Case Report

A Unique Case of Transient Spontaneous Regression Complicated with Tumor Lysis Syndrome of T-cell Lymphoblastic Lymphoma in HIV-Infected Patient without Antiretroviral Therapy

Pairaya Rujirojindakul MD*, Kanita Kayasut MD**,
Montanan Rohitoprakarn MD***, Arnuparp Lekhakula MD*

** Department of Medicine, Faculty of Medicine, Prince of Songkla University, Songkhla*
*** Department of Pathology, Faculty of Medicine, Prince of Songkla University, Songkhla*
**** Department of Radiology, Faculty of Medicine, Prince of Songkla University, Songkhla*

Spontaneous regression in high-grade non-Hodgkin lymphoma is rare. Herein, the authors report the case of a 26-year-old asymptomatic HIV-infected patient presenting with bleeding per gum after a dental extraction. Initially, a complete blood count showed lymphoblasts and thrombocytopenia. Laboratory investigations were compatible with acute tumor lysis syndrome. Without any steroid or chemotherapy, both clinical and laboratory abnormalities were spontaneously returned to normal limits. However, three weeks later he developed generalized lymphadenopathy. A submandibular gland biopsy revealed to be T-cell lymphoblastic lymphoma. This was followed by the second episode of spontaneous tumor lysis syndrome and spontaneous regression of lymphadenopathy again. At this time, he was treated with cyclophosphamide, adriamycin, vincristine, and prednisolone (CHOP) with whole brain irradiation. During seven months of chemotherapy, the physical examination and blood chemistry were normal. Unfortunately, after seven courses of CHOP, the disease rapidly progressed and ultimately lead to his death.

Keywords: *Spontaneous regression, Tumor lysis syndrome, HIV, T-cell lymphoblastic lymphoma, carcinomatous meningitis*

J Med Assoc Thai 2007; 90 (9): 1930-3
Full text. e-Journal: *http://www.medassocthai.org/journal*

Spontaneous regression of low-grade malignant lymphoma has been reported relatively frequently[1]. However, this phenomenon rarely occurs in high-grade malignant lymphoma[2]. In HIV-associated lymphoma, regression occasionally occurs after antiretroviral agents are given and the immune function is improved, but without treatment the spontaneous regression is rarely observed[3].

A tumor lysis syndrome, characterized by hyperuricemia, hypocalcemia, hyperkalemia, lactic acidosis, hyperphosphatemia, and azotemia, usually occurs after chemotherapy or steroid use. This syndrome has rarely been reported in cases without any treatment[4]. To the best of the authors' knowledge, tumor lysis syndrome has never been recognized when complicated by the situation of spontaneous regression. Here, the authors report the case of an asymptomatic HIV-infected patient with T-cell lymphoblastic lymphoma suffering from repeated episodes of regression and tumor lysis syndrome occurring simultaneously without any related medication being administered.

Correspondence to : Rujirojindakul P, Department of Internal Medicine, Faculty of Medicine, Prince of Songkla University, Hat Yai, Songkhla 90110, Thailand. Phone: 074-451-481, Fax: 074-239-670, E-mail: rupairay@medicine.psu.ac.th

Case Report

In September 2001, a previously healthy 26-year-old man presented to a community hospital with bleeding of his gums for seven days after a dental extraction. He was admitted at that hospital and results of the physical examination showed generalized

petechiae and purpura without any lymphadenopathy or hepatosplenomegaly. A complete blood count (CBC) showed normal hemoglobin (Hb 14.9 g/dl), thrombocytopenia (15 x 10^9/l), leukocytosis (72.8 x 10^9/l) and 90% of lymphoblasts. Unfortunately, there was no immunophenotype confirmation due to the limited facilities of the hospital. During admission, he had received only platelet and packed red cell (PRC) transfusion without steroids or chemotherapy. Four days later, he developed acute renal failure and pulmonary hemorrhage and was subsequently transferred to Songklanagarind Hospital.

