Diagnosis and Management of Brachial Plexus Lesions in Cancer Patients

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By S. H. Kori, MD [2]

Brachial plexus dysfunction is a well-known complication of cancer. Metastatic brachial plexopathy (MBP) and radiation injury to the brachial plexus (RBP) are the most common causes. The distinction between MBP and

Introduction

Neurologic symptoms and signs of brachial plexus dysfunction are well-recognized disabling complications of cancer that are caused by unrelated acute brachial neuritis [1,2], trauma to the plexus during surgery or anesthesia [3], metastatic spread of tumor [4], radiation injury [5-9], or radiation-induced plexus tumors [10]. Metastatic brachial plexopathy (MBP) and radiation injury to the brachial plexus (RBP) are by far the most common causes.

Distinguishing between radiation injury to the brachial plexus and metastatic brachial plexopathy is very important so as to determine both prognosis and treatment, but the distinction is not easy to make. Several investigators have attempted to define clinical criteria to distinguish between the two conditions [11-14], while others have assessed the utility of imaging studies [15-19] and electrophysiologic studies [20-23] in this regard. All of these attempts have met with limited success. In this article, I will review the incidence, clinical features, prognosis, and treatment options for each of these conditions, and attempt to identify features that aid in differentiating the two.

Anatomy of The Brachial Plexus

The brachial plexus is formed by the anterior primary rami of the C5 through T1 nerve roots. Occasionally, the C4 and T2 roots contribute to the plexus. After leaving the spinal canal through the intervertebral foramina, the roots pass behind the scalenus anterior muscle and unite at its lateral margin to form the trunks of the brachial plexus. The C5 and C6 roots form the upper trunk, C7 forms the middle trunk, and C8 and T1 unite to form the lower trunk.

Each trunk splits into an anterior and a posterior division in the floor of the posterior triangle in the neck. At the upper border of the first rib, the divisions unite to form the cords. All the posterior divisions link to form the posterior cord, the anterior divisions of the upper and middle trunks unite to form the medial cord, and the anterior division of the lower trunk forms the lateral cord. The cords located further laterally in the axilla give off branches, which form the peripheral nerves supplying the upper extremity. The brachial plexus is in close proximity to the scaleni muscles, first rib, apex of the lung, vertebral artery and venous plexus, lateral group of axillary lymph nodes, and axillary vessels in the neck and axilla.

Radiation Injury to the Brachial Plexus

Incidence

Even though improvements in radiation techniques have dramatically reduced acute and external radiation injuries, long-term complications, such as brachial plexopathy, are still an important cause of discomfort and disability following radiation therapy to the upper chest and neck area. Conservative surgery and radiation therapy have been used with increasing frequency in the treatment of early-stage breast cancer over the past 2 decades, thus increasing the incidence of radiation-induced brachial plexus injury. Pierce et al [5], in their review of 1,624 patients receiving radiation therapy for breast cancer, encountered brachial plexus involvement in 1.8% of patients. Other investigators [24-26] have found the incidence of this complication to be less than 1%.

Predisposing Factors
The radiation dose used, treatment technique, and concomitant use of chemotherapy were all significantly associated with the development of radiation injury to the brachial plexus in Pierce's series. The incidence of brachial plexopathy was significantly higher when the axillary dose of radiation therapy was more than 50 Gy than when it was 50 Gy or less (5.6% vs 1.3%, \( P = 0.004 \)). This is consistent with our own observations. All 22 patients with brachial plexopathy in our series had received more than 60 Gy of radiation to the plexus [12]. In another series, the rate of brachial plexopathy was reduced from 73% to 15% by decreasing the radiation dose from 63 to 57 Gy [6]. Several other series concur with this finding [7,8,27]. The dose alone, however, does not determine whether a given patient will develop radiation damage. For example, two of our patients were treated bilaterally with the same radiation dose but suffered radiation damage on only one side. The treatment technique also seems to play a role. In Pierce's series, none of the 507 patients who were treated with two-field technique developed RPB, whereas 20 of the 1,117 patients treated with three-field technique did (\( P = 0.0009 \)).

