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Prostate Monomorphic PTLD After Stem Cell Transplantation for Plasma Cell Myeloma: A Case Report

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ABSTRACT

PTLD (Post-transplant lymphoproliferative disorder) are lymphoid or plasmacytic proliferations that develop as a consequence of immunosuppression in a recipient of a solid organ or stem cell allograft. Involvement of lymph node, gastrointestinal tract, lungs and liver is common, but disease can occur at almost any site of the body. In this case report we present an Epstein-Barr virus (EBV) with PTLD manifesting in the prostate after hematopoietic stem cell transplantation (HSCT) to treat plasma cell myeloma.

Keywords: *PTLD, Prostate, HSCT, Myeloma*

Introduction

PTLD is a rare life-threatening lymphoproliferative disorder, generally associated with Epstein-Barr virus (EBV) infection (LaCasce, 2006). EBV tends to infect B-lymphocytes and, whereas it usually is asymptomatic among immunocompetent patients, it can cause serious viremia, followed by EBV-positive polyclonal or monoclonal PTLD among immunocompromised patients, secondary to a lack of activation of cytotoxic T lymphocytes (CTL), especially after HSCT (Ru *et al*., 2018; Jagadeesh *et al*., 2012). The overall incidence is about 1-2% (Bhatia *et al*., 1996), with the highest incidence during the first year after the transplantation. PTLD following allogeneic HSCT generally involves lymph nodes and extranodal sites like the gastrointestinal tract, lungs and liver and can cause a multiorgan involvement (Cockfield, 2001). In hematopoetic stem cell recipients, the majority of PTLD occurs less than one year after transplantation and the risk factors include HLA-mismatch between the donor and the recipient, the use of strong immunosuppressive agents after the transplantation (e.g. anti-lymphocyte antibodies such as anti-

thymocyte globulin, ATG), T-cell depleted donor marrow transplantation and infection with cytomegalovirus (CMV) (Cockfield, 2001). The clinical presentation as well the morphological type of PTLD (early lesions, polymorphic, monomorphic, classical Hodgkin lymphoma) can be highly variable. Whereas early lesions of PTLD regress with reduction of immunosuppression, monomorphic lesions which fulfill the criteria for a lymphoma and some polymorphic lesions usually fail to regress and need further treatment with an anti-CD20 monoclonal antibody therapy (Rituximab) and/or chemotherapy (Al Hamed *et al*., 2020).

Rituximab represents the first treatment choice to prevent PTLD (Abbas *et al*., 2020), especially among high-risk patients, who can be monitored by measuring levels of EBV viral load in the blood (Coppoletta *et al*., 2011).

Case Report

We report on a 63-year old male patient with plasma cell myeloma IgG kappa (Stadium III A Salmon/Durie) with high risk cytogenetics (17p deletion) and a translocation t (11;14); (q13;q32), who underwent allogeneic stem cell transplantation (allo-SCT) from his HLA-identical sister in July 2017 following high dose melphalan therapy and autologous stem cell support. ATG, cyclosporine A (CyA) and mycophenolate mofetil (MMF) were used as prophylactic immunosuppressive medication, no significant complications occurred during the in-patient period. In terms of the plasma cell myeloma, sustained complete remission could be confirmed via multiple bone marrow biopsies after allo-SCT.

In the further course, the patient experienced a Graft-versus-Host disease (GvHD) grade 2, mainly located in the upper intestinal tract and in the skin, initially responding to steroid therapy. Moreover, he developed a CMV reactivation, which was treated successfully with valganciclovir. EBV reactivation occurred 4 weeks post-allo-SCT and five cycles of Rituximab were administered leading to full clearance of the EBV load in the peripheral blood, a minor amount of EBV was still detectable in the PCR though in a later performed follow-up bone marrow biopsy.

In the further outpatient setting, 12 months after the allo-SCT, the patient complained about dysuria, urinary retention and pain in the perineal region, which was attributed to the already known benign prostatic hyperplasia. After consulting the urologist, a transrectal ultrasonography (TRUS) confirmed an enlargement of the prostate as well as the presence of a hypoechogenic area. The prostate-specific antigen (PSA) level was elevated with 14,9 ng/mL.

For these reasons, a prostatitis was suspected and the patient was treated with a broad-spectrum antibiotic therapy (Piperacillin/Tazobactam). Despite the antibiotic therapy and escalation to carbapeneme treatment, the patient did not show any clinical or sonographic improvement. To further characterize the nature of the mass, magnetic resonance imaging (MR) was performed (Fig. 1 a,b), showing a mass lesion in the prostate which was suggestive of an abscess or prostate cancer, with no lymph node swelling or other suspect findings. TRUS-guided biopsies were performed and send for histopathological evaluation.

