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Rituximab as immunotherapy following autologous stem cell transplantation (ASCT) in a 17-year-old boy with diffuse large B cell lymphoma - a case report

Agnieszka Zaucha-Prażmo[1], Jolanta Stefaniak[1], Agnieszka Brodzisz[2], Beata Wójcik[1], Katarzyna Drabko[1], Marta Chroma[1], Jerzy R. Kowalczyk[1]

[1]Department of Paediatric Oncology and Haematology, Medical University, ul. Chodźki 2, 20-093 Lublin, Poland, [2]Department of Paediatric Radiology, Medical University, ul. Chodźki 2, 20-093 Lublin, Poland

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Summary

Rituximab is a human-mouse chimeric monoclonal antibody with specifity for the CD20 antigen expressed on B-lineage cells.

We are reporting a 17-year old boy diagnosed with diffuse large B cell lymphoma, CD20(+). He was treated by standard chemotherapy and megachemotherapy with ASCT. The boy relapsed in the mediastinum and lungs one year after the treatment was completed. He underwent secondary treatment: surgical procedure, chemotherapy and immunotherapy with rituximab, second ASCT and again immunotherapy in the post-transplantation period. No severe complications during the treatment with rituximab were observed except for leukopenia and central venous catheter infection.

The CT scans performed one year after the therapy was completed showed regression of changes previously observed.

Słowa kluczowe: rituximab, stem cell transplantation, B cell lymphoma.

Immunochemioterapia z zastosowaniem Rituximabu po przeszczepie autologicznym (ASCT) u 17-letniego pacjenta z rozpoznaniem chłoniaka - opis przypadku

Streszczenie

Rituximab (Mabthera) jest ludzko-mysim przeciwciałem monoklonalnym skierowanym wybiórczo przeciwko antygenowi błonowemu CD20 limfocytów B. Potwierdzona jest jego skuteczność w leczeniu agresywnych chłoniaków nieziarniczych u dorosłych razem z konwencjonalną chemioterapią oraz w połączeniu z megachemioterapią i autoHSCT, również jako terapia podtrzymująca remisję.

Przedstawiamy przypadek 17-letniego chłopca ze wznową chłoniaka olbrzymiokomórkowego śródpiersia rozpoznaną rok po zakończeniu leczenia konwencjonalną chemioterapią i megachemioterapią z auto PBSCT. Wznowę chłoniaka stwierdzono w śródpiersiu i płucach. Po operacyjnym usunięciu guza śródpiersia i mnogich przerzutów w płucach przeprowadzono chemioterapię (IVAC) z immunoterapią (Rituximab), planując kolejną megachemioterapię z autoPBSCT. Po przeprowadzeniu megachemioterapii i auto PBSCT zdecydowano się na immunoterapię Mabthera (4 cykle co 4 tygodnie, dawka jednorazowa 375mg/m^2). Przebieg immunoterapi bez powikłań, z odchyleń w badaniach dodatkowych stwierdzaliśmy jedynie leukopenię, dwukrotnie będącą przyczyną wydłużenia odstępu między kolejnymi dawkami leku.

Aktualnie chłopiec jest rok po zakończeniu immunoterapii, w remisji choroby zasadniczej.

Key words: rituximab, przeszczepienie komórek macierzystych, chłoniak B-komórkowy.

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Introduction

Rituximab (MabThera) is a human-mouse chimeric monoclonal antibody with specifity for the CD20 antigen expressed on B-lineage cells [1,2]. Its mechanism of action differs from other antineoplastic agents. CD20 antigen is expressed on more than 95% of B-cell NHL, but is not expressed on stem cells or plasma cells. Cell lines not expressing the CD20 antigen are unaffected by rituximab. The antibody destroys CD20-expressing cells mainly by cytotoxicity: complement-dependent cytotoxicity, antibody-dependent cell-mediated cytotoxicity and induction of apoptosis [1]. Clinical trials in adults treated for CD20+ NHL demonstrated the efficacy and safety of rituximab, both as a single-agent and in combination with chemotherapy [3,4,5].

Case report

We report a 17-year-old boy diagnosed with diffuse large B cell lymphoma localised in the mediastinum. At the time of diagnosis a large mediastinal mass and superior caval vein syndrome were observed. Immunophenotype of malignant cells was: CD20 (+), CD3 (-), CD30 (+), ALK (-), HLADR (+), CD43 (-), CK (-). CT scans showed a large mediastinal mass and enlargement of cervical nodes *(Figure 1)*. The first line chemotherapy was given according to the B-NHL-LBM 89 protocol, therapeutic group C. After completion of standard chemotherapy and achievement of complete remission, high-dose chemotherapy was given (BEAM) followed by autologous stem cells transplantation. CT scans confirmed regression of changes previously observed *(Figure 2)*.

