Spinal Extramedullary Hematopoiesis Causing Spinal Cord Compression in Radiation-induced Bone Marrow Aplasia: A Case Report

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ABSTRACT

In rare cases with no clinical practice guidelines available, the approach heavily relies on small studies, reports, and professional experience based on sound clinical judgement from available data.

We present a case of a 52-year-old male radiation technologist with a 5-year history of pancytopenia diagnosed with radiation-induced marrow aplasia after presenting with bilateral lower extremity weakness and numbness. MRI revealed spinal EMH along T3 to T12. He was given steroids and radiation therapy (RT) of 18Gy in 10 fractions with improvement in sensory status at 4th session of RT and was discharged with steroid on tapering and maintenance of eltrombopag.

BM aplasia following chronic low-level radiation exposure results from the accumulation of cytogenetic abnormalities over time. EMH is a compensatory mechanism for BM aplasia, the diagnosis of which is established by MRI. In spinal EMH, transverse myelopathy occurs from spinal cord compression (SCC). As of writing and with our literature-search, spinal EMH has never been reported in patients with aplastic anemia or radiation-related BM aplasia. With the paucity of available data, there is currently no specific guidelines in managing BM aplasia from radiation and consequent SCC. However, as with most cases of SCC, radiotherapy, steroids, and surgical decompression are viable options. This case report will add to the very small pool of information on EMH from radiation-induced BM aplasia and its approach to management especially in this rare, never-before-reported presentation.

Keywords: spinal extramedullary hematopoiesis, radiation, marrow aplasia, case report

INTRODUCTION

Bone marrow aplasia following chronic low-level radiation exposure results from the accumulation of cytogenetic abnormalities over time. However, its true prevalence is not clearly known owing to its rarity. As a compensation of disrupted marrow function, EMH occurs and rarely appears axially. More infrequently, it presents as acute transverse myelopathy from spinal cord compression. We describe a case of a 52-year-old radiation technologist with radiation-induced bone marrow (BM) aplasia presenting with spinal cord compression with partial resolution of symptoms immediately after radiation therapy.

CASE PRESENTATION

A 52-year-old male radiation technologist initially presented five years prior to admission with anemia requiring supportive transfusions of unrecalled frequency. Initial workup revealed peptic ulcers and was given unrecalled

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meds resulting in resolution of ulcers but with persistence of transfusion-requiring anemia. Bone marrow biopsy done two years prior revealed a markedly hypocellular marrow with markedly decreased trilineage hematopoiesis supportive of aplastic anemia. Cyclosporin 300mg/day was started, however, onset of neuropathy on hands and lower extremities, and chest pain prompted its discontinuation. Six months prior to admission, he gradually developed thoracolumbar pain, constipation, dysuria with sensation of incomplete voiding, and bipedal edema. He subsequently developed lower extremity weakness described as buckling of knees when standing and difficulty in lifting heavy objects with attendant worsening of thoracolumbar pain. This was later associated with gradually progressing numbness in the lower extremities starting from the feet going to the abdomen.

He is a known diabetic maintained on insulin 70/30 with acceptable blood glucose monitoring but has no other co-morbidities. He has a family history of diabetes and endometrial cancer but is otherwise unremarkable. He is a non-smoker, non-alcoholic beverage-drinker and denies illicit drug use. He worked as a radiation technologist for 12 years and denies using protective equipment during radiologic imaging and procedures. Both frequency and average number of procedures were unrecalled but exposure level was characterized as high.

Physical examination revealed pale palpebrae and distended abdomen with no palpable hepatosplenomegaly. Neurologic examination showed lower extremities with slight atrophy (left), hypotonia (bilateral), hyporeflexia (left), hyperreflexia (right), and muscle strength (manual muscle test, MMT) of 0/5 (bilateral). Sensory testing with light touch and pin-prick revealed 100% in C2-T4 (bilateral), 80% in T5-T11 (bilateral), 70% in T12 (left), and 40% in L1-S2. Both position and vibration senses were impaired bilaterally and sphincter tone was noted to be lax.

