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Case Report

Two Rare Clinical Spectrums in a Hodgkin Lymphoma Patient: Super-acute Tumor Lysis Syndrome and Syndrome of Inappropriate Antidiuretic Hormone

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ABSTRACT

Tumor lysis syndrome (TLS) can be seen in hematological malignancies before and during treatment. Rapid tumor cell lysis by chemotherapy causes electrolyte abnormalities in patients, which can lead to organ failure and death. We aimed to present a case of a patient with super-acute TLS, which is not an expected finding in Hodgkin lymphoma patients. A 44-year-old male patient was admitted to the infectious diseases ward due to a fever of unknown origin. He had complaints of periodically recurring fevers, night sweats, fatigue, and weight loss for the last year. Excisional lymph node biopsy was performed because of the patient's B symptoms and multiple lymphadenopathy. The patient's excisional lymph node biopsy was reported as Classical Hodgkin lymphoma, mixed cellular type. Standard Hodgkin lymphoma chemotherapy: adriamycin-bleomycin-vinblastine-dacarbazine was planned after staging. However, the patient developed clinical and laboratory superacute TLS after bleomycin and vinblastine treatment. The patient could not receive adriamycin and dacarbazine treatment. The patient experienced a deterioration in general condition and seizures. During the follow-up, vinblastine-associated syndrome of inappropriate antidiuretic hormone was also observed while waiting for the general condition to improve before starting chemotherapy again. Both clinical conditions, which are rarely seen in patients with Hodgkin lymphoma, are potentially fatal. Treating physicians should be alert to the many manifestations of this potential Hodgkin lymphoma sequela.

Keywords: Hodgkin lymphoma, super-acute tumor lysis syndrome, inappropriate antidiuretic hormone syndrome

Introduction

One metabolic problem that might occur after starting cancer treatment is tumor lysis syndrome (TLS). Rapid tumor cell lysis causes metabolic abnormalities such as hyperuricemia, hyperkalemia, hyperphosphatemia, and hypocalcemia, which can result in severe renal impairment, cardiac arrhythmia, seizures, and death [1,2]. In patients with hematological and other malignancies, oncologic emergency encounters are among the situations that result in mortality [3]. Chemotherapy or spontaneous cytolysis of malignant cells is two possible causes [4,5]. Hematological malignancies such as lymphoma and leukemia are most commonly linked to TLS [4,6,7]. On the other hand, hyponatremia, a common electrolyte disease, is frequently caused by the syndrome of inappropriate antidiuretic hormone (SIADH) in oncologic patients. Chemotherapy drugs are among the causes of SIADH. A few documented examples currently link vinorelbine to SIADH [8,9]. In this study, we aim to present a case of a Hodgkin lymphoma patient who developed TLS immediately after vinblastine and bleomycin treatment. Additionally, our patient developed SIADH after vinblastine treatment. Only 1-2 cases of TLS have been reported in the literature in Hodgkin lymphoma patients. We aimed to present this case because Hodgkin lymphoma patients rarely experience super-acute TLS findings.