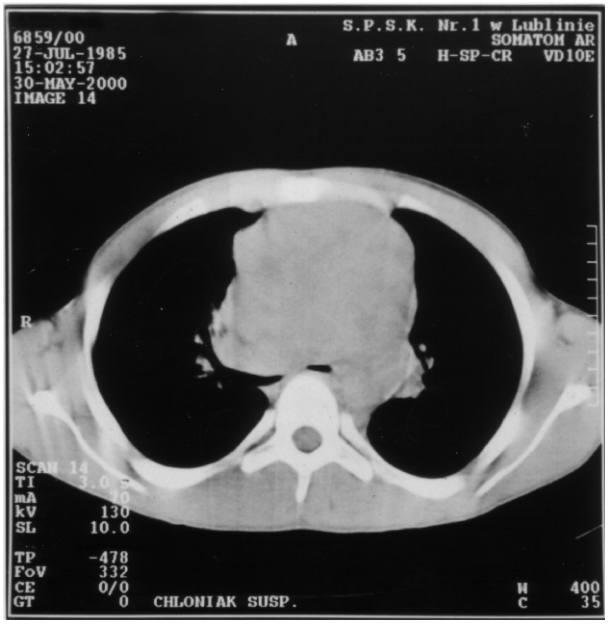

Figure 1. CT scans at the diagnosis with large mediastinal mass.

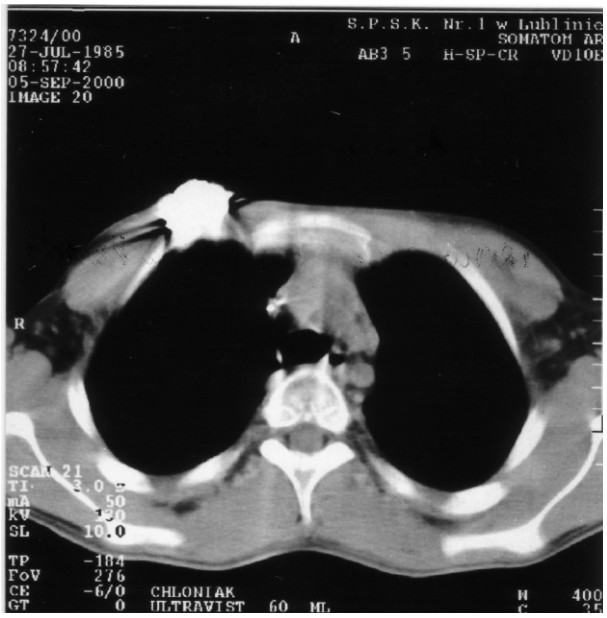

Figure 2. Complete remission.

The boy relapsed in the mediastinum and lungs one year after completion of primary treatment. Immunophenotype of malignant cells at the relapse was the same as that at the first diagnosis: CD20 (+), CD3 (-), CD30 (+), ALK (-), HLADR (+), CD43 (-), CK (-). CT scans showed a large mediastinal mass with multiple pulmonary metastases *(Figure 3)*. Treatment of the relapse was started. The first surgical procedure extirpation of the anterior mediastinal tumour and pulmonary metastases was performed to reduce the tumour mass. Only partial resection was possible. Afterwards

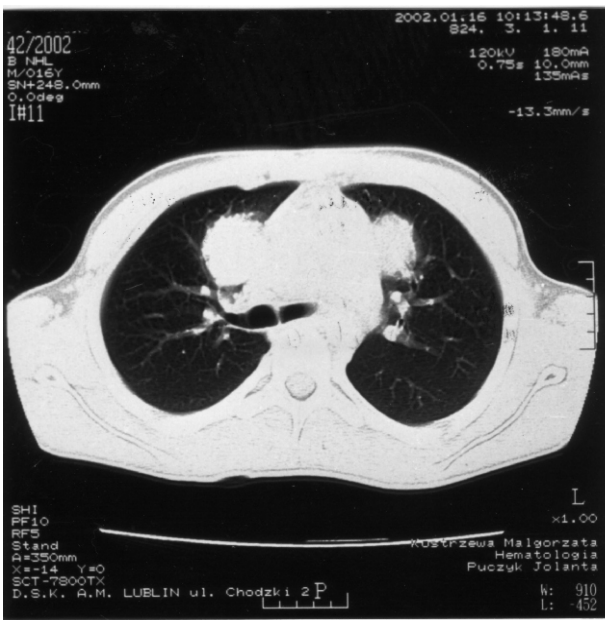

Figure 3. Relapse. CT scans show large mediastinal mass with multiple pulmonary metastases.

chemotherapy (IVAC) with immunotherapy (rituximab) was started (four cycles every four weeks with a single dose of 375 mg/m^2), followed by high dose chemotherapy (Treosulfan + Fludara) with second autologous stem cells transplantation. Cells used for the second transplantation were harvested during the first line therapy. Immunotherapy with rituximab was continued after the recovery of hematopoesis. From week 8, following ASCT, four doses of rituximab (375 mg/m^2) every 4 – 8 weeks were given. CT scans performed before the second transplantation showed partial regression of mediastinal and pleuropulmonary changes seen on previous CT scans *(Figure 4)*. During the treatment with rituximab no severe complications were observed. The consecutive dose of rituximab was delayed due to neutropenia. After the second rituximab course central venous catheter had to be removed because of its infection.

