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Letters

TO THE EDITOR

Belatacept as an Emerging Option in Immunosuppression-Induced Thrombotic Microangiopathy After Heart Transplantation

We read with great interest the case series by Massad et al[1] on tacrolimus-induced thrombotic microangiopathy (TMA) in patients after orthotopic heart transplantation. Their report emphasizes that calcineurin inhibitors (CNI), while cornerstone agents in immunosuppression, may precipitate TMA and necessitate alternative regimens.

The investigators correctly highlight mammalian target of rapamycin inhibitors (mTORi) as one of the most commonly used substitutes when CNI-induced TMA develops. However, emerging evidence and our own experience underscore that mTORi are not exempt from this complication. Both sirolimus and everolimus have been linked to de novo or recurrent TMA in solid organ transplant recipients.[2,3] Thus, switching from CNI to mTORi may not eliminate the underlying risk but may merely exchange one potential trigger for another.

This therapeutic dilemma points to the need for novel strategies. One emerging option is belatacept, which works by selectively blocking T-cell costimulation, a necessary second signal for T-cell activation and proliferation, to prevent organ rejection. Initially developed for renal transplantation, belatacept demonstrated improved renal outcomes with comparable rejection rates to CNI-based regimens in the BENEFIT (Belatacept and long-term outcomes in kidney transplantation) trial.[4] Its use in heart transplantation is still limited, but accumulating experience suggests that it can serve as a viable alternative in challenging clinical scenarios, such as patients with immunosuppression-induced TMA, CNI/mTORi intolerance, or CNI-associated renal injury.[5]

In our case, belatacept was successfully introduced after sequential CNI- and mTORi-associated TMA, providing effective rejection prophylaxis without recurrence of TMA (**Figure 1**). Although anecdotal, this observation adds to the growing body of evidence supporting its safety and utility in highly selected heart transplant recipients.

In conclusion, although Massad et al[1] emphasize early recognition and drug withdrawal as cornerstones of managing immunosuppression-induced TMA, we propose that clinicians should also be aware of the potential for mTORi to cause similar complications.[2,3] In this clinical scenario, belatacept may represent a promising alternative in heart transplant recipients who should avoid both CNI and mTORi.

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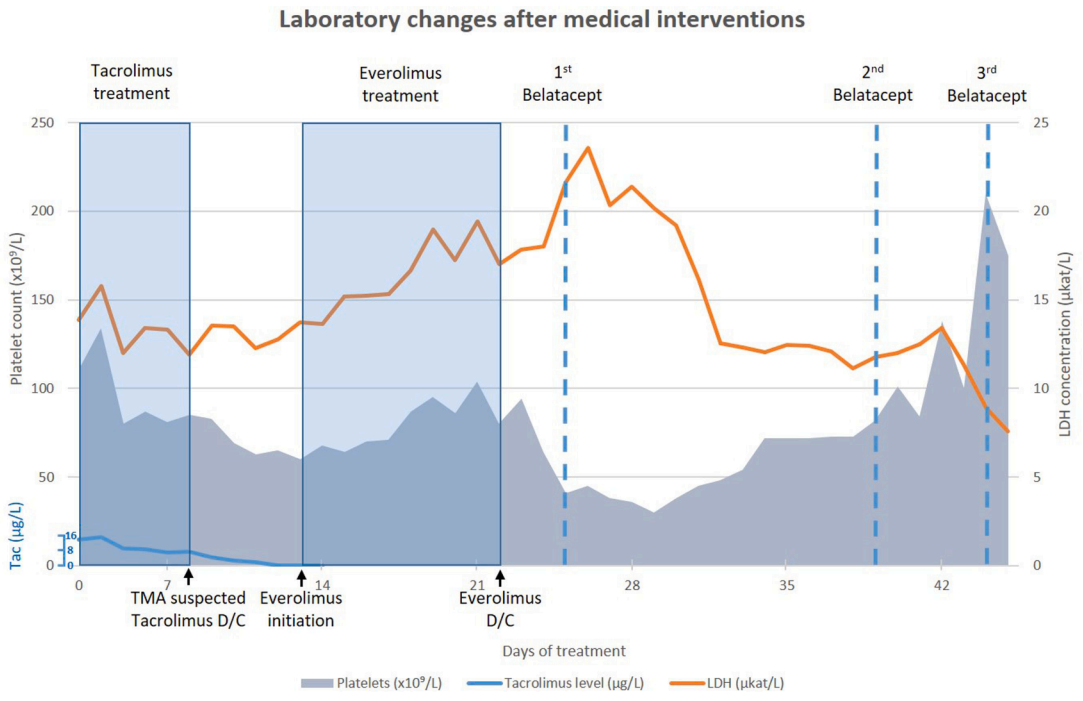
The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

FIGURE 1 **Clinical Course of TMA Under Different Immunosuppressive Treatment Regimens**



D/C = discontinuation; LDH = lactate dehydrogenase; Tac = tacrolimus; TMA = thrombotic microangiopathy.

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