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Case Report

A 44-year-old male patient was admitted to the department of infectious disease with an unknown fever. He had fevers recurring periodically over the last year, accompanied by night sweats, fatigue, and weight loss. The painless swelling on his neck had been gradually growing for a year. Its size gradually grew throughout the few weeks before the presentation. In his past medical history, he had a history of hypertension only. When asked about his family history, it was learned that his mother had Hodgkin lymphoma. On physical examination, fixed painful lymphadenopathy (LAP) was detected, measuring approximately 2 cm in the left cervical chains and extending to the supraclavicular region. Laboratory tests revealed C-reactive protein 171 mg/L, ferritin 2000 ng/mL, hemoglobin 10.7 g/dL, leukocyte $11x10^3/mm^3$, neutrophil $8x10^3/mm^3$, platelet $173x10^3/mm^3$, and lactate dehydrogenase level 335 U/L. Contrast-enhanced neck magnetic resonance imaging revealed multiple lymph nodes in the left cervical chain, the largest of which was at level 4, (13x10 mm in size), some round in appearance, and with increased cortical thickness. Due to the patient's B symptoms and multiple pathological LAP, an excisional lymph node biopsy was performed with the preliminary diagnosis of lymphoma. The patient's excisional LAP biopsy revealed the following histomorphological and histochemical findings: high Ki-67 index, Epstein-Barr virus positive, CD30, CD15, PAX 5 (faint), BCL6 (weak) positive, compatible with 'Classical Hodgkin lymphoma, mixed cellular type'. The patient underwent bone marrow aspiration and biopsy for staging purposes, and positron emission tomography/computed tomography (PET/CT) was performed. On PET/CT, lymph nodes measuring 13x10 mm in size and showing fluorodeoxyglucose (FDG) uptake [maximum standardized uptake value (SUV_{max}) 6.60] were observed in the left upper, middle, and lower cervical regions. Lymph nodes measuring 11×10 mm with FDG uptake (SUV_{max} 5.08) were observed in the left supraclavicular region adjacent to the left thyroid lobe. Lymph nodes measuring 27×16 mm in size and showing FDG uptake (SUV_{max} 11.64) were observed in the abdomen adjacent to the liver hilum and the paraaortic and paracaval regions. Focally increased FDG uptake was observed in the spleen (SUV_{max} 12.09). The patient was evaluated as stage IIIBS as depicted in Figure 1. After echocardiography, adriamycin, bleomycin, vinblastine, and dacarbazine treatment was planned for the patient. The patient had a seizure immediately after receiving vinblastine and bleomycin treatment, and developed TLS. Although the patient was started on allopurinol for TLS prophylaxis a few days before the start of chemotherapy, acute TLS was observed. Adriamycin and dacarbazine treatments could not be given. In biochemical findings, uric acid reached 17 mg/dL, creatinine 3.5 mg/dL, potassium 6 mmol/L, calcium 6 mg/dL, and phosphorus 12 mg/dL (Table 1). The patient was given rasburicase and supportive treatment. The patient's renal function tests and electrolytes returned to normal during follow-up. Hemodialysis treatment was not required. However, the patient was admitted to the intensive care unit with a sodium level of 105 mEq/L and a potassium level of 2 mmol/L as depicted in Figure 2. At the same time, the patient developed high creatinine levels again. The patient was initially considered to have SIADH due to vinblastine treatment. The patient was treated with isotonic saline and hypertonic saline. Close monitoring of fluid intake and output was performed. Fluid intake was restricted, and tolvaptan treatment was applied. The patient's serum sodium value reached 131 mEq/L after 4-5 days. We present this case because TLS is rarely seen in Hodgkin lymphoma.