Investigations

Investigations revealed hemoglobin of 85 g/L (normal range 135-180 g/L), WBC count 4.5 x 10^9/L (normal range 4.5-11 x 10^9/L), platelet count 17 x 10^9/L (normal range 150-450 x 10^9/L), mean corpuscular volume of 84.8 fL (normal range 80-96 fL), mean corpuscular hemoglobin of 29.0 pg (normal range 27.0-31.0 pg), and reticulocyte count of 1.2% (normal range 0.5-1.5%). Consistently, peripheral smear showed normocytic, normochromic RBCs with marked thrombocytopenia at 2-3 per oil immersion field. Serum chemistry showed lactate dehydrogenase of 294 U/L (normal range 120-246 U/L), alanine transaminase of 98 U/L (normal range <50 U/L), globulin of 39 g/L (normal range 15-35 g/L), and potassium of 3.3 mmol/L (normal range 3.5-5.1 mmol/L). Creatinine, uric acid, aspartate transaminase, total protein, albumin, bilirubins, sodium, and chloride were all within normal range.

Repeat bone marrow aspiration and biopsy revealed a markedly hypocellular marrow with markedly decreased trilineage hematopoiesis supportive of a hypoproliferative process such as the clinical consideration of acquired aplastic anemia (radiation-induced) (Figure 1).

MRI of the thoracic spine with and without gadolinium showed (1) heterogeneous, patchy to confluent bone marrow signals along the thoracic spine, likely from reconversion to red marrow, and (2) multiple, discrete, enhancing, bilateral paravertebral lesions, T3 through T12 levels and multiple, discrete, extradural spinal lesions, T4 through T12 levels (Figure 2), resulting in moderate spinal canal stenosis (Figure 3B), suggestive of extramedullary hematopoiesis. Abdominal MRI showed diffuse, hepatosplenic hemosiderosis with no EMH in the lumbar spine and spleen.

Differential Diagnosis

Differential diagnoses for extramedullary spinal cord compression, as in this case, would include a neoplasm, degenerative disc disease, vertebral fracture or infectious

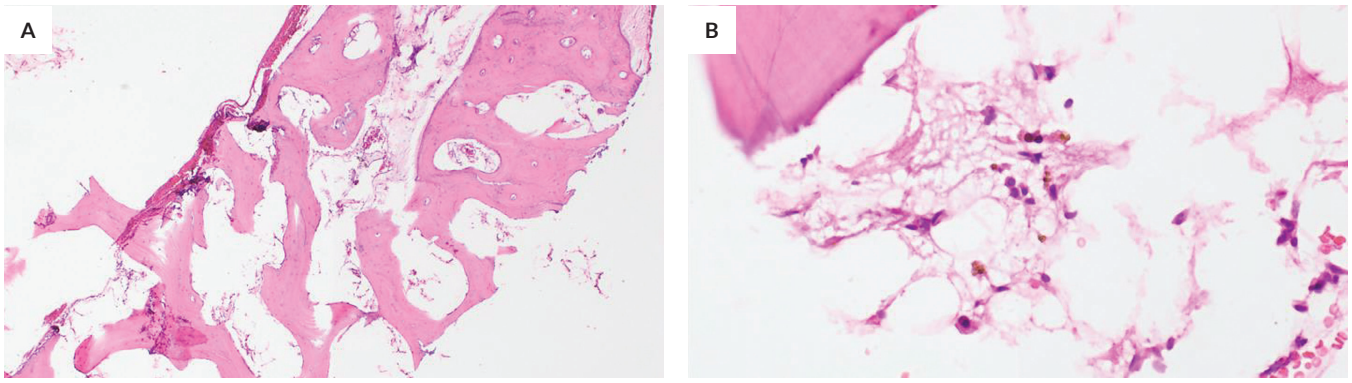

Figure 1. BM core bone biopsy in **(A)** scanning magnification (40x) showing markedly hypocellular marrow for age with 5-10% cellularity, and in **(B)** high power magnification (400x) showing markedly decreased erythrogranulopoiesis with maturation and absence of megakaryocytes.

