CASE REPORT

Spontaneous Tumor Lysis Syndrome in a Patient with Mantle Zone Cell Lymphoma

Ikram A. Burney[1*] and Syed Azhar Rizvi[2]

[1]Department of Medical Oncology, Sultan Qaboos Comprehensive Care and Research Center, Muscat, Sultanate of Oman
[2]Department of Oncology, Milton Keynes University Hospital, NHS Foundation Trust, Standing Way, UK

Abstract

We describe the case of a patient diagnosed to have Mantle cell lymphoma (MCL), who underwent spontaneous tumor lysis syndrome, with overwhelming metabolic acidosis and acute kidney injury, was managed conservatively without the need for hemodialysis and went on to receive cytotoxic chemotherapy. ATLS is rare in patients with MCL, and spontaneous ATLS is even rare.

Keywords: *Mantle cell lymphoma, spontaneous, tumor lysis syndrome, acute kidney injury, CD20, cyclin-D1.*

INTRODUCTION

Acute tumor lysis syndrome (ATLS) results from a sudden and rapid release of cellular breakdown products after the treatment of cancer. The extra-cellular release of intra-cellular contents could lead to alterations in metabolic profile. Renal function may be severely impaired and a high anion gap metabolic acidosis ensues, leading even to death [1]. ATLS occurring spontaneously, *i.e.* without antecedent cytotoxic therapy, is rare. We report the case of a patient diagnosed with Mantle Cell Lymphoma (MCL), who developed ATLS spontaneously while undergoing staging investigations.

CASE REPORT

A 65-year-old gentleman was admitted through the emergency room with a 2-month history of cervical and axillary lymphadenopathy, weight loss, and low-grade fever. There was no history of drenching sweats. On examination, the gentleman appeared cachectic and had generalized lymphadenopathy. Examination of the chest was unremarkable; however, examination of the abdomen revealed a palpable spleen 5 cm below the subcostal margin and an epigastric mass, nodular in surface, measuring 6.5 x 5 cm.

Laboratory investigations revealed the following: Hb 10.1gm/dl; WBC 13.5 x 10^9/l; ANC 2.5 x 10^9/l; absolute lymphocyte count 9.8 x 10^9/l; platelets 350 x 10^9/l; urea 5.0 mmol/L; creatinine 126 µmol/L; Na 133 mmol/L; K 4.1 mmol/L; Cl 105 mmol/L; HCO3 23 mmol/L; LDH 390 IU/L; Uric acid 0.26 mmol/L; bilirubin 16 mmol/L; ALT 9 IU/L; AST 25 IU/L ; ALP 76 IU/L; Albumin 23 gm/L; Ca 2.61 mmol/L; PO4 1.13 mmol/L. A chest x-ray revealed bilateral pleural effusion and mediastinal lymphadenopathy. The peripheral blood smear showed large atypical lymphocytes and a few smudge cells. The diagnosis of a lymphoproliferative disorder was suspected and the patient was started on allopurinol. Peripheral blood flow cytometry revealed the lymphocyte population to be positive for CD5 and CD20, and negative for CD10 and CD23, consistent with a diagnosis of MCL.

Staging CT investigations revealed mediastinal and hilar lymphadenopathy, bulky retroperitoneal, para-aortic, para-iliac, and inguinal nodes, and splenomegaly. The liver was not enlarged, and there were focal lesions within the spleen. The patient was staged to have stage IIIBSX disease.

On the 3rd day of admission and before the treatment could be instituted, the patient developed hypotension, tachycardia, and desaturated, necessitating transfer to ICU for monitoring and institution of supportive management. The ECG was unremarkable, and an urgent CT angiogram of the chest did not show evidence of pulmonary embolism. However, serum urea and electrolytes revealed the following: urea 10.5 mmol/L; creatinine 196 µmol/L; Na 133 mmol/L; K 5.1 mmol/L; Cl 110 mmol/L; HCO3 16 mmol/L; Urate 0.36 mmol/L Ca 2.46 mmol/L; PO4 2.07 mmol/L. A diagnosis of ATLS with normal anion gap metabolic acidosis was made and the patient was treated with normal saline at 200 ml/hour, along with loop diuretics, to maintain a urine output of 120-150 ml/hour. The baseline and subsequent serum creatinine and electrolytes are shown in **Fig. (1)**. The patient became clinically stable by around the third day of the treatment and was started on combination chemotherapy, consisting of non-cross resistant alternating weekly cycles of prednisolone, mitoxantrone, cyclophosphamide, etoposide, and bleomycin and vincristine (PMitCEBO). Biochemical features of tumor lysis syndrome were monitored. No further rise in K, PO4, or urate was observed.

