We thank Drs Stöllberger, Schneider, and Finsterer for their interest in our case report on Takotsubo cardiomyopathy in a young adult with transplanted heart. The authors of the letter correctly request some additional clinical information, which could help clarify or, at least, attempt at improving the understanding of the underlying physiopathology possible culprit of the occurrence of Takotsubo cardiomyopathy in our young adult with transplanted heart.

Takotsubo syndrome (also defined as broken heart syndrome or stress-induced cardiomyopathy) is a reversible acute heart failure event that predominantly affects post-menopausal women. As we underline in our case report, this is in contrast to our case in which the event occurs in a young woman. It is worth underlining however that cardiac allograft vasculopathy occurs in >50% of orthotopic heart transplant patients by 10 years, thus providing an ‘ideal substrate’ for the occurrence of Takotsubo syndrome and to help understand how Takotsubo syndrome may affect transplanted patients also at younger ages.

We nonetheless agree that additional details on the heart donor clinical characteristics might provide useful insights. It is worth underlining that the heart transplant was performed approximately 10 years before the occurrence of the Takotsubo event, and thus, given the denervation occurring at time of transplant and the (hypothesized) re-innervation occurring in the first post-transplant years, we believe that age and sex of the donor would be very unlikely to have an effect on the event. Nonetheless, as the question is quite intriguing, we have reviewed the patient’s chart and found that the donor was a 16-year-old boy, who died in a motorcycle accident. Considering that the reported occurrence of Takotsubo syndrome is in overwhelmingly higher in women than in men (90% vs. 10% approximately), the evidence of a male donor reinforces the hypothesis that the Takotsubo event that occurred in our patient might be more strongly related to recipient rather than donor characteristics.

Unfortunately in our case report, recognition of Takotsubo cardiomyopathy was delayed for a couple of days, as the first hypotheses for the patient event were acute myocardial infarction and acute graft rejection. Thus, direct measurements of serum catecholamine levels during the acute phase of the event were not available.

We also recognize that combined immunosuppressive therapy might have contributed to the development of Takotsubo syndrome; however, it should be noted that the patient had not changed her immunosuppressive regimen in the last 2 years prior to the event (cyclosporine 75 mg b.i.d. and everolimus 0.75 mg b.i.d.), and the patient had no cardiovascular medications. Eventually, the temporal occurrence of the event, immediately following an angry debate, strongly supports the hypothesis of stress-induced event. In further support of this hypothesis, the myocardial biopsy performed in the patient apart from presenting no clear signs of rejection reported increases in CD68+ macrophages and few contraction band necrosis, both compatible with a catecholamine-mediated cardiac injury.

In conclusion, despite the fact that no established pathophysiologic mechanism for the occurrence of Takotsubo cardiomyopathy has been established yet, we believe that correlation of Takotsubo with a surge in catecholamines is well evidenced in literature and thus that re-innervation of the graft represents a necessary phenomenon for its occurrence in transplanted heart patients.
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