On admission to Songklanagarind Hospital, the patient was pale, febrile, tachycardic, and normotensive with endotracheal intubation. The CBC showed a normal leukocyte count (5.7 x 10^9/l) with leucoerythroblastic features (nucleated red blood cell 2%, myelocyte 2% and metamyelocyte 2%), Hb was 7.9 gm/dL, and the platelet count was 67 x 10^9/l. Bone marrow aspiration was non-diagnostic. The laboratory investigations indicated acute tumor lysis syndrome. The following test results were found: blood urea nitrogen (BUN) 123.9 mg/dL, creatinine (Cr) 9.3 mg/dL, potassium (K) 7.4 mmol/L, bicarbonate (HCO_3) 17 mmol/L, calcium (Ca) 7.2 mg/dL, and phosphate (P) 14.5 mg/dL, uric acid 34 mg/dL. The serum lactate dehydrogenase (LDH) was also found to be elevated (1,036 U/L). Human immunodeficiency virus (HIV) antibodies were positive by ELISA. Ultrasonography of the urinary system revealed bilateral nephromegaly with a significant increase of renal echogenicity and preserved corticomedullary differentiation that was compatible with infiltrative parenchymal disease. Microbiologic studies for bacteria and fungus were negative. After ventilator support with platelet and PRC replacement, both the CBC and all of the above laboratory results returned to normal within eight days.

The patient's medical history was unremarkable. Although there was disclosure of a remote sexual liaison with a female prostitute many years earlier, no other risk factor for HIV infection was identified. At that time, neither chemotherapy nor antiretroviral agents were prescribed due to no confirmatory histological evidence of malignancy.

Three weeks later, the patient visited the Hematology Clinic at Songklanagarind Hospital and the physical examination revealed bilateral cervical, submandibular, and preauricular lymphadenopathy. The CBC was normal. Surprisingly, a lymph node biopsy showed lymphoid depletion and negative acid-fast and fungus stains. However, one week later the patient was admitted to our hospital again because of developing tonic-clonic seizure. He still had generalized lymphadenopathy. Apart from papilledema, no neurological deficit was detected. Computer Tomography (CT) of the brain without contrast media administration showed multiple hypodense lesions (Fig. 1). The CBC was found normal but again acute tumor lysis syndrome was detected. The laboratory results were as follows: BUN 36.5 mg/dL, Cr 4.49 mg/dL, K 4.6 mmol/L, HCO_3 16 mmol/L, Ca 10 mg/dL, P 6.6 mg/dL, uric acid 37.4 mg/dL. In addition, the serum LDH was also high (2,062 U/L).

By that time, a submandibular gland biopsy revealed lymphoblastic lymphoma (Fig. 2). An immunohistochemical study indicated there was T-cell origin with staining present for LCA and CD45RO but not for CD20. A bone marrow biopsy did not detect any malignancy. Spontaneously, all enlarged lymph nodes significantly decreased in size after the biopsy and simultaneously in addition the laboratory results were normal with only the administration of intravenous saline and allopurinol.

After the patient was treated with a regimen of CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisolone), all the lymphadenopathy completely disappeared. In addition, on completion of a whole brain radiation, no abnormalities were detected from the CT brain images. During his visits to the Hematology Clinic, the patient had been asymptomatic and

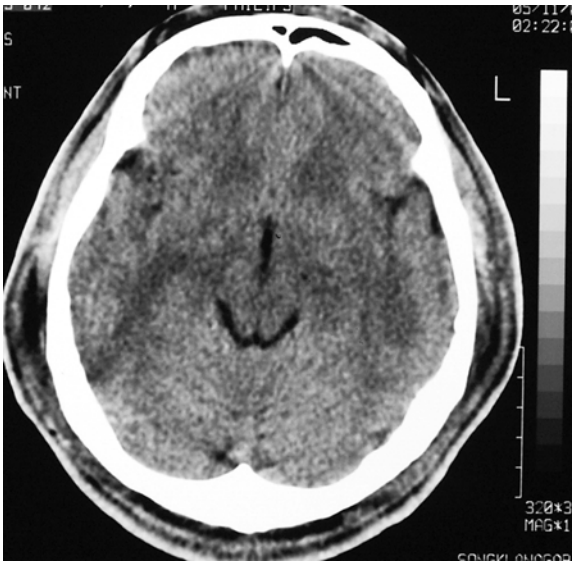
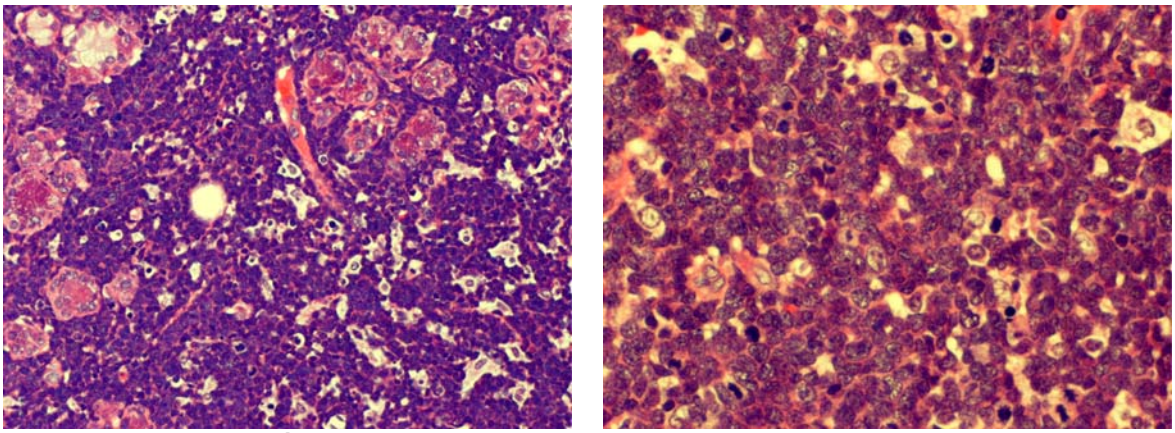