Meanwhile, the cervical lymph node biopsy was reported to reveal large irregular nodular areas, within which

*Corresponding author: Ikram A. Burney, Department of Medical Oncology, Sultan Qaboos Comprehensive Care and Research Center, Muscat, Sultanate of Oman ; Emai: i.burney@cccrc.gov.om; ikramburney@hotmail.com
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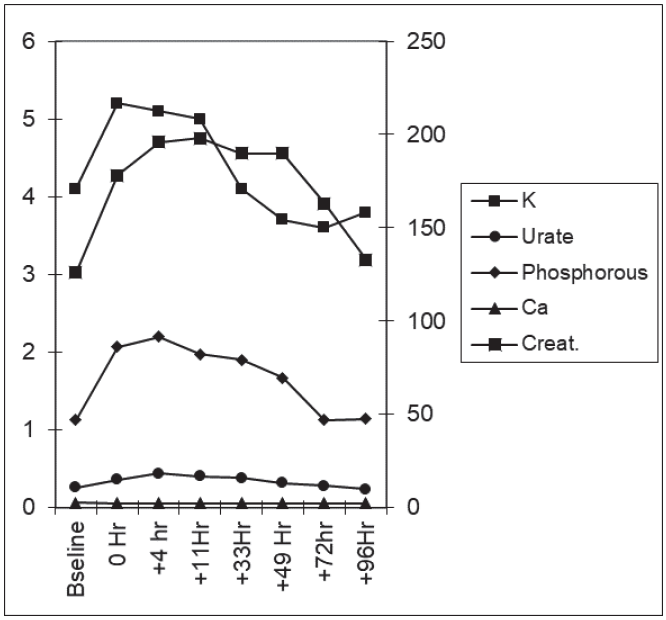

Fig (1): Graph showing serial measurements of Creatinine and other markers of acute tumor lysis syndrome. Calcium levels are corrected for albumin. The X-axis shows time, 0 hours being the time when the patient became acutely unwell and electrolytes and creatinine were measured. The Y- axis shows Potassium, urate, phosphate, and calcium (mmol/L), and the Y- axis on the right side shows serum creatinine (µmol/L).

was the diffuse proliferation of monomorphic lymphoid cells, moderately large, and showing increased mitotic activity. Immunohistochemistry revealed the cells to be positive for CD20 antigen. CD5 and CD3 positivity was seen around the nodular region of CD20-positive cells. Although the cyclin D1 stain remained negative, the morphological and immunohistochemical features were consistent with the diagnosis of MCL and corresponded to the immunophenotypic pattern of the peripheral blood. Bone marrow flow cytometry also revealed features similar to the peripheral blood; the bone trephine revealed a population of small lymphocytes staining positively for the CD5 and CD20 antigens and negative for the cyclin D1 stain.

The patient continued to receive the weekly chemotherapy for 4 weeks and was returned to the ward. Subsequently, he developed sepsis secondary to candidemia and passed away.

DISCUSSION

ATLS occurs due to the rapid destruction of tumor cells and a subsequent release of cellular breakdown products. The cardinal features of ATLS are hyperkalemia, hyperphosphatemia, hyperuricemia, and hypocalcemia. The constellation of these biochemical features may result in acute kidney injury and high anion-gap metabolic acidosis [1]. Factors that predispose to ATLS include a chemo-sensitive tumor, bulky disease, a large number of ischemic areas within the tumor, high lactate levels, high LDH levels, and impaired renal function [2]. ATLS has been known to occur most frequently following induction chemotherapy for Burkitt's lymphoma [3] but has also been reported to occur following the treatment of aggressive lymphoproliferative disorders and occasionally after treatment of solid tumors [1, 4]. More recently, ATLS has been described in patients with chronic lymphocytic leukemia using novel targeted agents [5].

