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CASE REPORT

Relapsed Hodgkin's Lymphoma after Autologous Bone Marrow Transplant

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ABSTRACT

This report describes a 28-year-old woman with stage IV Hodgkin's lymphoma with nodular sclerosis and bone marrow involvement. The patient received four cycles of adriamycin, bleomycin, vinblastine, and dacarbazine combination chemotherapy and achieved only partial response. Salvage therapy with cytarabine, cisplatin, and dexamethasone followed by autologous bone marrow transplantation improved control of the disease partially, but the patient ultimately had a relapse. Further options for salvage therapy in stage IV Hodgkin's lymphoma are discussed, and the patient's response to these therapies is described.

Key Words: *Bone marrow transplantation; cAC10-vcMMAE; drug therapy, combination; Hodgkin disease; recurrence; transplantation, autologous*

中文摘要

自體骨髓移植後出現復發性霍奇金淋巴瘤

夏頌賢

本文報告一名28歲女性，她患有第四期霍奇金淋巴瘤（結節硬化型）並有骨髓轉移。病人接受利用adriamycin、bleomycin、vinblastine和dacarbazine的合併化療共四個療程，但只有部份緩解。使用cytarabine、cisplatin和dexamethasone後再以自體骨髓移植的補救治療亦只改善部份病情，但病人最終出現復發。本文會討論第四期霍奇金淋巴瘤的補救療法，以及研究病人對這些療法的反應。

INTRODUCTION

Advanced Hodgkin's lymphoma can be a challenge to treat. While around two-thirds of patients with advanced disease are cured,[1] the remaining one-third may have relapses or are refractory to the available treatment options. This report describes a young woman who presented with large bilateral neck masses and dyspnoea, and who was diagnosed with advanced Hodgkin's lymphoma. This case highlights the challenges involved in treating a patient with advanced disease who achieves only partial response to chemotherapy, and who later has a relapse. The report outlines the treatments selected for this patient, including use of the new chemotherapeutic agent brentuximab vedotin.

CASE REPORT

A 28-year-old woman presented to the Accident and Emergency Department in March 2011 with neck masses that had increased in size over two to three

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months and progressive dyspnoea for the previous few days. Physical examination showed that the patient was in severe respiratory distress, with a borderline oxygen saturation level despite being given high-flow oxygen. She had facial oedema and large bilateral neck masses, each measuring approximately 10 cm. The patient did not smoke or drink alcohol, and had good past health.

In March 2010, the patient had presented to another hospital with bilateral enlarged cervical lymph nodes, but refused further investigation. She discharged herself from the hospital against medical advice, and consulted a traditional Chinese medicine practitioner who prescribed a herbal remedy.

The patient was intubated shortly after arrival and transferred to the intensive care unit (ICU). She underwent an urgent contrast computed tomography (CT) scan and incisional biopsy of the neck masses. The CT scan revealed extensive lymphadenopathy over the bilateral cervical, axillary, mediastinal, mesenteric, retroperitoneal, and left external iliac regions (Figure). The right lung and superior vena cava were collapsed. The lymph node biopsy showed that the patient had classical Hodgkin's lymphoma with nodular sclerosis. Bone marrow involvement was also observed. The patient was diagnosed with stage IV disease.

The patient received chemotherapy consisting of adriamycin, bleomycin, vinblastine, and dacarbazine (ABVD) while in the ICU. Clinical improvement was observed, with a reduction in the size of the neck tumours. The patient was extubated after seven days and discharged from hospital after two to three weeks. She received four cycles of ABVD between March and July 2011, which resulted in a decrease in the size of the neck tumours; however, significant residual lymphadenopathy remained, with the bilateral neck

