are living longer following cancer treatments, physicians are becoming more aware of late neuromuscular complications of therapy, especially radiation therapy. Side effects are essentially related to the dose of radiation and the volume of normal tissue that receives radiation [32].

The pathognomonic EMG finding of radiation-induced neuropathic damage is the myokymic discharges, which are clusters of motor unit potentials firing spontaneously with regular interburst and intraburst frequencies. The absence of myokymic discharges however does not exclude radiation damage, and while the presence of myokymic discharges and fasciculation potentials confirms a radiation-induced contribution to plexus injury, it does not exclude the possibility of tumor involvement [34]. Even in the setting of classic EMG findings, follow up imaging of the brachial plexus with MRI is warranted to exclude a concomitant compressive or infiltrating lesion, which could be due to local recurrence or new metastases. In a patient with a history of prior radiation therapy to the axillary or supraclavicular lymph nodes, secondary radiation-induced neoplasms such as sarcomas should also be considered.

Mononeuropathy

Focal mononeuropathies directly related to cancer most often result from the external compression or invasion from tumor, such as an isolated radial neuropathy caused by a primary osteogenic sarcoma or a bone metastasis involving the spiral groove of the humerus. Malignant nerve sheath tumors arising from plexiform neurofibromas can also result in focal mononeuropathies. The presence of secondary sarcomas compressing or infiltrating nervous system structures, resulting from previous radiation therapy, needs to be excluded. NCS and needle EMG should correspond to clinical abnormalities, limited to the distribution of the individual nerve, involving both sensory and motor fibers depending on the composition of the particular nerve involved.

Although uncommon, damage to the peripheral nervous system during the perioperative period can occur in the surgical cancer patient. Because the nature of these procedures is likely to be more complex than in non-oncologic surgeries, it is postulated that the likelihood of neuromuscular complications is greater in oncologic surgeries. There are no studies

however comparing the incidence of unintentional nerve injury in the cancer surgery population to that in the general population. In addition, peripheral nerves are sometimes intentionally sacrificed in the cancer surgery patient in order to obtain local disease control, especially the spinal accessory nerve to the trapezius in radical or modified neck dissection for head and neck malignancies or in limb-salvage surgery for extremity sarcomas. The pattern and extent of neurologic involvement following surgery depends on the location of the tumor, patient positioning during surgery, and the patient's overall preoperative status and propensity to nerve injury [23].

Perioperative neurapraxic injuries, resulting from either compression or traction of peripheral nerves, are well-recognized phenomena. It is felt that these injuries result from the patient's position during anesthesia and surgery or during the immediate post-surgical recovery period [24]. Common sites of injury and associated surgical procedures include brachial plexus injury during thoracotomy or mastectomy, given the abducted position of the involved upper extremity. Abduction of the upper extremity greater than 90 degrees during surgery can cause the humeral head to sublux inferiorly, resulting in compression of the lower part and traction of the upper part of the brachial plexus. Patients upon awakening report varying degrees of pain, weakness, and numbness in both the upper and lower trunk distribution. Complete, spontaneous recovery within weeks is common; even in cases of severe plegia. Ulnar neuropathies at the elbow, resulting from arm boards used to secure intravenous lines; and radial neuropathies at the spiral groove, resulting from prolonged time in the lateral decubitus position are also noted following thoracic surgery. Findings of focal slowing, temporal dispersion, or conduction block across the level of injury can be demonstrated on motor NCS.

Compression of the femoral nerve or lumbar plexus can result from traction during pelvic surgery. Patients undergoing hip arthroplasty or acetabular reconstruction are especially susceptible to injury of the peroneal division of the sciatic nerve. Injuries to the superior gluteal, obturator, and femoral nerves have also been reported [25]. A cancer patient having undergone a significant amount of weight loss may be more susceptible to a perioperative peroneal neuropathy at the fibular head, resulting from positioning following a prolonged surgery and post-operative recovery period. Finally, delayed post-operative hemorrhages and hematomas should be excluded in all patients who develop new neuropathic symptoms 24–48 hours after surgery.