Radiation injury to the brachial plexus has also been shown to occur more frequently in patients who receive concomitant chemotherapy [5,23]. Given the demonstrated benefits of chemotherapy in breast cancer patients, it is important to assess the risks and benefits of adding the supraclavicular or axillary area to the regular radiation fields in patients scheduled to receive chemotherapy.

**Onset of Symptoms**

The interval from the last dose of radiation to the first symptom of plexus disorder varies widely. In our series, the interval varied from 3 months to 26 years, with a median of 4 years and an average of 5.5 years. Others have reported the average interval to range from 7.5 months to 6 years [6,12,13,22,23]. The interval tends to be shorter with higher radiation doses. Bagley et al [13] suggested that this interval may be shorter for radiation-induced plexopathy than for metastatic plexus lesions, a factor that may help differentiate between the two. In their series, the mean symptom-free interval was 9 months for the group with radiation-induced injury and 5.5 years for those with metastatic lesions. None of the other series, including ours, could confirm this finding. There was no significant difference between the two groups in the median symptom-free interval in our series.

**Clinical Features**

Sensory symptoms, such as numbness, paresthesia, and dysesthesia, along with swelling and weakness of the arm, are the predominant presenting symptoms of RBP. In our series, 55% of patients presented with paresthesia and 45%, with arm swelling and weakness. Only 18% of patients presented with any significant pain, and in only 35% was pain ever a major symptom. This finding is consistent with other series [8,11,15,20,21,23]. In contrast, pain was the presenting symptom in 98% of our patients with metastatic plexopathy. The significant difference in presentation of these two groups (\( P = 0.05 \)) can be very useful in establishing a clinical diagnosis. In addition, Horner's syndrome is not usually seen in radiation injury to the brachial plexus, and can be another useful sign to distinguish it from metastatic plexopathy [12]. The importance of the anatomic distribution of weakness, atrophy, and sensory changes in the differentiation of the two types of plexopathies is controversial. There is a consensus that by the time brachial plexopathy is diagnosed, a majority of patients have diffuse plexus involvement in both conditions [6,11-13,20,21,23]. We found, however, that in the earlier stages, radiation injury to the brachial plexus is manifested predominantly by upper trunk involvement, in contrast to the predominantly lower trunk involvement of metastatic plexopathy ([C] Table 1). In 34 patients with radiation neuropathy, Stoll and Andrews [6] also noted more involvement of the upper plexus but did not detail the findings or compare them with tumor plexopathy. Even though Pierce et al did not make an attempt to identify the trunks involved in their series, only three patients had grip weakness (C8 to T1 involvement), suggesting that most of their patients had upper trunk involvement.5

Other series have found no such correlation between the anatomic distribution of the neurologic dysfunction and the type of plexopathy [20,21,23]. We still feel that this can be an important clinical finding to distinguish between the two conditions, however. We hypothesize that since the divisions of the lower trunk run a shorter course through the radiation port, they are partially protected by the clavicle and thus are less likely to be damaged by radiation.

**Diagnostic Studies**
Imaging studies, such as routine plain films, tomograms, and bone scans, are not helpful in either diagnosing brachial plexopathy or establishing its etiology [12,15,20,21]. Computed tomography of the brachial plexus area can be very helpful in confirming the plexus lesion but is positive in only 50% of cases [12,15,17,20]. A diffuse, ill-defined loss of tissue plane is consistent with radiation injury to the brachial plexus, in contrast to the discrete mass lesion seen in tumor plexopathy [15,20]. Magnetic resonance imaging provides a better direct multiplanar imaging capability than CT and superior soft-tissue resolution. The presence of a mass in the brachial plexus area can be detected earlier and more consistently with MRI than with CT [18,19], but differentiation of radiation injury from metastatic brachial plexopathy is not always possible.

Electromyographic studies can be very useful in making the diagnosis of brachial plexopathy [20-23]. Nerve conduction velocities help differentiate brachial plexopathies from other types of neurologic dysfunction, such as radiculopathy and neuropathy, but are not helpful in differentiating radiation injury to the brachial plexus from metastatic brachial plexopathy. F-wave recordings and Erb's point stimulation are also helpful in distinguishing brachial plexopathy from other neurogenic lesions. Harper et al [20] found fibrillation potentials in 23% of RBP patients' paraspinal muscles on needle examination, compared to only 2% of MBP patients' muscles. They also found myokymic discharges to be common in RBP (63%), compared to metastatic brachial plexopathy (4%). Lederman and Wilbourn [21] also noted the presence of myokymia predominantly in RBP patients. However, Mondrup et al [23] were unable to demonstrate myokymia in any of their 17 patients with RBP.