Fig. 1 Axial CT images shows multiple hypodense lesions at both basal ganglia, and the right parietal lobe and both posterior occipital areas



A B

Fig. 2 Microscopic section showing pleomorphic tumor cells with large nuclei and a coarse chromatin pattern. A 'starry sky' pattern is seen (hematoxylin and eosin stain A x200, B x1,000)

no evident disease had been found for more than a six-month period. Unfortunately, after the seventh course of CHOP he was admitted to the hospital again because of developing a severe headache and right lateral rectus palsy. Samples of cerebrospinal fluid revealed numerous lymphoblasts. At the same time, the systemic manifestation progressed rapidly, which ultimately led to his death.

Discussion

In HIV-infected patients, NHL occurs with a 60-fold increased frequency when compared with HIV-negative patients[5] and it frequently presents as an advanced stage III or IV disease where extranodal involvement is common, including the bone marrow (25-40%), and the central nervous system (CNS) (17-32%)[6]. Further, prognosis without antiretroviral agents is also very poor. When treating with doxorubicin-containing regimens, in non-HIV-infected patients with advanced aggressive lymphomas the disease-free-survival and overall survival is approximately 45% and 50%, respectively[7]. In contrast, fewer than half of HIV-infected patients were alive one year after treatment[8].

Regarding spontaneous regression of aggressive NHL, the regression in HIV-infected patients has been observed after antiretroviral therapy with improvement in immunologic status, such as in the primary central nervous system lymphoma[9] and T-cell non-Hodgkin's lymphoma[10]. However, the presented case seemed to be unique, with suspected temporary regression repeatedly occurring without any antiretroviral agents or steroids. Unfortunately, tests for the patient's CD4 count were not performed for confirmation of the host immune status due to lack of financial support. Even the patients' adequate absolute lymphocyte counts (mean 1321/ mm^3, 786-1152/mm^3) have been noted, the authors have no confirmatory evidence to show that the host's immune response was sufficient for this phenomenon.

The mechanism of spontaneous regression remains obscure. A number of potential coincident events, infection, or biopsy, may result in an augmented host response that results in an immunologically mediated tumor regression[11,12]. Other proposed mechanisms include apoptosis, angiogenesis inhibitor, induction of differentiation, and hormonal effects[13].

References

1. Horning SJ, Rosenberg SA. The natural history of initially untreated low-grade non-Hodgkin's lymphomas. N Engl J Med 1984; 311: 1471-5.
2. Kumamoto M, Nakamine H, Hara T, Yokoya Y, Kawai J, Ito H, et al. Spontaneous complete regression of high grade non-Hodgkin's lymphoma. Morphologic, immunohistochemical, and gene amplification analyses. Cancer 1994; 74: 3023-8.
3. Karnad AB, Jaffar A, Lands RH. Spontaneous regression of acquired immune deficiency syndrome-related, high-grade, extranodal non-Hodgkin's lymphoma. Cancer 1992; 69: 1856-7.
4. Jasek AM, Day HJ. Acute spontaneous tumor lysis syndrome. Am J Hematol 1994; 47: 129-31.
5. Beral V, Peterman T, Berkelman R, Jaffe H. AIDS-associated non-Hodgkin lymphoma. Lancet 1991; 337: 805-9.
6. Tirelli U, Spina M, Vaccher E, Errante D, Tavio M,

