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Antibodies to biotherapeutic drugs as one of the possible mechanisms for reducing the effectiveness of targeted therapy

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Introduction.

Monoclonal antibodies have become mandatory for neoplastic targeted therapies as well as chronic inflammatory and autoimmune diseases. Rituximab is a chimeric monoclonal antibody directed against CD20 antigen that is expressed on normal and malignant human B cells [1,2]. It was the first monoclonal antibody to be approved for therapeutic use [2]. Treatment with rituximab at standard weekly dosing is effective in more than 50% of patients with relapsed or refractory CD20-positive follicular non-Hodgkin's lymphoma, but is not curative. It is less effective in other subtypes of CD20-positive lymphoma and for retreatment, even with CD20 still expressed [3]. Thus, binding of rituximab to CD20 is not sufficient to kill many lymphoma cells, indicating that there are mechanisms of resistance.

Many observations show that antibodies to rituximab are generated in some patients during rituximab treatment and may be associated with a less favourable response to treatment. [4-7]. However, antibodies that bind a drug are sometimes found in pre-treatment serum samples, with the amount depending on drug, assay, and patient population. The accurate prediction and assessment of (clinically relevant) immunogenicity remains a challenging endeavor [4].

Purpose of the study - to determine the incidence of anti-rituximab antibodies (ARA) in patients with chronic lymphocytic leukemia (CLL) treated by rituximab.

Materials and methods.

The study involved 32 patients with nHL (11 newly diagnosed, 21 - resistant / recurrent form), aged from 36 to 70 years (average age 49,5 years), of which 18 women and 14 men and 13 practically healthy individuals, matched by age and sex.

In 55% of patients, stage 2 of the disease was detected, in 45% of patients - stages 3 and 4. Patients with refractory / relapsing forms have previously received 4-6 courses of R-FC therapy. Determination of anti-rituximab antibodies in peripheral blood serum was performed by enzyme-linked immunoassay using a test system manufactured by Bender Medsystems (Austria) (semi-quantitative analysis).

Results.

None of the patients with newly diagnosed disease have ARA. Positive results were recorded in 7 (33%) patients who received rituximab earlier. Of particular note is a patient with a very high antibody level (74,7 c.u.) who received 6 courses of combination therapy and showed pronounced progression of the disease. At the same, in the group of practically healthy persons, positive results were obtained in 2 (15,4%) cases, in particular, with a procedural nurse who regularly contacts the drug.

Conclusion.

ARA have been found in patients with lymphoproliferation and other diagnoses but the data on clinical implications of the development of these antibodies are limited. The data obtained in this study demonstrated that they are revealed in 33% of patients with resistant forms of the disease treated by rituximab. Besides, pre-existing anti-rituximab antibodies were detected in several serum samples in control group. Of course, it should be borne in mind that the effect of ARA on the therapeutic efficacy of the drug can be different: it could be targeting predominantly the idiotype and thus clinically relevant, or due to pre-dose

antibodies that can bind the therapeutic antibody, but are often irrelevant. If we suppose that immunogenicity is an important factor that should be considered in the overall treatment strategy, we should take actions to reduce antidrug antibodies formation: modifying drug administration; increasing dose; decreasing immunogenicity by adding immunosuppressive agents to the regimen or using new drugs which are supposed to be less immunogenic such as humanized or fully human monoclonal antibodies.

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Evaluation of influencing factors (age, sex, number of teeth, type and quality of teeth) on the development of dry socket (alveolar osteitis) after tooth pull (clinical study)

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Abstract

A dry socket (alveolar osteitis) is a painful dental condition that sometimes happens after you have a permanent adult tooth pulled. Dry socket is the most common complication following tooth pull, such as the removal of third molars (wisdom teeth). Over-the-counter medications alone won't be enough to treat dry socket pain. Your dentist or oral surgeon can offer treatments to relieve your pain. In this study, we investigated the influential factors (age, sex, number of teeth, type, and quality of teeth) on the formation of the dry socket after tooth pull (as a clinical study) and analyzed each of the factors. This research was conducted in the Russian federation in 2018-2020 as a case study.

Keywords: Dry socket, dentistry, alveolar osteitis, case study.

1. Introduction

A dry socket (alveolar osteitis) may be a painful inflammation that will develop within the jawbone's open tooth socket after a tooth has been removed [1]. Dry sockets often develop after pull and are more common after pull of the third molars, or wisdom teeth removal. (Fig.1 and 2).