Case Report

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Malignant Pleural Effusion and Advanced-Stage Low-Grade Non-Hodgkin's Lymphoma Successfully Treated with Intrapleural Instillation of Rituximab

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ABSTRACT

We report a patient with an advanced-stage low-grade B cell lymphoproliferative disorder with malignant pleural effusion. Because of the patient's age and reluctance to submit to intensive chemotherapy, we administered rituximab via the intrapleural route in the hope that not only would it control the patient's pleural effusion, but that the rituximab instilled in the pleural cavity would also be absorbed and have a systemic effect to control the disease. Following four monthly courses of intrapleural Rituxan therapy, the patient's pleural effusion resolved completely, and the patient has stayed effusion- and effusion-related-symptom-free for eight months. In addition, there was a regression of his disease as evidenced by CT scan. Intrapleural rituximab therapy may be a promising treatment, both to control the malignant pleural effusion in patients with B-cell non-Hodgkin's lymphoma (NHL), and also to control the disease and help foster progression-free survival in patients who are not willing to receive intensive chemotherapy or for whom such therapy could be hazardous because of age.

Introduction

Rituximab, a chimeric mouse/human anti-CD20 monoclonal antibody targeting the pan-B-cell antigenic marker CD20, was the first monoclonal antibody licensed for use in the treatment of cancer. Rituximab has proven its important role in the management of B-cell NHL under various situations and has emerged as a useful biological agent in lymphoma. The antibody is only approved to be administered intravenously, although intrapleural [1], intraperitoneal [2], and intralesional [3], injection have recently been employed with positive response. We present the case of an advanced-stage low-grade B-cell NHL who presented with marked right-sided pleural effusion, hugely swollen lower extremities-particularly the legs-as well as massive underlying disease/lymphadenopathy. Intrapleural Rituximab therapy made it possible both to control his pleural effusion and halt the progression of his disease, and also to cause regression of his disease.

Case Report

The patient is an 85-year-old white male who was admitted to our hospital with a history of progressive shortness of breath associated with cough, but without expectoration, and massive swelling of both legs and lymphadenopathy. During his hospital admission, his CBC was found to be normal, with WBC 9.1 x 109/L, hemoglobin 13.4 g/dl, and platelet count 223 x 109/L, with a normal differential count. A CT of the chest revealed massive right-sided pleural effusion associated with right, middle, and right lower lung collapse and shift of the heart and mediastinum to the left. There was also right axillary adenopathy, as well as right paraspinal

musculature and thoracolumbar junction. A CT of the abdomen and pelvis with contrast revealed a small pericardial effusion and a moderate right pleural effusion with extensive airspace disease, as well as extensive mesenteric and retroperitoneal lymphadenopathy with infiltration of the right-sided muscular plane. There was also bilateral inguinal lymphadenopathy. The patient underwent a right inguinal lymph node biopsy, which revealed diffuse large B cell lymphoma (20%) and follicular lymphoma (80%), Grade III follicular pattern. The lymphoma cells were positive for CD20 Pax 5, CD23 BCL 16; they were negative for CD3, CD30, and cyclin D1. The flow cytometry of the lymph node biopsy revealed CD10+/ CD20+ B cell lymphoproliferative disorder.

The patient also underwent a bone marrow examination, which revealed follicular lymphoma, low-grade, focally involving cellular bone marrow. Flow cytometry of the bone marrow aspirate revealed CD20+ B cell lymphoproliferative disorder. Cytogenetic was normal. He then underwent pleurocentesis, and as his condition improved, he was discharged home. However, about a week later, his condition deteriorated, and he was again admitted to our hospital, again with considerable pleural effusion. On that occasion, a PleurX catheter was placed, over 1500 mL of fluid was drained and 100 mg of Rituximab was instilled in the right pleural cavity. He was then discharged home with a PleurX catheter in place with an order for the VNA nursing association to drain the pleural fluid three times per week. At that time, he also had considerable leg edema, which appeared to be lymphedema, possibly due to blockage in the lymph drainage. Following his discharge, the patient continued to have intrapleural Rituximab therapy on a monthly basis, and following three such courses of treatment, his condition improved considerably. Before the beginning of his treatment, he was extremely short of breath and had difficulty in ambulation due to swollen legs. After treatment, he started walking with a cane. The swelling of his legs had lessened considerably, and he needed pleural fluid drainage only once a month instead of three days per week.

Following six monthly courses of intrapleural rituximab therapy the patient is completely mobile with little or no swelling of his legs. CT scan of the chest, abdomen, and pelvis have revealed considerable regression of the disease.

Discussion

Rituximab is a chimeric monoclonal antibody that binds to the CD20 antigen, which is expressed on 95% of the B cell lymphoma cells and normal B cells. The efficacy and safety of rituximab in the treatment of most types of CD20+ non-Hodgkin's lymphoma - either as a single agent (monotherapy) or in combination with other chemotherapeutic agents - have now been well established [4]. Conventionally, rituximab is administered almost exclusively via the intravenous route, although the intrapleural route to control malignant pleural effusion, intraperitoneal route to control malignant ascites, as well as intralesional use to control cutaneous B cell lymphoma have been reported. Although it has been reported that rapid pleural instillation of even large doses of rituximab (400 mg bolus) can be tolerated without any adverse effects and may be effective in controlling malignant effusion [1], we used only a modest dose (100 mg of Rituxan in 60 ml of normal saline) to control the pleural effusion as well as the disease, to avoid any potential adverse events. Although the serum levels of rituximab were not measured, after intrapleural rituximab instillation the gradual reduction in the pleural effusion as well as regression of lymphadenopathy demonstrate that significant amounts of the antibody were absorbed and reached the circulation in an active form resulting in a systemic effect.

Thus, the therapeutic effect of rituximab in this case may be seen in the destruction both of infiltrating lymphoma cells in the pleural cavity and also of the affected lymph nodes, thus cleansing the inguinal lymphatic drainage vessels, as evidenced by regression of the patient's edematous legs. In summary, we report a case of low-grade CD20+ non-Hodgkin's lymphoma in which intrapleural rituximab was used both to control the pleural effusion and also to treat his disease. Thus, the intrapleural instillation of rituximab may provide a novel approach not only to control malignant pleural effusions in CD20+ low-grade non-Hodgkin's lymphoma patients, but also to treat them with a view to controlling the disease, improving the quality of life and providing progression-free survival.

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