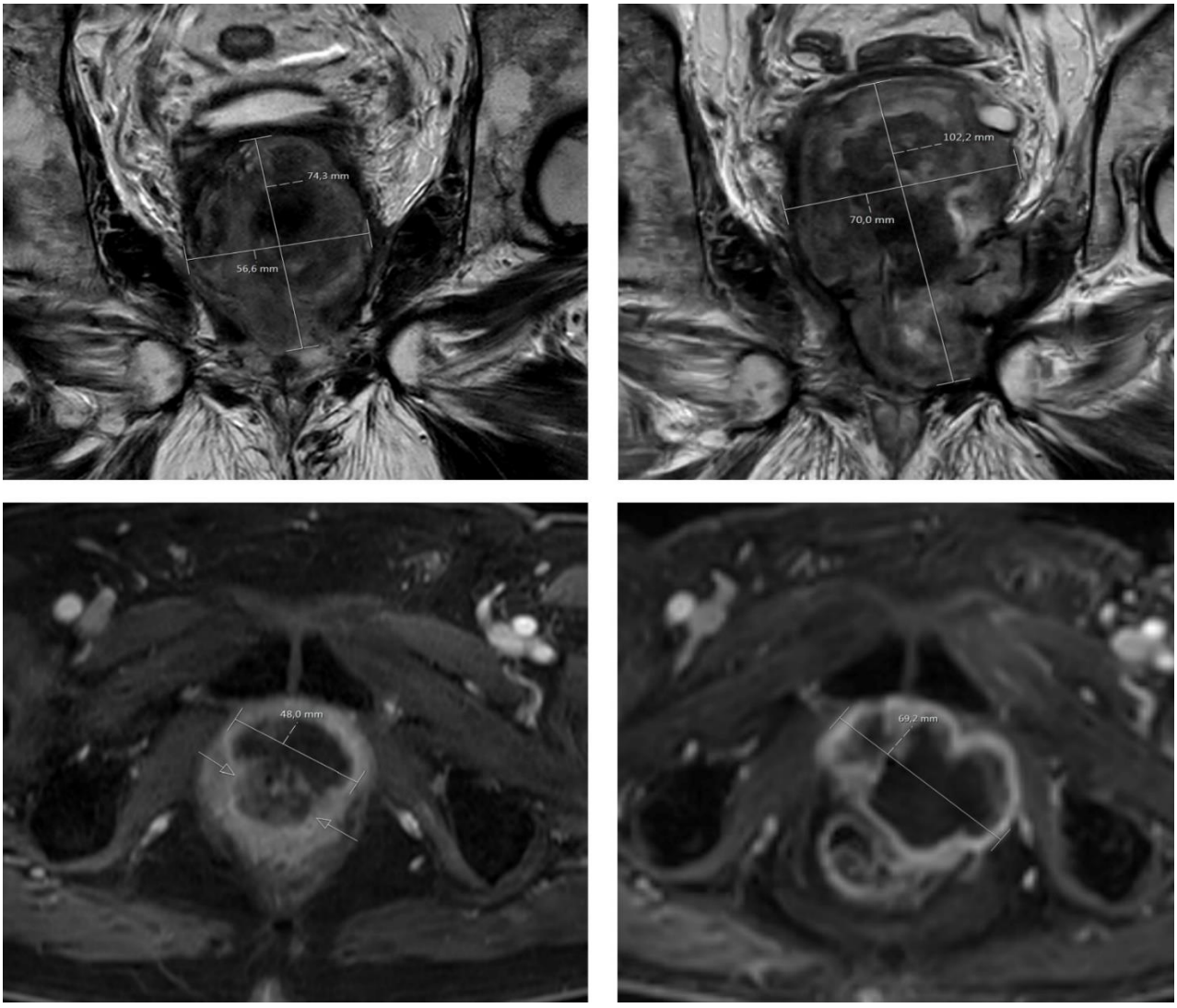

Figure 1: Magnetic resonance imaging findings of the prostate mass (A, B) coronal T2-weighted images showing a prostate mass before (A; 56,6 x 74,3 mm) and after two cycles of chemotherapy (B; 70 x 102,2 mm). (C, D) axial T1-weighted FS images after Gd-DTPA administration showing the prostate mass before (C; 48 mm) and after the treatment (D 62,2 mm).

The histopathological examination revealed prostate biopsies with widespread necrosis and a proliferation of blasts arranged mainly around blood vessels with some diffuse areas and some

plasmacytic differentiation (Fig. 2 a). The blasts were pleomorphic with often prominent central nucleoli and sometimes centroblastic morphology. In immunohistochemistry the blasts were positive for CD79a, Mum1, kappa light chain and CD30 and only very faint staining for CD20 and CD138 in some cells. The proliferation rate was >90%. EBV- in situ hybridization revealed EBV-positivity of the blasts. Cyclin D1 immunohistochemistry was negative in the blasts and the plasmacytic differentiated cells and no translocation t(11;14) (q13;q32) could be detected by FISH. In the bioptic sample a high EBV load was found as well (3,4 x 105 Geq/105). Thus, the diagnosis of an EBV positive monomorphic B-cell PTLD with plasmablastic/plasmacytic differentiation was made.