Rapid weight loss is a common symptom of malignancy, and thus there is a higher risk of focal compression neuropathy, especially the peroneal nerve at the level of the fibular head. This is because the nerve in that location is no longer protected by soft tissue, and is more easily compressed against bony structures. A history of habitual leg crossing is sometimes elicited. Focal slowing, temporal dispersion, and conduction block across the fibular head on peroneal motor NCS are characteristic findings. There may be additional predisposition to injury given exposure to neurotoxic chemotherapy.

Polyneuropathy

Chemotherapy-induced peripheral neuropathy is a well-described and well recognized phenomenon, and is the most common neuromuscular condition associated with cancer. Side effects tend to be dose-dependent, although it is important to recognize pre-existing sub-clinical neuropathies or a family history of neuropathy, such as in the case of the hereditary sensory and motor neuropathies. The neurotoxic effects of chemotherapy in these susceptible patients can occur earlier than expected in the treatment course and symptoms can be severe and permanently disabling [26, 27, 28]. Although almost all agents have been associated with neuropathies, there are a select number of chemotherapeutics that are especially prone to causing neuropathy. These notably are the vinca alkaloids, the taxanes, and the platinum-based compounds.

The vinca alkaloids; such as vincristine, vinblastine, and vinorelbine; are used in the treatment of solid tumors, lymphomas, and leukemias. They are usually given in combination with other chemotherapeutic agents. The mechanism of action with the vinca alkaloids is to arrest dividing cells in metaphase by binding tubulin and preventing its polymerization into microtubules. This is also the proposed mechanism of inducing neuropathy, by inhibiting anterograde and retrograde transport via microtubules and causing axonal Wallerian degeneration. Taxanes such as paclitaxel and docetaxel are also used to treat solid tumors such as breast and ovarian cancer. As in the vinca alkaloids, the taxane-induced neuropathy results from damage to the axonal microtubule system [29]. Bortezomib, used in the treatment of multiple myeloma, is also highly associated with an axonal peripheral neuropathy.

Chemotherapy induced axonal neuropathy generally is characterized by subacute onset, length-dependent, symmetric, sensory greater than motor deficits. NCS reveal normal or low amplitude CMAPs and low amplitude or absent SNAPs; with the lower extremities more affected than the uppers. Needle EMG findings include fibrillation potentials, reduced recruitment, and large, polyphasic MUPs in distal limb muscles; again more prominent in the lower limbs. The prognosis for neurologic recovery, upon discontinuation of the offending agent, is generally favorable but depends on the severity of symptoms.

Platinum based compounds such as cisplatin, carboplatin, and oxaliplatin are used in the treatment of solid tumors such as ovarian, testicular, and bladder cancer. While platinum toxicity can also result in a distal, symmetric, sensorimotor polyneuropathy through microtubule disruption; it can also cause preferential apoptosis-related damage to the dorsal root ganglia, causing a pure sensory neuronopathy or ganglionopathy with clinical and electrodiagnostic features including sensory ataxia and upper extremity SNAPs being more affected than in the lower extremities. CMAPs are preserved in a sensory neuronopathy, and needle EMG findings are normal, although patients may demonstrate poor volitional motor unit activation due to profound proprioceptive sensory loss. A “coasting phenomenon” may be noted, where symptoms can progress for months following discontinuation of the platinum based agent. Prognosis for neurologic recovery in a sensory ganglionopathy is poor [30].

Diffuse peripheral nerve infiltration directly from cancer, either in a distal symmetric pattern or in a mononeuritis multiplex pattern, is rare but has been reported in hematologic malignancies such as cutaneous T-cell lymphoma and chronic lymphocytic leukemia [9, 10]. Amyloid deposition in systemic amyloidosis and multiple myeloma can also result in diffuse polyneuropathy, as well as generalized proximal myopathies. [11,12]. Neuropathies associated with paraproteinemias and plasma cell dyscrasias warrant special consideration, as there is a high association of neuropathies with these disorders and the presence of monoclonal proteins. These disorders include monoclonal gammopathy of unknown significance (MGUS), Waldenström's macroglobulinemia, cryoglobulinemia, multiple myeloma, osteosclerotic myeloma, primary amyloidosis, non-Hodgkin lymphoma, and the chronic leukemias [25]. A diagnosis of MGUS should raise concern, as approximately 20% of these patients will at some point develop a malignant plasma cell disorder.

