INTRODUCTION

Gemtuzumab ozogamicin is a chemotherapeutic agent containing a recombinant humanized IgG4κ antibody conjugated with a cytotoxic anti-tumour antibiotic calicheamicin that is isolated by fermenting the bacterium Micromonospora echinospora sub-sp. calichensis.¹ The antibody portion of gemtuzumab ozogamicin binds specifically to the CD33 antigen, a sialic acid-dependent adhesion protein found on the surface of leukaemic blasts and immature normal cells of myelomonocytic lineage but not on normal haematopoietic stem cells. Gemtuzumab ozogamicin injection contains amino acid sequences, of which approximately 98.3% are of human origin. The constant region and framework regions contain human sequences, while the complementarity determining regions are derived from a murine antibody that binds CD33.² This antibody is linked to N-acetyl-γ calicheamicin via a bifunctional linker. Gemtuzumab ozogamicin contains approximately 50% of the antibody loaded with 4-6 moles of calicheamicin per mole of antibody. The remaining 50% of the antibody is not linked to the calicheamicin derivative. A new complication related to its use is described hereby.

CASE REPORT

We report the case of a 22-year-old Saudi male patient who was treated extensively in the past with various regimens for acute promyelocytic leukaemia that was refractory to all standard treatments. He was ultimately administered Gemtuzumab to induce remission and subjected to an allogeneic bone marrow transplant. However, he developed orchitis, which has not been previously reported with this agent.

Key words: Promyelocytic leukaemia. Gemtuzumab. Orchitis.

DISCUSSION

Over the last 25 years, general prognosis of APL has changed from a disease that was fatal for a majority of patients to one of the most curable sub-types of acute myeloid leukaemia. Improvements in supportive care have also been achieved through the introduction of novel targeted therapies.³ APL is characterized by a specific chromosome translocation t(15:17) that results in the formation of the promyelocytic leukaemia-retinoic acid receptor-α (PML-RARA) fusion gene and by the terminal differentiation of leukaemic promyelocytes after ATRA treatment. Arsenic trioxide has recently been identified as an alternative therapeutic agent for APL,⁴ ATRA and arsenic trioxide, which are the major molecularly targeted therapeutic agents for APL, affect
or degrade the PML-RARA fusion protein and cause APL cell differentiation and apoptosis. Gemtuzumab ozogamicin is a calicheamicin-conjugated monoclonal antibody directed against CD33, a cell-surface antigen that is highly expressed on APL cells. Engagement of CD33 by this monoclonal antibody results in the internalization of the immunoconjugate and hydrolytic release of calicheamicin, which in turn causes irreversible DNA damage and cell death. A number of preliminary reports have highlighted the sensitivity of APL to gemtuzumab administered alone or with other agents. The high efficacy of gemtuzumab against APL may be because of several reasons, including the fact that CD33 is detectable in almost 100% APL cases.5 Studies have shown sustained molecular remission after low-dose gemtuzumab ozogamicin therapy in elderly patients with advanced APL, especially in those who were not candidates for high-dose chemotherapy.

In the transplant setting, there are reports of successful mobilization of peripheral blood stem cells in APL patients after gemtuzumab ozogamicin therapy.6 Gemtuzumab has shown good efficacy in the treatment of relapsed or refractory APL. In some studies, combination therapy with arsenic trioxide, ATRA and gemtuzumab ozogamicin has resulted in prolonged remission in patients with recurrent APL.7 A combination of ATRA and gemtuzumab ozogamicin was used successfully in elderly patients with APL and severe cardiac failure, and this combination resulted in good overall survival of patients who were at a high risk with standard combination chemotherapy.8,9 The use of gemtuzumab has been associated with various adverse effects in the past because of its targeted action and prolonged myelosuppression; however, there are no published reports of gemtuzumab-induced orchitis.

REFERENCES


