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LETTER TO THE EDITORS

Elimination of norovirus in a chronic carrier under immunosuppression after heart transplantation – effect of everolimus

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Dear Sirs,

Immunosuppression is a valuable tool to enable transplantation of solid organs, but it is also strongly connected to infectious problems. Susceptibility to bacterial and viral infections, amongst others norovirus, is significantly higher under immunosuppression. Norovirus can be life-threatening in patients after heart-transplantation and is difficult to treat, particularly in chronic carriers. We would like to present the case of a 24-year-old woman who was first admitted to our department in December 2008, when severe postpartal cardiomyopathy was diagnosed. EF was 19% with dyspnoea at rest post partum of her first child, before pregnancy capacity was not restricted at all. Apart from a heparin-induced thrombocytopenia type II, there were no relevant pre-existing diseases. At the end of January 2009, an LVAD had to be implanted as bridging to transplant, and there were no signs of recovery of LV-function under full CHF-medication. The patient was discharged during mid of April 2009 and lived at home until she underwent heterotopic heart-transplantation in April 2010. FK506, mycophenolic acid and prednisolone was used as immunosuppression. At the end of December 2010, the patient suffered from an acute norovirus infection with diarrhoea, vomiting and severe weight loss (from 64 to 54 kg). Norovirus was confirmed using qualitative PCR. During the following weeks, the patient continuously suffered from recurrent diarrhoea, and PCR for norovirus was continuously positive, and thus she was chronic carrier for norovirus. At the end of February 2011, immunosuppression was switched to Everolimus + mycophenolic acid + prednisolone because of significant decrease of renal function (reduction of glomerular filtration rate from >60 to minimal 20 ml/min/1.73 m^2). Under this immunosuppressant regime, diarrhoea stopped. Eight weeks after switching of to Everolimus, PCR for norovirus became negative in several consecutive measurements. Renal function significantly improved within few weeks. Everolimus was well tolerated by the patient. Finally, the mechanism of this action remains unclear and we can only speculate. It is well documented that there is a significant lower rate of cytomegalovirus-infections under everolimus and other proliferation signal inhibitors [1–3]. It has also been shown that this is not because of a direct effect of PSI on viral replication pathways, as there is no relevant effect of PSI in isolated cell-cultures infected with cytomegalovirus [4]. It is generally accepted that the cytomegalovirus-reducing effect is because of indirect affection of viral amplification by blocking cellular proliferation and impairing the phosphatidylinositol 3-kinase pathway. In our opinion, this is probably also the mechanism leading to elimination of Norovirus in our patient. In addition, attenuation of immunosuppression might have played a role in viral eradiation.

In conclusion, everolimus could – because of this 'pleiotrophic side effect' – be a valuable alternative to 'classical' immunosuppressive drugs in selected patients early after heart-transplantation with chronic viral infectious problems.

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Conflicts of Interest

No conflict of interest.

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