Electrodiagnostic studies are usually consistent with an axonal process, although in the case of osteosclerotic myeloma and POEMS syndrome (Polyneuropathy, Organomegaly, Endocrinopathy, M protein, Skin changes), findings of both axonal loss and multisegmental demyelination can be seen. The electrodiagnostic findings in POEMS syndrome can be similar to those seen in chronic, inflammatory demyelinating polyradiculoneuropathy [26]. The monoclonal gammopathy in these disorders can involve IgM, IgG, or IgA proteins, and there is some evidence to suggest that the type of paraproteinemia correlates to the clinical and electrophysiologic characteristics of the neuropathy [36]. That being the case, characterizing the pathophysiology of the neuropathy on NCS and needle EMG can help guide the hematologist/oncologist whether or not to initiate treatment.

Neuromuscular paraneoplastic syndromes cause damage to the peripheral nervous system as a result of remote effects from a malignant neoplasm or its metastases. Almost all tumor types have been associated with paraneoplastic syndromes, and any part of the nervous system can be affected. Although rare, it is important to recognize these syndromes. The clinical presentation is usually more rapidly progressive and severe than what would normally be expected in a non-cancerous etiology. They often precede the diagnosis of cancer, and early recognition may increase survival. Treatment of the underlying malignancy usually results in improvement of neurologic symptoms. In some disorders, neuronal antigens expressed by the tumor result in an autoimmune response against both the tumor as well as healthy neural tissue, and identification of these markers can facilitate diagnosis of the primary tumor. For example, the presence of anti-Hu antibodies, sometimes detected in paraneoplastic sensory neuronopathies, has a strong association with small-cell lung cancer, neuroblastoma, or prostate cancer [13]. Although some syndromes are associated with an identifiable neuro-oncologic auto-antibody, frequently no such marker is detected.

Paraneoplastic sensory neuronopathy or ganglionopathy can present with either an acute or insidious onset of pain and sensory loss. Clinical findings of sensory ataxia and pseudoathetosis are often present at various levels of severity. Both the clinical and electrodiagnostic findings can be diffuse but commonly are more severe in the upper extremities and may be asymmetric. Motor dysfunction is usually absent, however sensory neuronopathy can sometimes be seen along with a more diffuse paraneoplastic neurologic syndrome involving encephalomyelitis, autonomic neuropathy, and motor neuronopathy [13]. A pattern of more severe sensory abnormalities on nerve conduction studies in the

upper extremities compared to the lower extremities helps distinguish this entity from a length-dependent sensory neuropathy. Needle EMG is usually normal, although poor volitional activation of MUPs may be noted, due to the severity of sensory abnormalities. The most common associated neoplasm is small cell lung cancer; however breast, prostate, renal, chondrosarcoma, and lymphoma have also been implicated.

The diagnosis of a true paraneoplastic distal, symmetric, sensorimotor polyneuropathy is difficult to confirm, as there are many more likely known etiologies that can cause this pattern of involvement; including diabetes mellitus, nutritional deficiencies, and toxic exposure such as chemotherapy. A subacute, sensorimotor polyneuropathy as a paraneoplastic syndrome is therefore a diagnosis of exclusion. Symptoms include pain, paresthesias, numbness, and weakness in a stocking-glove distribution, along with hyporeflexia. A more rapidly progressive course may be the only distinguishing factor differentiating a paraneoplastic syndrome from an idiopathic or diabetic etiology. Electrodiagnostic findings are consistent with an axonal process, with reduction in motor and sensory amplitudes on NCS and the presence of fibrillation potentials and large, polyphasic motor unit potentials in distal limb muscles on needle EMG. This syndrome has been associated with lung and breast cancer [15]. A peripheral neuropathy resembling a chronic inflammatory demyelinating polyradiculoneuropathy affects up to 50 percent of patients with the osteosclerotic form of plasmacytoma (the polyneuropathy, organomegaly, endocrinopathy, M protein, and skin changes [POEMS] syndrome) [13]. Motor fibers seem to be preferentially affected, with marked slowing of conduction velocities, prolonged distal latencies, and evidence of temporal dispersion on NCS [16].