Simonelli C, et al. Clinical evaluation of 451 patients with HIV related non-Hodgkin's lymphoma: experience on the Italian cooperative group on AIDS and tumors (GICAT). Leuk Lymphoma 1995; 20: 91-6.
7. Fisher RI, Gaynor ER, Dahlberg S, Oken MM, Grogan TM, Mize EM, et al. Comparison of a standard regimen (CHOP) with three intensive chemotherapy regimens for advanced non-Hodgkin's lymphoma. N Engl J Med 1993; 328: 1002-6.
8. Little RF, Gutierrez M, Jaffe ES, Pau A, Horne M, Wilson W. HIV-associated non-Hodgkin lymphoma: incidence, presentation, and prognosis. JAMA 2001; 285: 1880-5.
9. McGowan JP, Shah S. Long-term remission of AIDS-related primary central nervous system lymphoma associated with highly active antiretroviral therapy. AIDS 1998; 12: 952-4.
10. Fatkenheuer G, Hell K, Roers A, Diehl V, Salzberger B. Spontaneous regression of HIV associated T-cell non-Hodgkin's lymphoma with highly active antiretro viral therapy. Eur J Med Res 2000; 5: 236-40.
11. Drobyski WR, Qazi R. Spontaneous regression in non-Hodgkin's lymphoma: clinical and pathogenetic considerations. Am J Hematol 1989; 31: 138-41.
12. Wiernik PH. Spontaneous regression of hematologic cancers. Natl Cancer Inst Monogr 1976; 44: 35-8.
13. Rappaport DC, Haider MA, Sternthal E. Spontaneous regression of intermediate-grade non-Hodgkin's lymphoma. AJR Am J Roentgenol 1999; 172: 131-3.

การเกิด spontaneous regression ร่วมกับ tumor lysis syndrome ในมะเร็งต่อมน้ำเหลืองชนิด T-cell lymphoblastic ในผู้ป่วยติดเชื้อ เอชไอวี ที่ไม่ได้ยาต้านไวรัส

ไปรยา รุจิโรจน์จินดากุล, คณิตา กายะสุต, มณฑนรรณ์ โรหิโตปการณ์, อานุภาพ เลขะกุล

การเกิด spontaneous regression ในมะเร็งต่อมน้ำเหลืองชนิด high-grade พบได้น้อยมาก รายงานกรณีผู้ป่วยรายนี้เป็นผู้ป่วยเอชไอวีที่มีเลือดออกจากรากฟันนาน 7 วันหลังจากถอนฟัน ผลการตรวจเลือดพบเกล็ดเลือดต่ำและ lymphoblast การสืบค้นทางห้องปฏิบัติการบ่งถึง ไตวายเฉียบพลันร่วมกับ tumor lysis syndrome ต่อมาทั้งอาการแสดงและผลการตรวจทางห้องปฏิบัติการกลับมาเป็นปกติ โดยที่ไม่ได้รับสเตียรอยด์ หรือ เคมีบำบัด ต่อมาผู้ป่วยมีต่อมน้ำเหลืองโตทั่วตัว ร่วมกับมีอาการชัก ผลการตรวจทางพยาธิวิทยาของต่อมน้ำเหลืองเป็นมะเร็งต่อมน้ำเหลืองชนิด T-cell lymphoblastic หลังการตัดชิ้นเนื้อต่อมน้ำเหลืองมีขนาดเล็กลงอย่างชัดเจน ร่วมกับมีผลการตรวจทางห้องปฏิบัติการ ที่บ่งถึง tumor lysis syndrome อีกครั้ง หลังจากนั้นผู้ป่วยจึงได้รับเคมีบำบัด ที่ประกอบด้วย cyclophosphamide, adriamycin, vincristine และ prednisolone (CHOP) ร่วมกับการฉายแสง ผู้ป่วยตอบสนองต่อการรักษาดี โดยตรวจไม่พบรอยโรค ตลอดระยะเวลา 7 เดือน อย่างไรก็ตามในเวลาต่อมาผู้ป่วยกลับมีรอยโรคที่ระบบประสาทส่วนกลาง และเป็นสาเหตุที่ทำให้เสียชีวิต