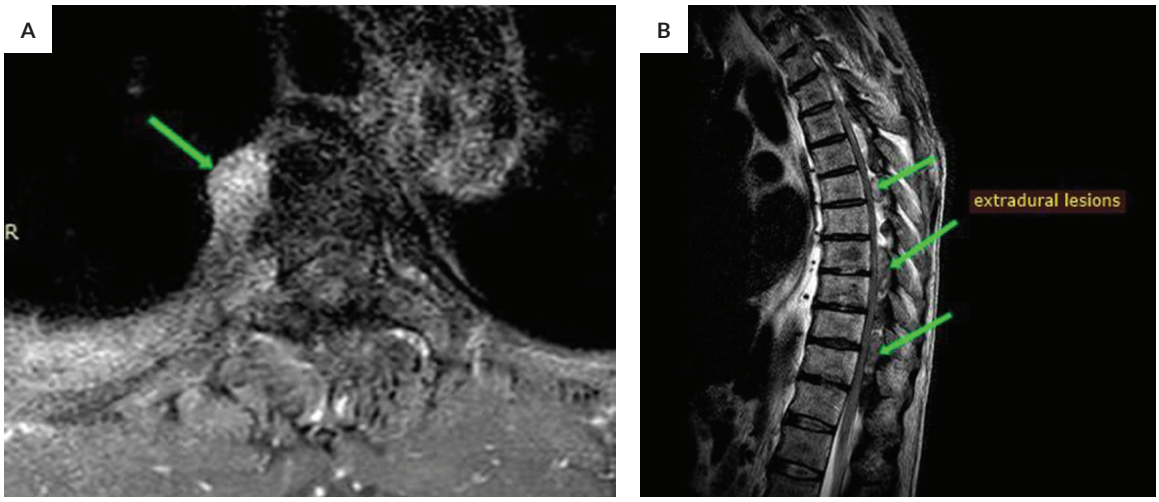

Figure 2. T2-weighted MR image of the thoracic spine with gadolinium showing paravertebral **(A, *transverse*)** and multiple, discrete, extradural spinal lesions, T4 through T12 levels **(B, *sagittal*)** *(green arrows)*.

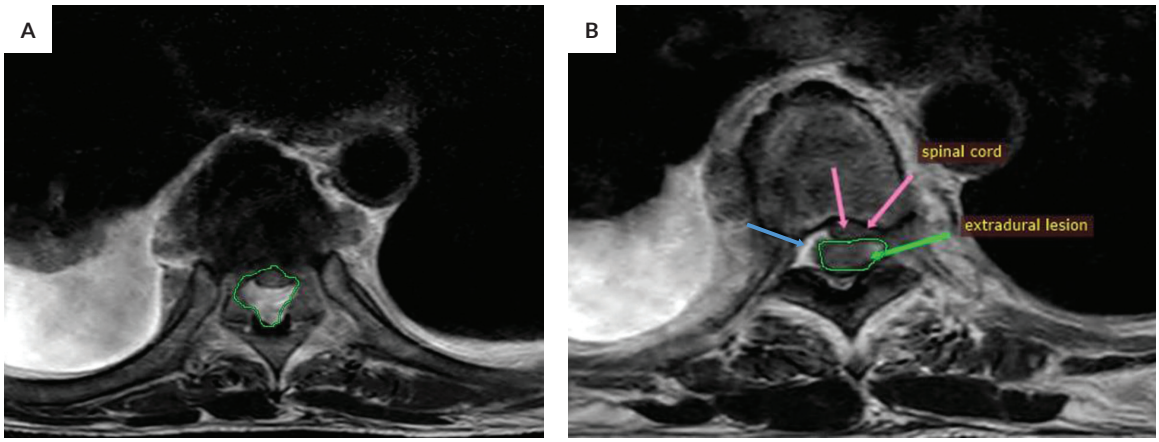

Figure 3. Axial T2-weighted MR image of the thoracic spine with gadolinium showing: **(A)** a normal spinal canal *(green outline)*; **(B)** an extradural lesion *(green arrow and outline)* displacing the spinal cord *(pink arrows)* and obliterating the CSF *(blue arrow)*.

process. Lesions on MRI, however, were not supportive of these entities based on the characteristic multiple, discreet, enhancing T2 hyperintense lesions, and absence of any disc or osseous structure abnormalities. The diagnosis of spinal EMH from radiation-induced BM aplasia with secondary spinal cord compression can therefore be established through the constellation of the patient's clinical history, laboratory investigations, BM biopsy results, and MRI findings.

