

Prolonged complete remission in a primary MALT lymphoma of the lung after rituximab monotherapy

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Abstract

Background: Primary pulmonary non-Hodgkin lymphoma (NHL) is a rare entity. Despite its favorable prognosis, an optimal treatment approach has not been established until today, as there are few debated heterogeneous data in the literature. Many therapeutic options such as surgery, radiotherapy, chemotherapy alone or in combination, immunotherapy and/or immunochemotherapy all with similar results, have been reported.

Case description: We report the case of a 68-year-old man diagnosed with a primary marginal zone B-cell pulmonary NHL, with a durable complete response to rituximab monotherapy.

Conclusion: We support the therapeutic application of rituximab monotherapy as an attractive option for this malignancy. This effective approach exhibits significant antitumor activity leading to long-term complete remission and minimal hematological toxicity in contrast to other intensive chemotherapies and/or radiotherapy, which might have serious side effects. HIPPOKRATIA 2017, 21(2): 108-110.

Keywords: Primary bronchial-associated lymphoid tissue lymphoma, BALT lymphoma, prolonged complete remission, rituximab monotherapy

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Introduction

Primary pulmonary non-Hodgkin lymphoma (NHL) is an extremely rare neoplasm (<1 % of all NHLs and 3-4 % of the extranodal ones)¹⁻³. The most common histological type is the B-cell marginal zone mucosa-associated lymphoid tissue (MALT) lymphoma, usually localized to the lung. The term bronchial-associated lymphoid tissue (BALT) lymphoma is equivalent. It has an indolent course, responds well to local or systemic therapy and has a favorable prognosis⁴. It is positive for CD19, CD20, CD22, CD79a, sIg (usually IgM, in 40 % of the cases) and negative for CD5, CD10, CD23. Despite its favorable prognosis, optimal therapy for primary pulmonary NHL has not been established until today, as there are few debated heterogeneous literature data⁵⁻⁷. Many therapeutic options such as observation alone, surgery, radiotherapy, chemotherapy alone or in combination, immunotherapy and/or immunochemotherapy all with similar results, have been reported⁵⁻⁹.

Case description

A case of a 68-year-old male smoker diagnosed with a pulmonary MALT non-Hodgkin lymphoma (NHL) with a durable complete response to rituximab monotherapy is described. The patient, who was suffering from

chronic obstructive lung disease, presented with dyspnea, cough, hemoptysis, and right chest pain. Lower right lung infiltration and pleural effusion were revealed. An open biopsy of the involved lung provided lesions immunohistochemically positive for CD19, CD20, CD22, CD79a, negative for CD5, CD10, and CD23, findings consistent with a marginal zone B-cell lymphoma of MALT type with focal transformation to high grade. The stage at diagnosis was I_{EA}. Computed tomography (CT) scan revealed no other sites of involvement and bone marrow biopsy was negative for infiltration. Extranodal primary marginal zone B-cell pulmonary lymphoma was diagnosed since no other sites of involvement were found. His laboratory diagnostic workout included hematocrit: 38.5 %, hemoglobin: 12.8 gr/dl, white blood cells: 8.1 x10⁹/μl with normal differential, platelets 234 x10⁹/μl, lactate dehydrogenase: 300 IU/l [normal range (NR): 280-480], β₂-microglobulin: 5.45 mg/l (NR: 1.42-3.21) and a small IgM paraprotein: 565 mg/dl (NR: 75-350).

The patient received one course of rituximab (375 mg/m²), dose-intensified cyclophosphamide (1,200 mg/m²), dose-intensified doxorubicin (60 mg/m²), vincristine (2 mg), and prednisone (100 mg x 5 days) (R-CHOP) three months after his diagnosis in another institution. Ten days later, while he was neutropenic, he developed

a severe lung infection with bilateral lung infiltration, and he was admitted to our institution. He recovered after six weeks of hospitalization, and at that time a lower right lung infiltration remained in the chest CT (Figure 1A). The patient refused to continue with R-CHOP, but accepted rituximab monotherapy (375 mg/m²) weekly, (six courses), starting almost five months after the initial diagnosis. He tolerated rituximab uneventfully, and re-evaluation after treatment completion showed clinical improvement and complete remission (CR) (chest CT - Figure 1B). He continued with maintenance treatment, rituximab 375 mg/m² every three months for two years. He is off treatment for the last ten years and remains in good performance status and CR.