With regard to motor neuron disease syndromes, the anti-Hu associated paraneoplastic encephalomyelitis/sensory neuronopathy/motor neuropathy syndrome has a strong link with small cell lung cancer. Subacute motor neuropathy and primary lateral sclerosis have been associated with lymphoma and breast cancer, respectively [21]. Sensory NCS in patients with pure motor neuron disease are normal. Motor responses will be either normal or reduced in amplitude. Needle EMG will demonstrate fibrillation and fasciculation potentials, reduced recruitment, and large, polyphasic, varying MUPs diffusely. There is no known association between cancer and amyotrophic lateral sclerosis, however in newly diagnosed motor neuron disease a screening for cancer should be part of the exclusionary diagnostic workup. Finally, a pattern of clinical and electrophysiologic involvement resembling mononeuritis multiplex may represent a paraneoplastic vasculitic neuropathy. This syndrome has been reported in association with small cell lung cancer and lymphoma [17]. The presence of an anti-Hu antibody can be seen with this syndrome as well [18].

Autoimmune neuropathies have also been associated with chronic graft versus host disease (GVHD), and can present as either a distal symmetric sensorimotor polyneuropathy with characteristic electrodiagnostic findings, or as a multifocal demyelinating polyneuropathy with features similar to Guillain-Barré syndrome [43, 44].

Neuromuscular junction disorders

Lambert-Eaton Myasthenic Syndrome (LEMS) is a presynaptic disorder of neuromuscular transmission, and is perhaps the best understood paraneoplastic neuromuscular syndrome. Clinically, patients present with fatigue, proximal weakness, hyporeflexia, and autonomic dysfunction. Repetitive strength testing may reveal a “warming-up” phenomenon, where one can display an initial increase in strength with repetition followed by eventual fatigue. Bulbar involvement is rare. LEMS can occur independent from cancer, but up to 40–60 percent of cases have been shown to be associated with small cell lung cancer [7]. LEMS has also been reported to be associated with lymphoma, breast, ovarian, pancreatic, and renal malignancies.

Electrodiagnostic studies are invaluable in the diagnosis of LEMS. Motor responses are reduced in amplitude at baseline. Repetitive stimulation of motor nerves at low frequency (2–3 Hz) demonstrates a further decrement in amplitude. Following brief isometric exercise, facilitation occurs and compound muscle action potential amplitudes show at least a 100 percent increase [19]. This finding is essentially pathognomonic for LEMS. Sensory responses and needle EMG findings are usually normal, except for the presence of varying, unstable MUPs. Anti-VGCC antibodies are seen in up to 92 percent of LEMS patients [7].

Myasthenia gravis (MG) in the setting of chronic GVHD usually develops between two and five years after transplantation during tapering of immunosuppressive drug therapy [42]. Clinically and electrophysiologically, the findings are similar to typical autoimmune MG; with decrement of baseline CMAP amplitude noted with slow 2–3 Hz repetitive stimulation and repair of the decrement following brief isometric exercise. Needle EMG findings are similar to those seen in LEMS. Acetylcholine receptor antibodies may or may not be present. There has not been a reported association with thymoma in patients with GVHD-associated MG. Treatment regimens of GVHD-associated MG are similar to those of autoimmune MG, with equal efficacy.

Myopathies

Focal myopathies from tumor involvement are rare, and usually result from direct muscle infiltration from underlying bony metastases or local lymph node involvement, rather than from hematogenous spread. The findings of a symmetric, proximal myopathy on clinical examination and electrodiagnostic testing can also lead to the discovery of an undiagnosed cancer. Myopathic findings on needle EMG typically include fibrillation potentials and rapid recruitment of small amplitude, short duration, polyphasic MUPs. Complex repetitive discharges may be present. Findings are usually more pronounced in proximal versus distal muscles. NCS are usually normal. Although their classification as a true paraneoplastic syndrome is controversial, polymyositis and especially dermatomyositis are associated with an increased incidence of malignancy compared with the general population [20]. Breast, lung, and gynecologic malignancies are most frequently implicated.