Treatment

During the patient's hospitalization, he was given supportive transfusions to target hemoglobin of 80 g/L and platelet count 20 x 10^9/L, in line with current restrictive transfusion guidelines. Eltrombopag 25mg once daily was continued and he was started on dexamethasone 20mg/day. Patient was ideally for decompressive spinal surgery but was deemed high risk for bleeding due to persistent thrombocytopenia. He was given external beam radiation therapy of 18Gy in 10 fractions administered to T3-T6 and T9-T12 vertebrae over a 16-day period.

Outcome and Follow-up

As early as the 4th session of radiotherapy, there was an observed improvement in the sensory testing now at 100% at the level of T8 from previously T4. However, no improvement was noted on the motor strength of the patient. At discharge, his hemoglobin was at 92 g/L with platelet count of 43 x 10^9/L, both sustained without transfusion support. The further plan was for monitoring of neurologic symptoms every two weeks and repeat whole spinal MRI after 2-3 months from the completion of radiotherapy and reassessment for need of additional interventions such as surgery.

DISCUSSION

After a single radiation dose, pancytopenia appears to be a more common late consequence than aplastic anemia (AA). However, in chronic low-level radiation exposure, cytogenetic abnormalities accumulate with time and may not be reliably related to dose. Repeated low dose radiation have been associated with AA but only a small proportion of exposed individuals develop hematologic disease.[1] Morphologically, marrow aplasia from various causes is indistinguishable. The diagnosis of secondary aplasia, as in the case of radiation-induced BM aplasia, is largely based on temporality of inciting events and causes.

EMH refers to hematopoiesis in locations other that the bone marrow and can either be physiologic or pathologic.[2] It is a compensatory phenomenon that occurs after bone marrow function is disturbed, commonly among patients with hematologic disorders that impair marrow hematopoiesis. It usually occurs in the spleen, liver, lymph nodes, and other sites including posterior mediastinum.[3]

Rarely, axial EMH occurs causing thoracic myelopathy and spinal cord compression. This was first reported by Gatto et al. in 1954. Theories on its pathophysiology include direct extension of hematopoietic material from the vertebrae and ribs, embolism of hematopoietic tissue, and anomalous activation of embryonic stem cells in the epidural space. This has been more commonly documented in thalassemia-associated EMH with an incidence of 11-15%.[4] However, as of writing and with our literature-search, spinal EMH has never been reported neither in patients with aplastic anemia nor among those with radiation-related BM aplasia.

Although tissue biopsy provides definitive diagnosis of EMH, it is only reserved for those with severe spinal cord compression scheduled for laminectomy or in cases with doubtful diagnosis.[5] MRI is currently the method of choice for diagnosis and monitoring, exceeding spinal CT scan.[5,6] It is also useful in assessing response to treatment an AA and other hematopoietic disorder. Signal characteristics follow differences in fatty versus hematopoietic marrow, with patterns described as (1) focal low-signal (both TI and T2) areas (likely representing islands of active hematopoietic cells) interspersed with high-SI areas in the marrow of the spine and (2) diffuse high-signal marrow without focal abnormalities in the pelvis and proximal femoral regions.[7]

With the paucity of available data, there is currently no specific guidelines in managing BM aplasia from radiation. Similarly, there are no guidelines or common consensus in the management of spinal cord compression from extramedullary hematopoiesis. However, as with most cases of spinal cord compression, the management involves radiotherapy and steroids. Supportive transfusions, hydroxyurea, and sometimes surgical decompression (laminectomy) were also used.

We elected to give steroid therapy and local radiation therapy to relieve spinal cord compression which resulted to clinical improvement of symptoms. However, it is difficult to make assumptions and generalizations on the intervention used due to the rarity of the case. While there was a documented improvement in the patient's sensory status, motor function remained unchanged and did not result in an overall improvement in his functional capacity in the immediate post-treatment phase. A long-term follow-up on the patient's clinical status, such as sensory and motor functions, is needed to fully assess durability of response and treatment outcomes.

CONCLUSION

In rare cases with no clinical practice guidelines available, the approach heavily relies on small studies, reports, and professional experience based on sound clinical judgement from available data. This case report will add to the very small pool of information on EMH from radiation-induced BM aplasia and its approach to management especially in this rare, never-before-reported presentation.

Informed Consent

An informed consent was obtained from the patient and his family for the creation of this manuscript and publication of information in a journal.

Statement of Authorship

All authors certified fulfillment of ICMJE authorship criteria.

Author Disclosure

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