Case Report

Development of acute promyelocytic leukemia in a patient with tetraplegia while in inpatient rehabilitation: A case report

Christopher A. Beal^{1,2}, Michael C. Krouse³, Jeffrey T. Tubbs^{1,2}

¹Spinal Cord Injury Service and Disorders, Hunter Holmes McGuire VA Medical Center, Richmond, Virginia, USA, ²Department of Physical Medicine and Rehabilitation, Virginia Commonwealth University, Richmond, Virginia, USA, ³School of Medicine, Virginia Commonwealth University, Richmond, Virginia, USA

Study Design: a single case report.

Objectives: To report a case of a patient with tetraplegia who developed acute promyelocytic leukemia (APL) while in inpatient rehabilitation after 10.5 months.

Setting: A VA Medical Center Spinal Cord Injury Service and Disorders Unit

Case Report: A 47 year-old male with a stage IV sacral pressure ulcer and C4 AIS A complete tetraplegia secondary to a motor vehicle collision, developed fever, thrombocytopenia, and anemia 20 months after his injury while in inpatient rehabilitation and was found to have APL, confirmed following bone marrow biopsy.

Conclusion: There is a wide differential for fever after a spinal cord injury. In this case report, the source of fever was APL. It is important as healthcare providers to not overlook fevers when otherwise common causes do not fit the clinical picture. Additionally, there has been no association found between traumatic spinal cord injury and the development of acute leukemia, however this is the first case report. Therefore, it is important to continue investigating to determine if an association exists.

Keywords: Tetraplegia, Spinal cord injury, Acute promyelocytic leukemia, Rehabilitation, Fever, Thrombocytopenia

Introduction

Fever is a common complication of spinal cord injury, occurring in nearly 50% of those undergoing inpatient rehabilitation.¹⁻² Urinary and respiratory tract infections are the most common etiologies, accounting for 70.6% and 9.6% of cases, respectively.² Other infectious causes include wound infection and abscess.¹⁻³ Noninfectious causes include deep venous thromboembolism, pulmonary embolism, heterotopic ossification, and thermoregulatory dysfunction.⁴⁻⁵ However, frequently there is no identified cause, as seen in 7–47% of cases.¹⁻²

In addition, fever with thrombocytopenia raises a high degree of suspicion for sepsis as an underlying cause. However, other etiologies ought to be considered, such as recently initiated medications, viruses such as

HIV and Hepatitis C, bone marrow infiltration, and acute leukemia,⁶⁻⁷ to only name a few examples.

In summary, the differential diagnosis for fever with and without thrombocytopenia is vast. The majority of cases are secondary to an apparent infection; however, in some cases, the fever may be from a less common source requiring additional investigation or the source may remain unidentified. In this case report, to the best of our knowledge, we present the first case of development of APL or any acute leukemia in a spinal cord injury patient while in acute rehabilitation.

Case report

A 47 year-old Caucasian male was involved in a motor vehicle collision resulting in C4 AIS A complete tetraplegia with C4 and C5 vertebral fractures. He reported no family history of leukemia; however, his maternal grandfather developed lung cancer after many years of smoking. Following his motor vehicle collision, he had numerous medical complications including failure to wean off the ventilator resulting in tracheostomy, as

Correspondence to: Christopher A. Beal, DO, Resident Physician, Virginia Commonwealth University Health System, Department of Physical Medicine and Rehabilitation, 1223 E. Marshall St., P.O. Box 980677, Richmond, VA 23284-0667, USA. Email: Christopher.beal@vcuhealth.org
Color versions of one or more of the figures in the article can be found online at www.tandfonline.com/yscm.

well as percutaneous endoscopic gastrostomy (PEG) tube placement for dysphagia during his initial hospital stay. Additionally, he developed a large stage IV sacral ulcer and underwent a gluteal rotation flap surgical repair eight months after his injury. The gluteal flap subsequently dehisced and received wound care including placement of a wound vacuum to aid in healing. He was transferred to Long-Term Acute Care (LTAC) two weeks after his rotation flap repair for continued wound care. He was transferred to the VA Medical Center's spinal cord injury unit one month later for further management. While in inpatient rehabilitation, he received extensive wound care for his sacral ulcer in addition to his intensive therapies.

