The role of radiation therapy in the treatment of malignancy remains extremely valuable. However, the presentation of side effects is often delayed, causing significant functional disability of varying extent, depending on the anatomical location and tissues involved. Studies have reported delayed myelopathy several years after radiation therapy, with clinical features ranging from weakness and diminished proprioception to hyperreflexia and spasticity. In addition to cervical myelopathy, radiation-induced brachial plexopathy has been reported following treatment of breast cancer. The effects of radiation therapy on normal tissue can result in localized damage with pseudomalignant transformation, producing a compressive effect on the spinal cord or exiting nerve roots. Infiltration of inflammatory cells and the subsequent fibrotic response can result in the development of an inflammatory pseudotumor (benign tumor-like lesion) with subsequent mass effect. Herein, the authors present a rare case of inflammatory pseudotumor with fulminant cervicothoracic cord compression, developing 7 years after radiation therapy for breast cancer. The lesion recurred following resection but subsequently displayed complete and rapid resolution following steroid therapy. To the best of the authors' knowledge, no previous studies have reported such an incident.

Herein, we present a rare case of IPT developing several years after radiation therapy for breast cancer. Recurrence following initial resection resulted in fulminant cord compression. Subsequently, the initiation of aggressive steroid therapy resulted in rapid resolution of the lesion. To the best of the authors' knowledge, no previous studies have reported such an incident.

**KEY WORDS** fulminant cord compression; steroids; inflammatory pseudotumor; radiation effects; oncology

**Case Report**

**History and Examination**

A 61-year-old woman presented with lower-neck and upper-back pain for 6 months. She had a history of left-sided breast cancer that had occurred 7 years earlier and was treated with resection and radiation therapy. The neck pain radiated down the medial aspect of the patient’s left upper extremity.

Seven years earlier, the patient had been diagnosed with...
left breast multifocal invasive ductal carcinoma with left axillary lymph node metastasis (Stage 2B, T2, N1). At that time, findings on CT and PET scans were negative for distant metastatic disease. The patient underwent neo-adjuvant chemotherapy, followed by left modified radical mastectomy. Subsequently, the patient received fractionated radiation therapy, consisting of 50 Gy to the chest wall and left supraclavicular area, and a total of 60 Gy to the surgical site.

Following these treatments, the patient remained clinically and radiographically cancer free. Seven years later, the patient experienced upper-back pain and lower-neck pain radiating down her medial left arm and fingers. She also reported left 5th digit numbness. She denied any weakness, difficulty ambulating, or other neurological symptoms.

On neurological examination, the patient had normal tone, full strength throughout, and no pathological reflexes. She had decreased sensation in the left T-1 dermatome. MRI revealed a contrast-enhancing spinal extradural mass at the T-1 level (Fig. 1). The mass displaced the thecal sac and spinal cord to the right, and extended into the left T1–2 foramen. The differential diagnosis included nerve sheath tumor, meningioma, metastasis, and lymphoma. The remaining neuraxis was unremarkable on imaging. The patient was started on a regimen of oral dexamethasone by the referring physician to alleviate her pain. One week later, she underwent surgery for biopsy and resection.

Operation

A left T1–2 hemilaminectomy and facetectomy with a transpedicular approach was used to approach the ventral component of the lesion. Upon opening the epidural space, the lesion was not the anticipated discrete mass, but rather a thick fibrovascular tissue around the left T1–2 epidural space with strong adherence to the left T-1 nerve root. This fibrous tissue was mildly compressing the thecal sac and left T-1 nerve root. Due to the consistency and tight adherence of the lesion to the dura and nerve root, only a near gross-total resection was achieved. The patient was discharged home the following day.

Pathological Findings

Initial histopathological examination revealed sclerotic fibrovascular tissue with acute and chronic inflammatory cell infiltrates. No malignant cells were identified.

Postoperative Course

At the 2-week follow-up, the patient was doing well, with complete resolution of her symptoms in her left upper extremity. However, at 2 months postoperatively, the patient started experiencing similar recurrent symptoms. MRI demonstrated a large recurrent enhancing mass. The differential diagnosis at this time was inflammatory pseudotumor, lymphoma, sarcoidosis, and postradiation sarcoma. Histological slides were then sent for further review and additional staining. Over the next 6 months, further workup was performed, including CT/PET studies, which revealed no evidence of recurrent cancer or metastasis. Hematological workup, including bone marrow biopsy, erythrocyte sedimentation rate, and C-reactive protein, revealed no abnormalities, and results were within normal limits. The patient then experienced weakness in the intrinsic muscles of her left hand, gait instability, and signs of myelopathy. A repeat MRI study showed a significant increase in the size of the mass, which contoured the thecal sac and extended to the contralateral side, with severe spinal cord compression (Fig. 2).

