A 49-year-old Hispanic male with stage IV non-squamous, non–small-cell lung cancer (NSCLC) on maintenance bevacizumab treatment, presented with progressive paresthesias over the back, abdomen, and chest; left foot numbness; unsteady gait; and mid-back pain. He had been diagnosed with advanced lung cancer 14 months prior, including bulky thoracic adenopathy, brain metastases, and malignant pleural and pericardial effusions. Imaging demonstrated no spinal, dural, or vertebral lesions. He was initially treated with pericardiectomy and whole brain radiation therapy (RT), followed by administration of six cycles carboplatin-paclitaxel plus bevacizumab then 12 cycles of bevacizumab maintenance monotherapy. To evaluate the patient’s neurologic symptoms, magnetic resonance imaging (MRI) of the spine was performed, which suggested the presence of intramedullary spinal cord metastases (ISCM) at the T4 level, with associated hemorrhage (Fig. 1A, B). Additional imaging revealed stable disease elsewhere. He was started on systemic steroids, and bevacizumab was discontinued. Neurosurgery was consulted with recommendation against surgical intervention. RT (45 Gray/25 fractions) was delivered to the intramedullary metastases. Back pain resolved, neurologic symptoms improved, and steroids were discontinued. MRI evaluation after RT demonstrated reduction in size of the metastases with resolution of hemorrhage. (Fig. 1C, D).

**DISCUSSION**

This could be the first reported case of bevacizumab-associated intramedullary hemorrhage in NSCLC. ISCM is a rare event, reported to affect only 0.1–0.4% of cancer patients and typically associated with poor prognosis. Of these cases, approximately 55% are attributed to lung cancer. Clinical
experience with bevacizumab in the presence of central nervous system (CNS) lesions can be extrapolated from that described with brain metastases. The rate of cerebral hemorrhage in NSCLC patients on bevacizumab is an equally rare event, ranging from 0.8% to 3.3%. Given the rarity of both ISCM and CNS hemorrhage associated with bevacizumab treatment, ISCM hemorrhage from bevacizumab should be an extremely rare event. In this case, with excellent prolonged control of his intracranial and extracranial disease, we surmise that this metastatic disease occurred or persisted at a site where chemotherapy generally has poorer penetration. Although there are concerns that bevacizumab can be associated with CNS hemorrhage, clinical data suggest bevacizumab should be considered safe to use in patients with pretreated brain metastases. Consistent with these reports, our patient, who had his brain metastases irradiated, never developed intracranial bleeding. Although intracranial experiences in NSCLC suggest that bevacizumab is safe to use in treated CNS metastatic lesions, specifically for ISCM, there is not enough experience to be certain of this. There is one report of a glioblastoma patient with intramedullary disease, treated with RT followed by bevacizumab, without report of bleeding events. However, this experience is limited in that the patient only survived 3 months. In our patient, bevacizumab was not resumed for safety concerns.

In summary, we present a patient with metastatic NSCLC who developed hemorrhage of ISCM while on bevacizumab. Although rare, ISCM hemorrhage should be considered, particularly in long-term survivors with metastatic NSCLC on bevacizumab presenting with concerning symptoms. Early recognition and prompt initiation of appropriate intervention may help reduce risk of lasting neurologic deficits.

REFERENCES