Originally thought to be relatively radioresistant, it is now known that skeletal muscle is also susceptible to late onset effects of radiation therapy. The direct effect of radiation on muscle

results in fibrosis and contracture [36]. There have been multiple reports of a late onset dropped head syndrome in patients who have received mantle field radiation therapy in the distant past as part of their treatment for Hodgkin lymphoma [37, 38]. Clinical features include slowly progressive atrophy of neck and shoulder girdle musculature. Neck flexor and extensor muscles are markedly weak, with remarkably preserved motor function in the shoulder girdle and upper extremities. Affected muscles have a firm, fibrotic character on palpation. The head tends to be in a forward-flexed position, with a secondary kyphotic spinal posture, due to anterior cervical muscle contracture. Needle EMG demonstrates low amplitude, short duration, polyphasic motor unit potentials in affected muscles, with normal or decreased insertional activity and rare, if any, fibrillation potentials. There may additionally be findings of a concomitant brachial plexopathy or cervical radiculopathy, depending on the extent of the prior treatment field [39].

Polymyositis, and to a lesser extent dermatomyositis, are well recognized but uncommon complications of chronic GVHD. The incidence of polymyositis in the GVHD population is greater than that of the general population [41]. The clinical presentation, electrodiagnostic findings, and pathologic findings in GVHD-associated polymyositis are identical to those found in idiopathic polymyositis.

Special Considerations

Hematopoietic stem cell transplantation is performed as part of the treatment for hematologic malignancies such as leukemias, lymphomas, and multiple myeloma; as well as for select solid tumors and non-malignant diseases. These patients will frequently receive additional chemotherapy and/or radiation therapy as part of their treatment regimen, and are susceptible to related neurotoxic effects as described earlier. Metabolic derangements such as steroid-induced diabetes and malabsorption syndromes are also common following transplantation, and can likewise result in secondary peripheral nervous system dysfunction. As mentioned previously, there are numerous autoimmune neuromuscular conditions associated with chronic GVHD, affecting any combination of peripheral nerves, muscles, or the neuromuscular junction.

Immunocompromised patients are at high risk for numerous infections and secondary complications. Sepsis with multisystem organ failure in the cancer patient is a common reason for intensive care unit admission. Often these patients will be diagnosed with critical illness polyneuropathy and/or critical illness myopathy based on electrodiagnostic findings [26]. Other acute weakness syndromes such as MG, LEMS, or steroid myopathy should also be considered. Needle EMG of the diaphragm and phrenic motor NCS can help guide the critical care team with regards to the potential of weaning of ventilatory support, or determine whether interventions such as phrenic nerve pacing would be appropriate.

Certain medical conditions associated with cancer warrant special attention with regards to planning the needle EMG component of the electrodiagnostic study. Patients with lymphedema are felt to be at increased risk for cellulitis, and are frequently cautioned to avoid needle puncture in the affected limb to prevent infection or worsening lymphedema. The actual risk of cellulitis associated with needle EMG in the setting of lymphedema

however is unknown. Given this, reasonable caution should be exercised in performing needle examination, and physicians should balance the potential risks with the need to obtain the information gained [45]. While there is no contraindication for performing NCS in the lymphedematous extremity, the need for adequate stimulus intensity to obtain an accurate nerve or muscle action potential may be greater depending on the limb volume and extent of fibrosis, and therefore could result in more discomfort for the patient.

Cancer patients often receive therapeutic agents that adversely affect platelet counts, or are anticoagulated for treatment of associated deep venous thromboses, all of which increase likelihood of bleeding. Mild reduction in platelet counts (below 50,000/mm³) increases the chance of bleeding, and more severe thrombocytopenia (below 20,000/mm³) markedly increases the risk [46]. There is a scant evidence-base to guide the electromyographer in these clinical scenarios. As with balancing the potential risks and benefits of performing needle EMG in the lymphedema patient, clinical judgment is warranted in the cancer patient with increased bleeding risk. Careful selection and minimal exploration of easily compressible, superficial compartment muscles is recommended.

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Key Points

- The cancer patient is prone to peripheral nervous system injury at multiple anatomic levels.
- A wide variety of nerve injuries can be caused by cancer and its treatments; either by direct effects from tumors, cancer treatment effects, paraneoplastic effects, or indirect effects associated with cancer symptoms.
- Electrodiagnostic studies are an invaluable tool in the evaluation of neuromuscular disorders in the cancer patient population.