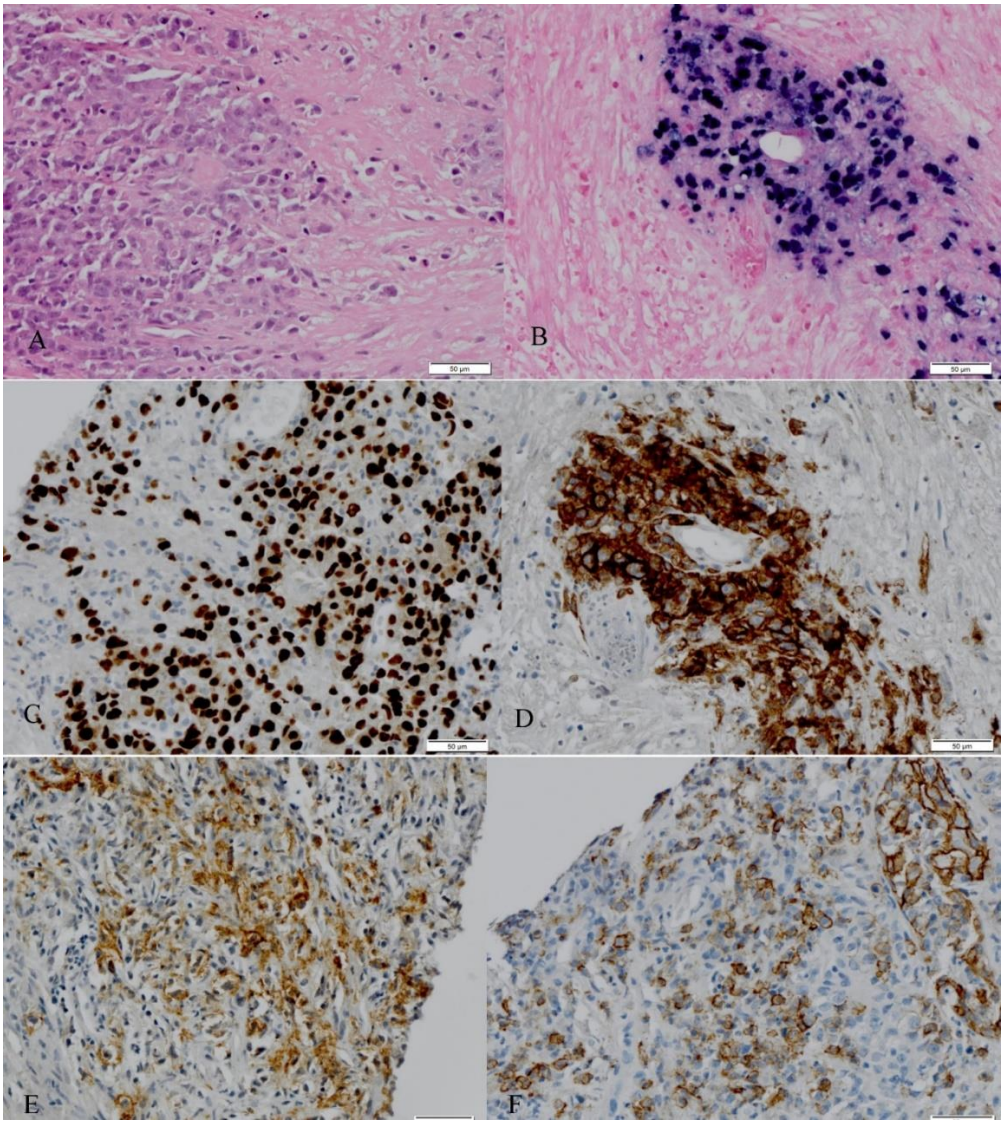

Figure 2: Histopathological examination of the prostate biopsy with hematoxylin and eosin staining (A). There is a widespread necrosis and a proliferation of blasts arranged mainly around blood vessels with some diffuse areas and some plasmacytic differentiation. The blasts are pleomorphic with often prominent central nucleoli and sometimes centroblastic morphology. EBV- in situ hybridization revealed EBV-positivity of the blasts (B). The immunohistochemistry of the shows positivity for CD79a, Mum1 (C), kappa light chain and CD30 (Fig. D) and only very faint staining for CD20 (E) and CD138 (F) in some cells.

As a result, a chemotherapy regimen based on the R-CHP scheme and Bortezomib was started, but the first MRT-staging after two cycles of chemotherapy and six cycles of Rituximab showed a progressive disease (Fig. 1 c,d), with a 10 x7 cm lobulated mass of the prostate with infiltration of the bladder and compression of the rectum. Therapy was then switched to R-CHOP scheme. In addition, third-party-EBV-specific T cells were administered, but due to relapsing infectious complications which required admission to the intensive care unit (ICU), the therapy could not be continued and the patient passed away 6 months after the diagnosis of prostate PTLD, 18 months after the allo-SCT.

Conclusion

To our best knowledge, this is the first case of an isolated prostate monomorphic PTLD after HSCT. The patient presented some known risk factors for PTLD, such as several transplant complications like GvHD and CMV reactivation and underwent a therapy with ATG. So far, it is not known which factors trigger the distribution of PTLD lesions and the presentation in unusual sites. The diagnosis of PTLD should always be considered in patients after organ or hematopoetic transplantation who are presenting with new lesions, even in atypical localizations.

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