Following discussion with the neuropathologist, further histological workup, including staining for specific tissue markers, was performed. The immunostaining demonstrated mixed lymphoid infiltrates, with no neoplastic cells identified. Stains for fungi, acid-fast organisms, and bacteria were negative. Immunophenotyping for CD20 (B-cell marker) and CD5 (T-cell marker) confirmed mixed infiltrate, with approximately equal numbers of each. The maximum Ki 67 labeling index was 30%. Additional immunophenotyping (Bcl-6, CD10) provided no support for lymphoma. The presence of mild lymphoid atypia may be at least partly accounted for by concomitant corticosteroid administration. The constellation of morphological and immunophenotypic features was characteristic of IPT. Upon further discussion with the patient and after review at the multidisciplinary tumor board, intravenous steroid therapy was initiated, with 1 g of intravenous Solu-Medrol given daily for 5 days, followed by 1-g monthly infusions for 1 year. The patient experienced immediate relief of symptoms after steroid infusion. MRI performed after steroid administration showed complete resolution of the lesion (Fig. 3). Over the next several months, the patient’s gait returned to baseline and she regained full strength in her hand. For the next 3 years, yearly MRI showed no evidence of recurrence.

Discussion

The differential diagnosis of a progressive and compressive enhancing epidural spinal mass includes metastasis, lymphoma, IPT, postradiation sarcoma, myeloid sarcoma, nerve sheath tumor, and meningioma. Of these, only lymphomas and myeloid sarcoma are sensitive to steroid therapy. Primary spinal lymphoma accounts for approximately 10% of epidural spinal tumors and carries a 5-year median survival of 69%. Standard treatment con-
sists of radiation therapy and chemotherapy, with protocols including prednisone. Myeloid sarcoma, also known as granulocytic sarcoma or chloroma, is rarely seen in the spine. It is very uncommon in nonleukemic patients, and 66%–88% of patients with isolated myeloid sarcoma go on to develop leukemia at a mean of 9–11 months after diagnosis.

Radiation-induced fibrosis is a known delayed complication of radiation therapy for breast cancer. With conventional therapies, the risk is considerably low. Radiation-induced fibrosis most commonly affects the skin, soft tissues, and mucosal surfaces, but it can affect connective and vascular tissues, usually at doses greater than 60 Gy. The condition typically appears 4 to 12 months following radiation therapy and progresses over years. Because the initial treatment was performed at an outside facility many years earlier, it was difficult to obtain records and confirm whether the spine or the left T-1 nerve root was in the radiation ports, as this would increase the baseline risk of postradiation therapy tissue damage. As such, the exact details of the radiation trajectory could not be obtained, which is a limiting factor in this report. Radiation-induced fibrosis in the epidural space has been rarely reported, likely due to reduction of the radiation dose around the spinal cord. One case of radiation-induced fibrosis of the atlantoaxial spine after treatment of a head and neck squamous cell cancer has been reported. This resulted in symptomatic epidural compression, which was successfully treated with odontoidectomy. A potential complication of radiation-induced fibrosis is the development of IPT, which can compress the spinal cord and nerve roots.

IPT is a rare, benign tumor-like lesion that can be radiologically and clinically indistinguishable from other malignant lesions. Despite the unknown etiology, local tissue response to trauma, infection, autoimmune phenomenon, and radiation-induced fibrosis, as seen in our patient, remain probable instigators. Histopathological studies have revealed varying degrees of cellularity, fibrotic changes, and inflammatory cell infiltration. In the absence of a tissue diagnosis, IPT can present potential management difficulties, as seen in our patient, in whom there was a significant recurrence following resection that caused progressive neurological deficits. This difficulty partly stems from the absence of preoperative characteristic features to distinguish this lesion from other pathological abnormalities.