**Prognosis and Treatment**

The natural course of radiation injury to the brachial plexus is variable. Pierce et al found that 80% of their RBP patients improved spontaneously, and only 20% suffered from progressive deterioration. This is in sharp contrast to our own observations and those of all other investigators. We have found that about a third of our patients deteriorate rapidly and exhibit significant weakness, lymphedema, and pain. The other two-thirds remain stable for months to years, with gradual worsening of paresthesias, weakness, and pain. Discomfort and disability are common.

No therapy is uniformly effective in patients with radiation-induced brachial injury. Early physical therapy is crucial, as it helps prevent lymphedema, frozen shoulder, posture-induced muscle spasms, and premature muscular atrophy. Tricyclics, antiarrhythmics, and anticonvulsants, when used appropriately, can control neuropathic pain. Transdermal electrical nerve stimulation (TENS) and dorsal column stimulators may be useful in rare, intractable cases. Neurolysis and neurolysis with omentoplasty have been suggested as surgical procedures to prevent clinical deterioration [28-30] but they have not been proved to be effective over the long term.31

**Metastatic Brachial Plexopathy**

**Incidence**

The exact incidence of metastatic plexopathy is unknown. In our review of 12,000 admissions to a cancer hospital during a 1-year period (prior to the availability of MRI), 52 patients were identified as having a brachial plexus lesion [12]. The tumors that commonly involve the brachial plexus are the lung, breast, and lymphoma [11-13,15,20]. Other tumors that can spread to the plexus are sarcoma, melanoma, unknown primaries, and laryngeal tumors (Table 2).

The exact mode of spread of the disease to the plexus is also unknown. In our series, 54 of the 78 patients with metastatic brachial plexopathy had lung or breast as the primary tumor site. Of the 24 other tumors, 16 had metastasized to the upper lobe of the corresponding lung before spreading to the plexus, and 3 involved the ipsilateral axillary lymph nodes. From these findings, we hypothesize that tumor metastasis involves the plexus mainly by lymphatic spread, with tumor most commonly situated in the area drained by the lateral group of axillary lymph nodes.

**Onset of Symptoms**

The interval from diagnosis of malignancy to the first symptom of plexus disorder varies widely. In our series, the interval varied from 3 months to 14 years, with a median of 1.5 years and an average of 3.5 years. In 15 of the 34 patients who had radiation therapy to the local area, tumor recurred in less than a year. In Harper's series, the interval ranged from 0 to 276 months, with a median of 18 months [20]. In 17 of their 55 patients, brachial plexopathy was the initial manifestation of cancer. The interval from diagnosis to development of metastatic brachial plexopathy symptoms tends to be shorter in patients with lung cancer than in those with other malignancies.
Clinical Features

Pain was the most common presenting symptom of metastatic brachial plexopathy in both our series (affecting 89% of patients) and Harper's series (76%). The pain is moderate to severe in intensity, begins in the shoulder girdle, and radiates to the elbow, medial side of the forearm, and the fourth and fifth fingers. Movement of the shoulder increases the pain. In some patients, pain is localized to the posterior aspect of the arm or to the elbow. Some patients complain of a burning or freezing sensation and hypersensitivity of the skin along the ulnar aspect of the hand. The differential diagnosis includes cervical osteoarthritis, bursitis of the shoulder joint, myofascial pain, or radiculopathy.

Horner's syndrome is a common finding in metastatic brachial plexopathy, which is not surprising, considering the relationship of the sympathetic ganglion to the T1 root. This syndrome was found in 56% of our patients with MBP and in 33% of Harper's series.