Spontaneous ATLS is a rare condition. It occurs due to the rapid cell destruction in patients who present with bulky widespread or metastatic disease. Only a few cases of spontaneous ATLS have been reported. Spontaneous ATLS has been described in acute leukemias, high-grade NHL, and myelofibrosis [6-10]. ATLS has also been reported in some solid tumor malignancies, such as cancers of the lung, breast, and colon [11-15]. Acute kidney injury (AKI) as a result of spontaneous ATLS has been reported in patients diagnosed to have Burkitt's lymphoma and acute myeloid leukemia [6, 8]. Our patient with Mantle cell lymphoma developed spontaneous ATLS leading to AKI and metabolic acidosis. Only a few cases of spontaneous ATLS have been reported, mostly in the blastoid variants [16-18].

MCL is a discrete clinicopathological sub-type of NHL. The clinical, immunophenotypic, and molecular characteristics are distinc [19]. Clinically, MCL has a failure-free survival rate of only around 10% at 5 years, and an overall survival rate of 15-20% at 5 years. However, several histologic subtypes of MCL have been described, such as nodular, diffuse, and blastoid variants and the clinical behavior is known to be variable [20]. The nodular and the diffuse variants follow an intermediate course, and the blastoid variant is clinically the most aggressive sub-type, exhibits a higher mitotic index, a higher proliferative rate, frequently over-expresses p53, and is more often tetraploid. Our patient had the blastoid variant, as suggested by the peripheral blood flow cytometry results.

The most important immunophenotypic characteristics of MCL are the expression of CD5 and a lack of expression of CD10 or CD23. In contrast to B-cell CLL, CD23 is absent, and in distinction from follicular lymphoma, CD5 is expressed. The tumor shows rearrangement of the *BCL-1* oncogene caused by (11;14) translocation [21]. This gene rearrangement leads to the over-expression of the cyclin D1 protein. Although cyclin D1 expression has a diagnostic value in MCL, occasionally, this expression may be absent [22]. For example, even using multiple breakpoint probes for *BCL-1* (MTC, p94PS) and cyclin D1, approximately 70% of MCL only, have a rearrangement consistent with a t (11;14) (q13; q32). Additionally, when using paraffin sections, as was the case here, occasionally fixation or other technical factors may lead to satisfactory staining. However, the morphologic, and immunophenotypic pattern in our case established the diagnosis of MCL, even in the absence of cyclin D1 expression.

CONCLUSION

MCL is a relatively rare type of non-Hodgkin lymphoma. Different sub-types have been recognized. The Blastoid variant is the most aggressive sub-type. ATLS is most often reported in Burkitt lymphoma, aggressive leukemias, and other chemo-sensitive tumors, presenting with bulky disease. Although spontaneous ATLS is rare, it can develop in patients with MC, as shown in this case. Cases like these need to be reported to the literature, so that rare manifestations of the disease and its treatment could be disseminated and recorded.

CONSENT FOR PUBLICATION

Verbal consent was taken from the patient.

CONFLICT OF INTEREST

None.