The patient completed the treatment and currently is being followed for 12 months. Last CT scans showed regression of changes previously observed *(Figure 5*).

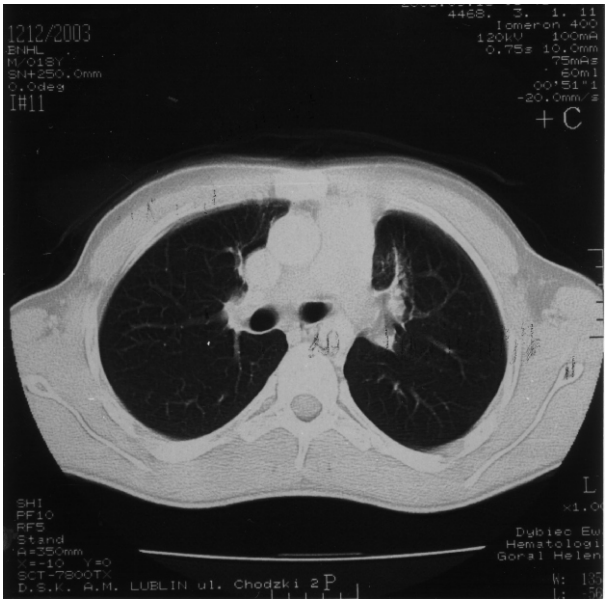

Figure 4. CT scans show partial regression of mediastinal and pleuropulmonary changes.

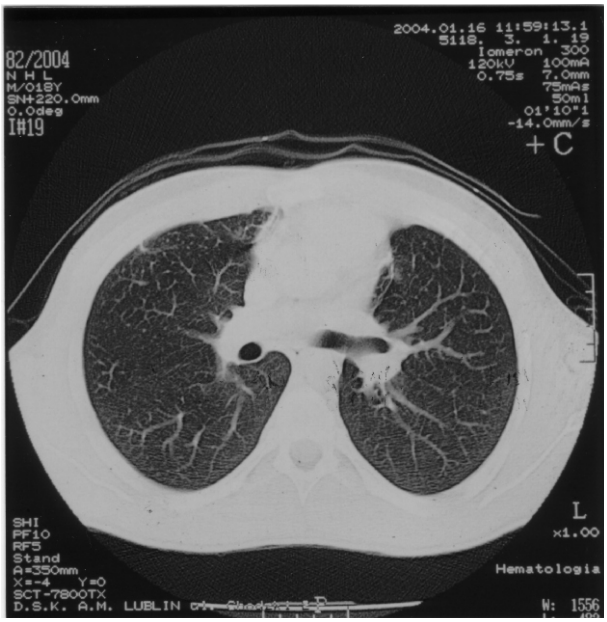

Figure 5. Regression of changes previously observed.

Discussion

Myeloablative chemotherapy combined with autologous stem cell transplantation (ASCT) is an effective treatment for aggressive non-Hodgkin's lymphoma (NHL). However the rate of relapse following transplantation remains a clinical problem despite advances in therapy [6,7]. Pan et al. [8] reports that rituximab is an effective and well tolerated treatment for aggressive NHL relapsing after or refractory to autologous stem cell transplantation. Bucstein et.al. [9] show good response to rituximab in patients with relapsed follicular or mantle cell lymphoma who previously had high-dose chemotherapy followed by ASCT. In their study, patients received rituximab before stem cell collection as *in vivo* purging in addition to eight maintenance infusions of rituximab after ASCT. Relapses after HSCT are due either to persistence of residual tumour cells after high-dose chemotherapy or to contamination of the stem cell product. Many studies have confirmed that *in vivo* purging using rituximab can reduce the rate of relapses following ASCT [9,10,11].

The efficacy and tolerability of rituximab have been confirmed in many studies, and relapsed patients in the post-transplant period can safely be retreated with rituximab [3,4,5]. In our case no severe complications were observed during the postransplantation treatment with rituximab except for leukopenia without severe infections.

Rituximab can be effective in a variety of settings. It can be used alone or in combination with chemotherapy in the first line treatment of CD20+ NHL, before stem cell collection as in vivo purging, or as a maintenance treatment following ASCT. It also appears to be an efficient and safe form of therapy in B-lymhoproliferative post-transplant disorders, e.g. severe complications following organ and bone marrow transplantation [12].

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