Horner's syndrome in metastatic brachial plexopathy patients can also serve as an indicator of more proximal spread of the tumor along the nerve roots to the epidural space. Of our 45 patients with MBP who underwent myelography, 25 demonstrated epidural metastatic deposits (Table 3). All 25 had Horner's syndrome, but only 12 of them had bony lesions at the site of epidural disease, 10 had long-tract neurologic signs, and 14 had pain over the vertebral body distinct from the brachial plexus pain. Two patients had no clinical signs, and epidural disease was demonstrated at autopsy. For this reason, we strongly recommend that any patient with metastatic brachial plexopathy and Horner's syndrome should be investigated with an MRI of the spine or a myelogram to rule out epidural spread, even if no other clinical signs of cord compression are present.

As noted above, a majority of patients with either radiation injury to the brachial plexus or metastatic brachial plexopathy present with diffuse plexus involvement [6,11-13,20,21,23]. We found, however, that in its earlier stages, MBP involves primarily the lower trunk. Of 78 patients, 56 with tumor plexopathy had focal weakness, atrophy, or sensory changes only in the distribution of the C7, C8, and T1 roots. When the anatomic relationship of the brachial plexus to the surrounding lymph nodes is considered, these findings are not surprising. In 73 of the 78 patients with metastatic plexopathy, the initial tumor was in an area that drains to the lateral group of the axillary lymph nodes that are in close contact with the divisions of the lower trunk.

Diagnostic Studies

Diagnosis of metastatic brachial plexopathy can be difficult when it is the only sign of tumor recurrence. In 29% of our patients, pain in the brachial plexus was the first symptom of recurrence, preceding other systemic or neurologic signs and delaying diagnosis for as long as 9 months. As discussed above, MRI, CT, and electrophysiologic studies are useful in diagnosing metastatic brachial lesions. Magnetic resonance imaging is also helpful in detecting epidural tumor spread. Bone scan is useful in demonstrating the presence of metastasis in other sites, as well as vertebral body involvement, but is not useful in demonstrating brachial plexus tumor.

Prognosis and Treatment

The prognosis of MBP is usually poor. Rapid progression of symptoms, particularly distressing pain, is the rule. Radiation therapy to the plexus, either alone or in combination with chemotherapy, can provide significant pain relief in up to 50% of patients [12]. However, 29 of 78 patients with metastatic brachial plexopathy in our series could not receive further radiation because they had already received a maximal dose to the area. Nor does radiation improve neurologic function. Paravertebral nerve blocks afford good pain relief in the limited number of patients who have involvement of only one to two nerve roots. Most patients with MBP have diffuse plexus involvement, however, and hence respond poorly to nerve blocks. Dorsal rhizotomy, dorsal root entry zone surgery, or high contralateral percutaneous cordotomies can be tried in patients with severe intractable pain.

Tricyclics, antiarrhythmics, anticonvulsants, nonsteroidal anti-inflammatory drugs, and steroids can serve as useful adjuvants when used appropriately. Narcotics should be used early and in adequate doses to help control the pain. Physical therapy, transdermal electrical nerve stimulation, and other supportive measures are also helpful in managing sympotms. Amputation and other destructive procedures are ineffective, can result in distressing phantom pain, and should be avoided.

Conclusions
As is evident from the discussion above, it is not always possible to distinguish metastatic from radiation-induced brachial plexopathy clinically, and occasionally it may be necessary to resort to surgical exploration of the area to arrive at a definitive diagnosis. Surgical exploration is expensive, uncomfortable, can cause further scarring of the area, and in our experience, can fail to detect tumor presence. There are some clinical findings that may strongly suggest one etiology over the other, and hence avoid the need for surgical exploration:

Pain as a presenting symptom of the brachial plexus dysfunction is strongly suggestive of metastasis.
The absence of pain, paresthesia, dysesthesia, and lymphedema suggests radiation injury.
The presence of Horner's syndrome favors MBP over RBP.
Predominant involvement of the lower trunk of the plexus and its branches is seen in MBP.
Predominant or exclusive involvement of the upper trunk of the plexus and its branches is characteristic of RBP.
A diffuse, ill-defined mass with loss of tissue planes on CT or MRI is a typical finding in patients with radiation injury to the brachial plexus.
A well-defined mass lesion on CT or MRI is suggestive of metastatic brachial plexopathy.
The presence of myokymic discharges on electromyelographic needle examination points to RBP.
A rapid deterioration of symptoms over a period of days to weeks is common in patients with metastatic brachial lesions.

References:


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