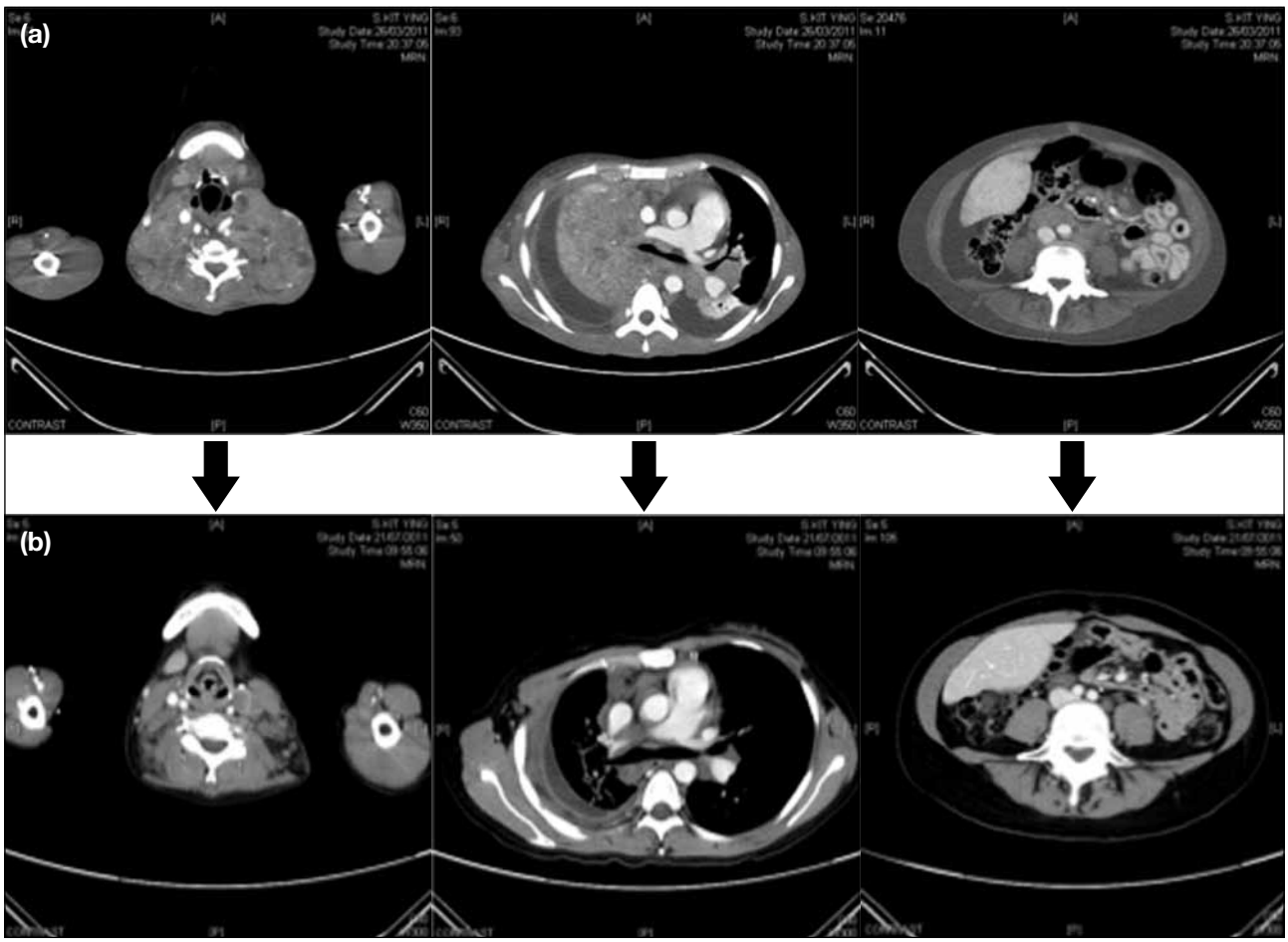

Figure. Computed tomography scan at (a) diagnosis; and (b) following four cycles of adriamycin, bleomycin, vinblastine, and dacarbazine, showing reductions in the size and number of lymphadenopathies and re-inflation of the right lung.

tumours measuring 3 to 5 cm. Restaging was performed in July 2011, which revealed reductions in the size and number of lymphadenopathies and re-inflation of the right lung (Figure); no lymphoma involvement was evident in the bone marrow.

Given the patient's age and partial response to four cycles of ABVD, salvage therapy was considered. The patient was given two cycles of cytarabine, cisplatin, and dexamethasone (DHAP) during August and September 2011, which resulted in some further improvement in the size of the neck masses, followed by an autologous bone marrow transplantation (BMT) with carmustine, etoposide, cytarabine, and melphalan conditioning in October 2011. Positron emission tomography CT scan done one month later revealed multiple small cervical lymph nodes, with standardised uptake value of 3.5; the salvage therapy had improved control of the disease.

However, three months after the autologous BMT, the size of the cervical lymph nodes increased again. Repeated contrast CT in February 2012 revealed that the tumours in the neck had recurred, while the abdominal and pelvic tumours remained static. Repeated lymph node biopsy returned the same diagnosis of Hodgkin's lymphoma with nodular sclerosis.

Gemcitabine-based chemotherapy (gemcitabine, prednisolone, and vinblastine) was commenced in March 2012, but the patient did not respond to treatment; there was progressive enlargement of the cervical lymph nodes.

A new chemotherapeutic agent, brentuximab vedotin, was tried. The patient was given the first dose of 1.8 mg/kg by intravenous (IV) infusion over 30 minutes in June 2012, eight months after the failed BMT, and had responded well after three days. However, on day 4 the patient deteriorated suddenly and could not be resuscitated. The family declined an autopsy, so the cause of death remains undetermined.

DISCUSSION

This patient had stage IV Hodgkin's lymphoma with nodular sclerosis and bone marrow involvement. At the time of diagnosis, the patient's International Prognostic Score was 4, and her predicted five-year freedom from progression was 51% and five-year overall survival was 61%.[1]

Given that the patient achieved only a partial response to ABVD, the use of salvage therapy was considered pertinent. Many different regimens for salvage therapy have been trialled in relapsed or refractory Hodgkin's lymphoma, but in most studies, the overall response rate is only in the range of 70 to 80%.[2] Two cycles of DHAP followed by autologous BMT showed initial improvement, but the disease recurred only a few months later.

As the patient was refractory to subsequent gemcitabine-based chemotherapy, the use of brentuximab vedotin was tried. This agent is an antibody-drug conjugate comprised of a monoclonal anti-CD30 and monomethyl auristatin E. Brentuximab vedotin has recently received US Food and Drug Administration approval for Hodgkin's lymphoma after failure of autologous BMT or ≥2 prior multi-agent chemotherapy regimens in patients who are not candidates for autologous stem cell transplantation. The overall response rate for brentuximab vedotin has been reported as 75%.[3] The recommended dose is 1.8 mg/kg by IV infusion over 30 minutes at three-week intervals. Commonly reported side-effects include infusion reaction, nausea and vomiting, marrow suppression, and peripheral sensory neuropathy. It is recommended that patients receive premedication for infusion reactions and anti-emetic agents, and that complete blood count is monitored before each cycle. While reports have demonstrated that brentuximab vedotin has been successful in patients with relapsed or refractory Hodgkin's lymphoma,[4] this outcome was unfortunately not achieved for the patient in the current report.

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