Early Detection of Richter’s Transformation: Stable Disease with Dose-Reduced Gemcitabine and Local Radiation

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Summary

Background: The occurrence of Hodgkin’s lymphoma (HL) as a second aggressive lymphoid malignancy (known as Hodgkin’s disease variant of Richter’s transformation) is rarely observed. Response rates, even with highly aggressive therapy such as stem cell transplantation, are limited, ranging from 4 to 43%, and the medium survival time ranges from 5 to 8 months. Case Report: A 72-year-old patient with a history of chronic lymphatic leukemia (CLL) was admitted with thoracic back pain and assumed progression of the CLL. The patient showed no fever, night sweats or weight loss. A computed tomography (CT) scan confirmed the progression of axillary and cervical lymph nodes. In addition, an intraspinal infiltration at the 8th thoracic vertebra (Th8) was detected. Surprisingly, histology of an extirpated lymph node demonstrated the existence of 2 tumors in the same lymph node. Infiltrates of small lymphocytes representing the pre-existing CLL (CD5-, CD20-, CD23-positive) coexisted with Reed-Sternberg Hodgkin’s cells (CD30-, CD15-positive). Chemotherapy was started, combined with palliative radiation of vertebrae Th7–Th10. 12 months after diagnosis of Richter’s transformation the patient is still alive without any progression of the underlying disease. Conclusion: We present a unique case of a Hodgkin’s disease variant of Richter’s transformation and CLL in the same lymph node, which was detected early because of spinal infiltration and was subsequently stabilized with reduced-dosage gemcitabine and local radiation. Additionally, we show unique pictures of 2 tumors coexisting in the same lymph node.
Introduction

Richter’s transformation (Richter’s syndrome, RS) represents rare cases of high-grade lymphoma in patients with pre-existing chronic lymphocytic leukemia / small lymphocytic lymphoma. The occurrence of Hodgkin’s lymphoma (HL) as a second aggressive lymphoid malignancy in RS (so-called Hodgkin’s disease variant of Richter’s transformation) is very uncommon. The mechanisms of the alteration of chronic lymphatic leukemia (CLL) to RS are not yet fully understood. Microorganisms, such as *Epstein-Barr virus*, may trigger RS, and an association with fludarabine treatment [1–4] has also been reported. Characteristic signs of RS are systemic symptoms (e.g. fever, weight loss and/or night sweats), rapid increase in the size of secondary lymphoid organs and elevated lactate dehydrogenase (LDH). Rarely, RS presents with extranodal involvement. Response rates, even with highly aggressive therapy including stem cell transplantation, are limited, ranging from 4 to 43%, and the medium survival time ranges from 5 to 8 months [1].

Here, we present the case of a patient with RS which was detected unusually early because of thoracic spinal infiltration. The patient’s disease was stabilized by a reduced dosage of gemcitabine and local radiation. The diagnosis was established by histology from a lymph node that showed the unique coexistence of both B-CLL and HL.

Case Report

A 72-year-old patient with a history of CLL was admitted because of thoracic back pain that was presumed to be a result of progressive disease. The initial diagnosis of CLL was made in 1994. The patient had received prednisone (75 mg on days 1 and 15, 50 mg on days 2 and 16, and 25 mg on days 3 and 17) and chlorambucil (0.4 mg/kg on days 1 and 15) between 1994 and 2002, fludarabine (25 mg/m²) in 2002, 5 cycles of a combination therapy with fludarabine (25 mg/m²), cyclophosphamide (250 mg/m²) and rituximab (375 mg/m²) between 2003 and 2004, and 6 cycles of R-CHOP (rituximab 375 mg/m², cyclophosphamide 750 mg/m², vincristine 1.4 mg/m², daunorubicin 50 mg/m², prednisolone 100 mg) between 2004 and 2005, together with involved field radiation of an abdominal bulk with good clinical responses.

At the time of admission, major complaints were severe thoracic paravertebral back pain, fatigue and energy loss. The patient did not suffer from night sweats, fever or weight loss. Physical examination revealed enlarged cervical and axillary lymph nodes. Laboratory values on admission to the hospital included decreased hemoglobin of 11.2 g/dl (reference range 13.5–17.5 g/dl), increased sedimentation rate (32 mm in 1 h), increased alkaline phosphatase (248 U/l), increased liver enzymes (AST 102 U/l, ALT 117 U/l, GGT 199 U/l), increased IgM (7.8 mg/dl, RR 46–304 mg/dl) and IgA (28.5 mg/dl, RR 5–83 mg/dl) and an association with fludarabine treatment [1–4] has also been reported. Characteristic signs of RS are systemic symptoms (e.g. fever, weight loss and/or night sweats), rapid increase in the size of secondary lymphoid organs and elevated lactate dehydrogenase (LDH). Rarely, RS presents with extranodal involvement. Response rates, even with highly aggressive therapy including stem cell transplantation, are limited, ranging from 4 to 43%, and the medium survival time ranges from 5 to 8 months [1].

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Fig. 1. CT scan of a thoracic spinal infiltration of Hodgkin’s lymphoma. A Infiltration at Th8. White arrows show lymphoma masses infiltrating the left intervertebral foramen. B Infiltration at Th2/3. White arrows show lymphoma masses infiltrating the right intervertebral foramen.

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ity > grade 2 according to common toxicity criteria (CTC) occurred during the following 12 administrations.

7 months after diagnosis of RS, a CT scan was performed showing stable disease with a minor reduction in the size of some lymph nodes. 5 months later (12 months after diagnosis of RS), the patient is still alive and in a clinically stable condition, with 4,000 leucocytes/µl, 100,000 thrombocytes/µl and 11.9 mg/dl hemoglobin, without detectable CLL cells in the peripheral blood.

Discussion

Most commonly, treatment regimens for patients with RS include conventional therapy (e.g. CHOP or its variants), radioimmunotherapy, and high-dose therapy followed by hematopoietic cell transplantation. Thus, patients with RS are generally treated similarly to patients with de novo aggressive lymphoma, lymphoma patients refractory to cyclophosphamide, vincristine, procarbazine and prednisone (COPP) or HL patients refractory to doxorubicin, bleomycin, vinblastine and dacarbazine (ABVD) [5–7].

However, patients who have received numerous pretreatments are normally unable to tolerate conventional treatment. For this reason and because of the age of our patient and the location of the tumor, we decided in the present case to use gemcitabine in combination with local radiation, as suggested in recent reports [6, 9]. With this third line regimen, the disease could be stabilized, and after a dose reduction that was necessary because of hematological toxicity, combination therapy (gemcitabine and local radiation) was well tolerated without hematological and infectious complications. Hence, the treatment employed was successful in this heavily pretreated RS patient.

References