During his admission, his complete blood count (CBC) remained relatively stable with white blood count (WBC) between $5\text{--}6 \times 10^9/\text{L}$, hemoglobin between 11–12 g/dL and platelets generally in the mid- $100\text{s} \times 10^9/\text{L}$. 20 months after his injury, and while participating in inpatient rehabilitation, the patient became increasingly confused and developed a low-grade fever. Labs were drawn at that time and were noted to have a downward trend of his CBC over the last two months with his platelets decreasing from 115 to $58 \times 10^9/\text{L}$, hemoglobin decreasing from 12.7 to 10.4 g/dL, and WBC decreasing from 5.9 to $4.8 \times 10^9/\text{L}$. Urine and blood cultures grew *proteus mirabilis*; therefore, he was placed on piperacillin-tazobactam. The hematology service was consulted. After a thorough workup, including Hepatitis B and C and HIV antibodies and a peripheral blood smear, which were all negative, the compilation of symptoms and changes in lab results appeared to be secondary to sepsis and antibiotic use. Piperacillin-tazobactam was changed to ertapenem and platelets mildly increased to $94 \times 10^9/\text{L}$. The patient's vitals remained stable over the next four weeks until he again developed a fever of 39.4°C . Workup included a CBC, which showed platelets decreased to $19 \times 10^9/\text{L}$, hemoglobin decreased to 9.4 g/dL and WBC decreased to $4.3 \times 10^9/\text{L}$ with an initial urinalysis not suggestive of an urinary tract infection. The patient was initially placed on piperacillin-tazobactam due to prior *proteus* bacteremia and urinary tract infection. There was also low suspicion that piperacillin-tazobactam was the original cause of thrombocytopenia, as there was a drop in platelets to $19 \times 10^9/\text{L}$ while not on antibiotics. Repeat hemoglobin was further reduced to 8.3 g/dL and platelets to $9 \times 10^9/\text{L}$. At that time, it was again thought the thrombocytopenia and fevers were secondary to infection, but hematology was consulted for assistance. Laboratory work-up was performed. Heparin induced thrombocytopenia (HIT) was not a suspected cause of

Figure 1 Myeloblasts with Auer rods.

thrombocytopenia secondary to enoxaparin, as he had presented to the VA Medical Center on enoxaparin and it had been continued throughout his inpatient rehabilitation stay. He had been on prolonged use of enoxaparin because of his significant wound burden from the chronic sacral ulcer. Therefore, HIT antibody or serotonin release assay (SRA) were not ordered.

A repeat peripheral smear was performed and demonstrated multiple blast cells with Auer rods, concerning for acute myeloid leukemia (AML), especially APL (Fig. 1). The patient was emergently transferred off the spinal cord injury unit to the medicine service for further workup and management. Since there was a high suspicion for APL, treatment was initiated with all-trans-retinoic acid (ATRA) and arsenic trioxide (ATO). APL was then confirmed with a bone marrow biopsy. He underwent treatment with ATRA and ATO including consolidation treatment. Hospital course was complicated by neutropenic fever secondary to *klebsiella* urinary tract infection (UTI) and adrenal insufficiency. Repeat bone marrow biopsy was performed and was suggestive of APL remission.

Discussion

In patients with spinal cord injury, fever can arise from common infectious sources as well as noninfectious sources. However, an etiology may not be found and further investigation into less common causes may be required. In this case report, we present the first case of APL, or any acute leukemia, in a spinal cord injury patient in acute rehabilitation. Diagnosing APL early is prudent, as it is associated with life threatening medical emergencies. APL has been strongly associated with disseminated intravascular coagulation (DIC), which places patients at risk for hemorrhage and thrombosis.⁸ Hemorrhages can manifest on a spectrum, ranging from petechiae to death associated with bleeding in the brain or lungs.⁹ Additionally, thrombosis

can include venous thromboembolism resulting in pulmonary embolism and arterial thrombosis resulting in ischemia of organs, potentially resulting in organ failure.⁹ If APL is diagnosed early and treatment is initiated, the prognosis improves, thereby making it one of the more curable forms of acute leukemia with a 90% long-term survival rate.⁹