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REFERENCES

1. Davidson MB, Thakkar S, Hix JK, Bhandarkar ND, Wong A, Schreiber MJ. Pathophysiology, clinical consequences, and treatment of tumor lysis syndrome. Am J Med 2004; 116(8): 546-54. DOI: https://doi.org/10.1016/j.amjmed.2003.09.045
2. Chasty RC, Liu-Yin JA. Acute tumor lysis syndrome. Br J Hosp Med 1993; 49: 488-92
3. Cohen LF, Balow JE, Magrath IT, Poplack DG, Ziegler JL. Acute tumor lysis syndrome: A review of 37 patients with Burkitt's lymphoma. Am J Med 1980; 68: 486-91. DOI: https://doi.org/10.1016/0002-9343(80)90286-7
4. Burney IA. Acute tumor lysis syndrome after transcatheter chemoembolization of hepatocellular carcinoma. South Med J 1998; 91(5), 467-470. DOI: https://doi.org/10.1097/00007611-199805000-00012
5. Cheson BD, Heitner Enschede S, Cerri E, Desai M, Potluri J, Lamanna N, Tam C. Tumor lysis syndrome in chronic lymphocytic leukemia with novel targeted agents. Oncologist 2017; 22(11): 1283-1291. DOI: https://doi.org/10.1634/theoncologist.2017-0055
6. Lotfi M, Brandwein JM. Spontaneous acute tumor lysis syndrome in acute myeloid leukemia? A single case report with discussion of the literature. Leuk Lymphoma 1998; 29(5-6): 625-8 DOI: https://doi.org/10.3109/10428199809050923
7. El-Sonbaty MR, Bitar Z, Abdulrazak A. Acute spontaneous tumor-lysis syndrome in a pregnant woman with non-Hodgkin's lymphoma. Int J Hematol 2001; 73(3): 386-9. DOI: https://doi.org/10.1007/bf02981967
8. Faheem B, Kollimuttathuillam S, Ashkar H, Maroules M. Spontaneous Tumor Lysis Syndrome in T-Cell Leukemia. Cureus 2020; 12(10): e11002. DOI: https://doi.org/10.7759%2Fcureus.11002
9. Wesemüller W, Taverna C. Spontaneous Tumor Lysis Syndrome. Case Rep Oncol. 2020; 13(3): 1116-24. DOI: https://doi.org/10.1159%2F000509643
10. Sile S, Wall BM. Acute renal failure secondary to spontaneous acute tumor lysis syndrome in myelofibrosis. Am J Kidney Dis 2001; 38(4): E21. DOI: https://doi.org/10.1053/ajkd.2001.27730
11. Weerasinghe C, Zaarour M, Arnaout S, Garcia G, Dhar M. Spontaneous tumor lysis syndrome in small-cell lung cancer: A rare complication. World J Oncol. 2015; 6(5): 464-71. DOI: https://doi.org/10.14740/wjon946w
12. Kanchustambham V, Saladi S, Patolia S, Stoeckel D. Spontaneous tumor lysis syndrome in small cell lung cancer. Cureus 2017; 9(2): e1017. DOI: https://doi.org/10.7759%2Fcureus.1017
13. Alan AM, Alan O. A case of spontaneous tumor lysis syndrome in extensive-stage small-cell lung cancer: A rare oncologic emergency. Turk J Emerg Med 2020; 20(3): 142-5. DOI: https://doi.org/10.4103/2452-2473.290061
14. Parsi M, Rai M, Clay C. You Can't Always Blame the Chemo: A Rare Case of Spontaneous tumor lysis syndrome in a patient with invasive ductal cell carcinoma of the breast. Cureus 2019; 11(11): e6186. DOI: https://doi.org/10.7759/cureus.6186
15. Shaforostova I, Fiedler R, Zander M, Pflumm J, März WJ. Fatal spontaneous tumor lysis syndrome in a patient with metastatic colon cancer: A clinical case of rare oncological emergency. Case Rep Gastroenterol 2020; 14(2): 255-60. DOI: https://doi.org/10.1159/000507648
16. Patel V, Case R. Spontaneous tumor lysis syndrome in blastoid-variant Mantle cell lymphoma: Considerations for the general internist. J Investig Med High Impact Case Rep 2020; 8: 2324709620944709. DOI: https://doi.org/10.1177/2324709620944709
17. Taha N, Bhaskar G. Spontaneous tumor lysis syndrome in Mantle cell lymphoma: A case study. Cureus 2022; 14(10): e29851. DOI: https://doi.org/10.7759%2Fcureus.29851
18. Wilson J. Spontaneous tumor lysis syndrome in hyperaggressive mantle cell lymphoma. eJHaem 2022; 3: 1060-61 DI: https://doi.org/10.1002/jha2.531
19. Harris NL, Jaffe ES, Diebold J, Flandrin G, Muller-Hermelink HK, Vardiman J, *et al.* World health organization classification of neoplastic diseases of the hematopoietic and lymphoid tissues: Report of the clinical advisory committee meeting-Airlie house. Virginia, November 1997. J Clin Oncol 1999; 17(12): 3835-49. DOI: https://doi.org/10.1200/jco.1999.17.12.3835
20. Majlis A, Pugh WC, Rodriguez MA, Benedict WF, Cabanillas F. Mantle cell lymphoma: Correlation of clinical outcome and biologic features with three histologic variants. J Clin Oncol 1997; 15(4): 1664-71. DOI: https://doi.org/10.1200/jco.1997.15.4.1664
21. Ott G, Kalla J, Ott MM, Schryen B, Katzenberger T, Müller JG, *et al.* Blastoid variants of mantle cell lymphoma: Frequent *BCL-1* rearrangements at the major translocation cluster region and tetraploid chromosome clones. Blood 1997; 89(4): 1421-9.
22. Swerdlow SH, Yang WI, Zukerberg LR, Harris NL, Arnold A, Williams ME. Expression of cyclin D1 protein in centrocytic/mantle cell lymphomas with and without rearrangement of the *BCL1*/cyclin D1 gene. Hum Pathol 1995; 26(9): 999-1004. DOI: https://doi.org/10.1016/0046-8177(95)90090-x