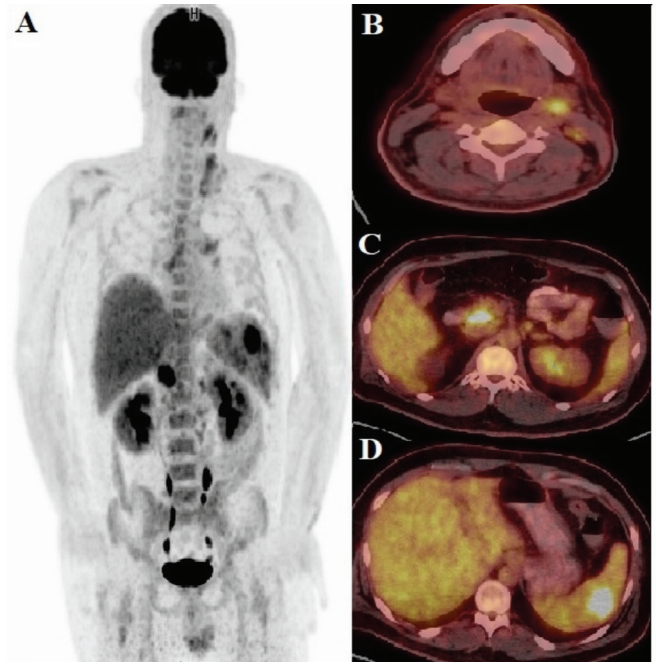

Figure 1. ^{18}F-FDG PET/CT maximum intense projection images (A) and transaxial fusion PET/CT images showed intense uptake of supra-diaphragmatic (B), infra-diaphragmatic (C) lymph nodes, and splenic nodal lesions (D) with increased ^{18}F-FDG uptake
^{18}F-FDG PET/CT: Fluorine-18-fluorodeoxyglucose positron emission tomography/computed tomography

Table 1. Biochemical findings after vinblastine and bleomycin treatment

Parameters	The patient's baseline values	Laboratory values within minutes after vinblastine and bleomycin treatment	Reference value
Creatinine (mg/dL)	0.82	3.5	0.7-1.2
Urea (mg/dL)	34	112	16.6-48.5
Calcium (mg/dL)	8.1	6	8.6-10.5
Phosphorus (mg/dL)	2.3	12	2.5-4.5
Uric acid (mg/dL)	4.1	17	3.4-7

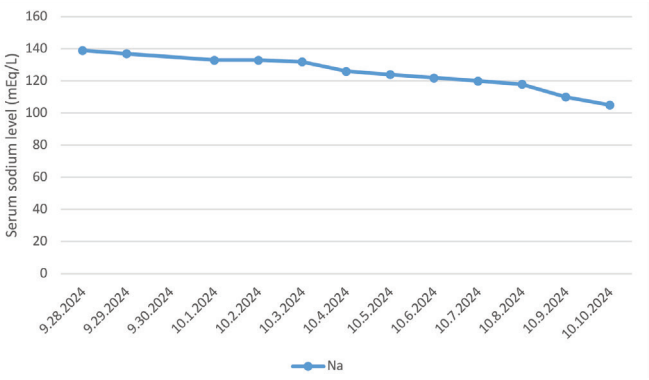

Figure 2. Serum sodium levels in the patient's follow-up after vinblastine and bleomycin treatment

Discussion

There are no universally validated diagnostic criteria or categorization system for TLS, even though it is generally agreed that a broad range of metabolic problems can arise in fast-growing neoplasms following the commencement of anticancer therapy. One kind of TLS that is characterized by biochemical alterations without clinical symptoms is laboratory-defined TLS. Severe metabolic disturbances might occur in patients without any symptoms. These need to be treated. Clinical TLS is characterized by manifestations of metabolic alterations requiring immediate treatment [1]. Some chemotherapy agents also have a higher risk of causing TLS. A recent study by Li et al. [10] reported that 164 antineoplastic agents precipitated TLS. Overall, rituximab was the most commonly reported antineoplastic agent in TLS reports, followed by cyclophosphamide, venetoclax, doxorubicin, and etoposide. TLS is more common in high-grade non-Hodgkin lymphoma (NHL) and acute leukemia. The following results from studies on children and adults in various facilities lend credence to this. To ascertain the frequency of TLS, Wasim et al. [11] examined 50 patients with hematologic malignancies. They found that acute leukemia, NHL, and chronic leukemia incidences were 14%, 4%, and 2%, respectively. Previous research has indicated that both elevated cytokine levels and heat cause tumor cell death. Patients with greater tumor sizes are at a higher risk [12]. Suzuki et al. [13] reported a case of super-acute onset of TLS accompanied by hypercytokinemia during treatment of Hodgkin's lymphoma with ABVD chemotherapy. It was reported that the patient developed a seizure within minutes of chemotherapy. Hypercytokinemia occurred with TLS, which led to pyrexia, convulsion, and loss of consciousness [13]. Similarly, in the case we presented, biochemical changes and clinical deterioration of the patient were observed within minutes after vinblastine and bleomycin treatment. Our patient also developed a seizure while neurological findings were observed. TLS is a rare clinical entity in Hodgkin lymphoma cases. According to reports, hypercytokinemia can occasionally accompany TLS [14]. Cancer chemotherapy (particularly in the treatment of hematologic malignancies) and several severe conditions (such as sepsis and trauma) can cause hypercytokinemia, which causes an overactive inflammatory response [15,16]. Recently, Hassan et al. [17] reported spontaneous TLS in a 7-year-old girl with Hodgkin lymphoma. The patient's condition deteriorated suddenly during his hospital stay for further work-up and treatment. Laboratory reports showed biochemical abnormalities confirming spontaneous TLS. He recovered completely with prompt stabilization and correction of electrolyte abnormalities. Spontaneous TLS is reported to be a life-threatening condition rarely seen in Hodgkin lymphoma patients [17]. The risk of developing spontaneous TLS is higher in patients with large tumors, high pretreatment uric acid levels, prior renal disorders, exposure to nephrotoxins, oliguria, acidic urine, and dehydration [18]. No risk factor increased the risk of developing TLS in our patient. Moreover, highly acute TLS was observed to have developed following the administration of only 2 of the 4 drugs included in the chemotherapy protocol.