Although there have been multiple case reports showing acute leukemia resulting in spinal cord injuries, to date there have been no case reports or associations between traumatic spinal cord injuries and the development of APL or other acute leukemias. For example, Kim *et al.*, among other researchers, have published case reports of acute leukemia infiltrating the spinal cord including the cauda equina.^{10–12} In addition, there have been other cases of leukemia infiltrating the epidural space resulting in compression of the spinal cord.^{13–15} Lastly, there have been numerous case reports regarding patients with spinal cord compressions caused by lymphoma.^{16–18}

According to a cross-sectional study by Saunders *et al.*, the lifetime prevalence of cancer in those with spinal cord injury is 6.3%.¹⁹ Within this study, skin cancer was the most common and was as common as “other” or “multiple” cancers at 32.1%.¹⁹ Acute leukemia was not specifically mentioned. The study indicated that cancer prevalence increased with age, but it did not compare the prevalence of cancer in the spinal cord injury population to that in the general population.¹⁹ In fact, bladder cancer remains one of the most commonly studied cancers in those with spinal cord injury. Nahm *et al.* recently observed an increased mortality risk secondary to bladder cancer in various ages, genders, and races.²⁰ Additionally, a literature review by Welk *et al.* demonstrated that bladder cancer tends to present earlier and at more advanced stages in the spinal cord injury population compared to the general population.²¹ However, Jensen *et al.*’s review of the prevalence of secondary health conditions in those with spinal cord injury concludes that bladder cancer was no more prevalent compared to that in the general population.²² In summary, the prevalence of acute promyelocytic leukemia within the spinal cord injury population compared to the general population remains unexplored.

Conclusion

In patients with chronic spinal cord injuries, there are many different causes of fever. When fevers present with thrombocytopenia, infection continues to be at the top of the differential, especially after the initiation of antibiotics. However, in this case, the source was APL. Even though development of acute leukemia in

an inpatient rehabilitation unit is rare, it is important as healthcare providers to continue to perform a thorough investigation for fever after spinal cord injury when otherwise common causes do not fit the clinical picture, as to potentially catch and treat life-threatening conditions. At this time in the current medical literature, there has been no association found between spinal cord injury and the development of acute leukemia, however very little attention has been brought to this subject. In order to obtain a better understanding of the prevalence of acute leukemias in the spinal cord injury population, we as clinicians must continue to report these events.

Acknowledgements

We would like to thank Hunter Holmes McGuire Research Institute and Spinal Cord Injury Services and Disorders, for providing resources and facilities to make this work possible. We would like to thank Dr. Ashraf Gorgey, Chief of Spinal Cord Injury Research, for his assistance of reviewing the manuscript. We would also like to thank the pathology department, including Dr. Caroline Martin, at Hunter Holmes McGuire Medical Center, for providing the picture of blast cells with Auer rods. We received no funding for this project.

Disclaimer statements

Contributors None.

Funding and Support

Hunter Holmes McGuire Research Institute and Spinal Cord Injury Services and Disorders provided resources and facilities to make this work possible. We received no funding for this project.

Please note, that this manuscript has not been previously published, is not being considered for publication elsewhere, and is being submitted exclusively for publication for The Journal of Spinal Cord Medicine. This case report was approved by the IRB at Hunter Holmes McGuire Medical Center.

Declaration of interest The authors report no declaration of interest.

Conflicts of interest None.

Ethics approval None.

References

- 1 McKinley W, McNamee S, Meade M, Kandra K, Abdul N. Incidence, etiology, and risk factors for fever following acute spinal cord injury. *J Spinal Cord Med* 2006;29(5):501–6
- 2 Unsal-Delialioglu S, Kaya K, Sahin-Onat S, Kulakli F, Culha C, Ozel S. Fever during rehabilitation in patients with traumatic spinal cord injury: analysis of 392 cases from a national rehabilitation hospital in Turkey. *J Spinal Cord Med* 2010;33:243–8