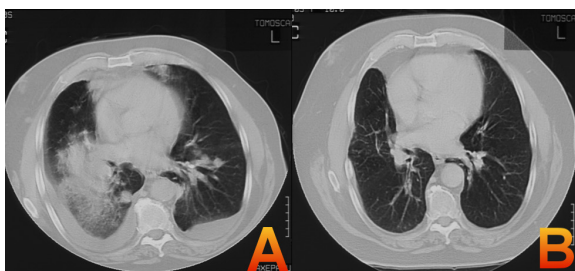


Figure 1: Axial sections of the computed tomography scan of the chest of the patient showing A) lower right lung infiltration and pleural effusion, and B) Clinical improvement and complete remission after rituximab monotherapy.

Discussion

The optimal treatment approach for BALT lymphoma has not been established, due to the rarity of this type of lymphoma and lack of randomized studies. Several therapeutic options such as surgery, radiotherapy, intensive chemotherapy, immunotherapy and/or immunochemotherapy all with similar results, have been reported. Observation only, even though appealing as an approach in low-risk patients, does not guarantee the stability of the disease.

All the above mentioned therapeutic choices and their combinations have been evaluated in the few published series with heterogeneous results. Controversy still exists. Our clinical experience indicates that surgery, radiotherapy or intensive chemotherapy are excessive options with unnecessary risks for this malignancy.

In the reported case, the disease was symptomatic, so observation alone could not be applied. Importantly, the prolonged exposure to rituximab, which included not just six cycles of monotherapy, but also a maintenance phase every three months for two years, may have resulted in the durable CR and the favorable outcome. Interestingly, the high-grade component of the histology of the MALT lymphoma has not affected the prognosis of the disease. A high-grade component may not confer poor prognosis in MALT lymphomas and could be treated with lower-intensity immunochemotherapy, based on the analysis of nine cases¹⁰.

In their retrospective study, Okamura et al also sug-

gest that rituximab monotherapy is the first-line treatment for primary BALT lymphoma¹¹. In the Japanese study, only one male patient was diagnosed at the age of 67, close to our case. The progression-free survival (PFS) of our patient is 144 months, much larger than the reported median PFS of 66 months, even larger than the upper limit range of 87.2 months¹¹. Differences in our patient are the pretreatment with R-CHOP (one cycle), while no patient received pretreatment in the published series and the application of six cycles of rituximab monotherapy, whereas eight cycles were given in the majority of the reported cases¹¹. We also used maintenance treatment (rituximab monotherapy) for two years, even though it is not clear if it should be applied and for how long. No such therapy was reported in the published series.

Kalpadakis et al have described 76 non-gastric extranodal marginal zone lymphoma cases from a single center and found that ten patients with BALT lymphoma had the worst prognosis, with a 5- and 10-year overall survival (OS) of 83 % and 63 %, respectively, vs 96 % and 88 % for non-lung localization (p = 0.05). Treatment was heterogeneous and included chlorambucil either alone or in combination with other agents¹².

Fludarabine and mitoxantrone-containing regimens have been proposed as the first-line treatment for BALT lymphoma in an Italian retrospective study¹³, while the combination of rituximab with bendamustine may provide a highly effective option, as recently suggested by Salar et al¹⁴. Moreover, the option of administering low-intensity chemotherapy [chlorambucil or Cyclophosphamide - Vincristine - Prednisone (CVP)] alone or in combination with rituximab monotherapy is probably another viable option for BALT lymphoma. The combination of rituximab with chlorambucil is supported by a recent randomized trial¹⁵. The same randomized trial, the IELSG-19, suggested that rituximab monotherapy is similarly effective to chlorambucil monotherapy in terms of PFS and remission duration, although both are inferior to the combination of rituximab with chlorambucil. However, OS was virtually the same in the 3 arms¹⁵.

However, we support the therapeutic application of rituximab monotherapy as an attractive option for this malignancy. In agreement with Okamura et al¹¹ and the IELSG-19 randomized trial¹⁵, we conclude that rituximab monotherapy is a viable first-line therapy for patients with pulmonary MALT lymphoma, because this effective approach exhibits significant antitumor activity leading to long-term CR and minimal hematological toxicity in contrast to other intensive chemotherapies and/or radiotherapy, which might have serious side effects. Larger prospective studies are necessary in order to confirm the aforementioned results.

Conflict of interest

The authors report that they have no conflict of interest.

Acknowledgment

Informed consent was obtained from the patient.

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