The patient was observed to have SIADH related to vinblastine. Hyponatremia, a common electrolyte disorder, is frequently caused by SIADH in oncologic patients. Chemotherapy drugs are among the several causes of SIADH. Three examples linking vinorelbine to the SIADH have been described, according to Hoang et al. [8]. Garrett and Simpson [9] reported that vinorelbine was being administered to a 50-year-old Caucasian woman who had a history of advanced breast cancer and had not responded to various forms of treatment. Within seven days, blood chemistries showed significantly reduced potassium and salt concentrations compared to a normal baseline. Hyponatremia was verified by a follow-up blood chemistry analysis. After being brought to the hospital, the patient received treatment for SIADH. Non-steroidal anti-inflammatory drugs, tricyclic antidepressants, selective serotonin reuptake inhibitors, alkylating agents, platinum compounds, and vinca alkaloids are among the pharmacological types that can cause SIADH. Vinorelbine, a semisynthetic vinca alkaloid, is a member of the same class as vincristine and vinblastine. These compounds function by preventing the development of microtubules, which are essential for cell division. Within this class, SIADH is known to be induced by vincristine and, to a lesser extent, vinblastine [9,19]. We propose that this case will contribute to the literature. There are only a few cases in the literature that have reported TLS in Hodgkin lymphoma. Treatment with adriamycin, bleomycin, vinblastine, and dacarbazine was planned for this patient. However, since the patient developed TLS only after vinblastine and bleomycin treatment, adriamycin and dacarbazine treatment could not be applied. The patient also has SIADH after vinblastine treatment, which is a rare finding.

Conclusion

In conclusion, super-acute TLS in the case of Hodgkin's disease is a rare phenomenon. TLS is rare, but if it develops, it carries a high risk of poor clinical outcomes. Hypercytokinemia occurs in TLS, which can lead to symptoms such as fever, convulsions, and loss of consciousness, as observed in our patient. Often, the vague and non-alarming nature of the complaints makes it difficult to diagnose this easily treatable condition,

potentially leading to a series of fatal outcomes. This case report aims to draw the attention of general physicians to the rare but important occurrence of super-acute TLS in cases of Hodgkin's lymphoma. Hypercytokinemia occurs in TLS, which can lead to symptoms such as fever, convulsions, and loss of consciousness, as observed in our patient. Regular monitoring of sodium levels during vinorelbine treatment allows clinicians to improve the quality of life for patients, and take action before serious neurological problems of SIADH appear.

Ethics

Informed Consent: Informed consent was obtained from the patient.

Footnotes

Authorship Contributions

Surgical and Medical Practices: R.Ç., Z.H., Concept: R.Ç., H.Ö., Design: R.Ç., Data Collection or Processing: R.Ç., Z.H., Analysis or Interpretation: R.Ç., H.Ö., Literature Search: R.Ç., Writing: R.Ç.

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