- 3 Beraldo P, Neves E, Alves C, Khan P, Cirilo A, Alencar M. Pyrexia in hospitalised spinal cord injury patients. *Paraplegia* 1993;31: 186–91
- 4 Sugarman B. Fever in recently injured quadriplegic persons. *Arch Phys Med Rehabil* 1982;63:639–40
- 5 Lee JW, Jo YS, Park JS, Kim JM, Kim SK. Heterotopic ossification in a tetraplegic patient with prolonged fever. *J Rehabil Med* 2015;47:669–71
- 6 Arnold DM, Lim W. A rational approach to the diagnosis and management of thrombocytopenia in the hospitalized patient. *Semin Hematol* 2011;48(4):251–8
- 7 Sekhon SS, Roy V. Thrombocytopenia in adults: A practical approach to evaluation and management. *South Med J* 2006;99 (5):491–8; quiz 499–500, 533
- 8 Tallman MS, Kwaan HC. Reassessing the hemostatic disorder associated with acute promyelocytic leukemia. *Blood* 1992;79: 543–53
- 9 Cicconi L, Lo-Coco F. Current management of newly diagnosed acute promyelocytic leukemia. *Ann Oncol* 2016;27(8):1474–81
- 10 Buakhao J, Tansawet A. Cauda equina involvement in acute myeloid leukemia relapse. *J Med Assoc Thai* 2011;94(10):1271–5
- 11 Olcay L, Aribas BK, Gökçe M. A patient with acute myeloblastic leukemia who presented with conus medullaris syndrome and review of the literature. *J Pediatr Hematol Oncol* 2009;31(6):440–7
- 12 Kim W, Min CK, Shim YS, Shon YM, Yang DW. Intramedullary spinal cord metastasis of acute lymphoblastic leukemia as the initial manifestation of relapse. *Leuk Lymphoma*. 2008;49(6):1214–6
- 13 Isome K, Matsubara K, Taki T, Nigami H, Yura K, Iwata A *et al*. Spinal cord compression by epidural involvement over 21 vertebral levels in acute lymphoblastic leukemia. *J Pediatr Hematol Oncol* 2011;33(2):153–7
- 14 Molina B, Lassaletta A, Andion M, Gonzalez-Vicent M, López-Pino MA, Madero L. A persistent epidural mass in a child with B-lineage ALL. *Pediatr Blood Cancer* 2010;55(4):727–9
- 15 Dimou J, Jithoo R, Tsui A, Morokoff AP. Spinal cord compression as the initial presentation of acute biphenotypic leukaemia. *J Clin Neurosci* 2009;16(12):1696–8
- 16 Harris E, Butler JS, Cassidy N. Aggressive plasmablastic lymphoma of the thoracic spine presenting as acute spinal cord compression in a case of asymptomatic undiagnosed human immunodeficiency virus infection. *Spine J* 2014; 14(7):1–5
- 17 Seo JY, Ha KY, Kim MU, Kim YC, Kim YH. Spinal cord compression by B-cell lymphoma, unclassifiable, with features intermediate between diffuse large B-cell lymphoma and Burkitt lymphoma in a patient seropositive for human immunodeficiency virus: a case report. *J Med Case Rep* 2014; 8:324
- 18 Lei Y, Zi L, Long S, Pei L, Wei L. Primary bone lymphoplasmacytic lymphoma presenting with spinal cord compression: a case report. *Turk J Haematol* 2013; 30(4):409–12
- 19 Saunders LL, Clarke A, Tate DG, Forchheimer M, Krause JS. Lifetime prevalence of chronic health conditions among persons with spinal cord injury. *Arch Phys Med Rehabil* 2015;96(4):673–9
- 20 Nahm LS, Chen U, DeVivo MJ, Lloyd LK. Bladder cancer mortality after spinal cord injury over 4 decades. *J Urol* 2015;193(6): 1923–8
- 21 Welk B, McIntyre A, Teasell R, Potter P, Loh E. Bladder cancer in individuals with spinal cord injuries. *Spinal Cord* 2013;51(7): 516–21
- 22 Jensen MP, Truitt AR, Schomer KG, Yorkston KM, Baylor C, Molton IR. Frequency and age effects of secondary health conditions in individuals with spinal cord injury: a scoping review. *Spinal Cord* 2013;51(12):882–92