Without tissue diagnosis, several preoperative MRI features define spinal epidural lesions. Metastatic lesions, myeloma, and lymphomas are homogeneously hyperintense lesions on T2-weighted MRI sequences and hypointense on T1-weighted images. Meningiomas are isointense on T2-weighted images and show homogeneous contrast enhancement on T1-weighted postcontrast images, with a characteristic (although not pathognomonic) dural tail. Epidural abscesses are usually ring enhancing. In our patient, the lesion was homogeneously contrast enhancing on T1-weighted images without discrete borders, and isointense on T1- and T2-weighted images with dumbbell features extending from the extradural space through the foramen outward to the extraspinal compartment. These imaging features are similar to those reported in previous studies on the radiological presentation of IPT.

Biopsy and histopathological examination remain the mainstay for IPT diagnosis. Prior studies have reported fibroinflammatory lesions with polymorphous inflammatory cells, mixed cellularity, fibrous matrix, high lymphoplasmacytic nature without mitotic activity or nuclear atypia. The lesion in this study displayed sclerotic fibrovascular tissue with acute and chronic inflammation and no identifiable malignancy. With further histological workup, there was an equal mixture of B cells and T cells, and immunophenotyping showed no evidence of lymphoma. The morphology, immunostaining, and immunophenotypic features were characteristic of IPT presenting in a delayed fashion, 7 years after radiation therapy for breast cancer.

Surgical decompression has been reported as the management option for extradural IPT and radiation-induced fibrosis presenting with myelopathy. Despite spinal decompression and subtotal resection of the lesion in our patient, there was rapid recurrence postoperatively causing severe cord compression and myelopathy. At 2 months postoperatively when symptoms recurred, the patient was not immediately treated because of the uncertainty of the recurrent pathology. She underwent a full systemic workup including CT/PET and hematological studies consisting of bone marrow biopsy, with negative results. Erythrocyte

FIG. 2. Sagittal (A) and axial (B) T1-weighted postcontrast MR images obtained 6 months postoperatively, showing fulminant growth of the enhancing lesion circumferentially compressing the spinal cord and extending to the contralateral foramen.

FIG. 3. Sagittal (A) and axial (B) T1-weighted postcontrast MR images obtained after initiating corticosteroid therapy, showing complete resolution of the lesion.
sedimentation rate and C-reactive protein levels were normal. Further histological evaluation excluded lymphoma or postradiation therapy tumor. Following an interdisciplinary discussion about management options for IPT, steroid therapy was initiated, which resulted in complete resolution of the lesion/symptoms, with no evidence or recurrence for at least 3 years (date of writing this paper).

Corticosteroids have a long history of use in radiation fibrosis treatment, secondary to their beneficial properties of inhibiting inflammatory cell recruitment, collagen synthesis, and prostaglandin and leukotriene production. However, no long-term effect on the underlying fibrosis has been convincingly demonstrated. Hirota et al. showed a significantly lower incidence of radiation-induced fibrosis in patients receiving corticosteroids together with chemotherapy than in patients not receiving corticosteroids. Other therapeutic modalities in the literature include the combination of panitumumab (PTX) and alpha-tocopherol (vitamin E), which was shown in several independent studies to significantly reduce radiation-induced fibrosis. Angiotensin-converting enzyme inhibitors and liposomal Cu/Zn superoxide dismutase have also been reported as beneficial in inducing clinical regression of radiation-induced fibrosis by interfering with the expression of tumor growth factor-β. These agents show promise in improving the quality of life of cancer patients with radiation-induced tissue damage. However, larger, multicenter, randomized controlled studies are needed to validate these treatment protocols.

This study showed that IPT could present remotely (up to 7 years) following radiation therapy. Biopsy for tissue diagnosis should be the first step toward management. Surgical decompression should be considered when there is a compressive effect on the spine or nerve roots. Once the diagnosis of IPT is made, nonsurgical options including corticosteroids and antiinflammatory agents should be initiated immediately to prevent disease progression and recurrence.

Conclusions

The differential diagnosis of epidural enhancing lesions in patients with a history of radiation therapy is diverse. IPT secondary to remote radiation injury should be considered. In most cases, surgical decompression is needed and yields tissue for histopathological diagnosis, but recurrence is possible, as seen in our patient with fulminant compression of the spinal cord and nerve roots. High-dose corticosteroids should be considered, with clinical and radiographic observation to assess regression of the lesion, which may obviate the need for invasive surgical intervention.

References


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