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LETTER TO THE EDITOR

Takotsubo syndrome during breastfeeding: Further insights into prolactin and its implications

Síndrome de Takotsubo durante a amamentação: mais informações sobre a prolactina e suas implicações

Takotsubo syndrome (TTS) is a multi-faceted phenomenon, particularly in terms of its morphological and pathogenetic characteristics.[1–4] Interestingly, estrogen depletion has been universally suggested for the creation of a predisposing milieu for the evolution of TTS in response to stressful triggers.[1,2,4] The recent report by Brás et al.[1] described an atypical case of TTS evolution in a young female patient while breastfeeding. The authors placed particular emphasis on the protective role of estrogen in the evolution of TTS.[1] We fully agree with the notion that estrogen depletion due to prolactin upsurge during breastfeeding might have significantly facilitated TTS evolution in response to emotional and/or physical triggers in the patient.[1] In other terms, she might possibly have been TTS-free despite the emerging stressful trigger(s) if she had not been breastfeeding her child.[1] We would, therefore, like to comment further on the implications of prolactin in the context of TTS evolution.

In recent years, prolactin, the nursing hormone, which is known to increase substantially during late gestation and in the post-partum period, has been thought to have a potential role in the evolution of certain cardiovascular conditions including peripartum cardiomyopathy (PCMP) and preeclampsia (PE), particularly in women with placental abnormalities (hypoperfusion, etc.) and/or primary or secondary disturbances in anti-oxidant protective mechanisms.[5–7] In this context, enhanced fragmentation of mature 23 kDa prolactin, largely due to overproduction of placental matrix metalloproteinases and/or augmented oxidative stress leading to overexpression of proteolytic enzymes including myocardial cathepsin D, generally results in substantial levels of 16 kDa prolactin fragment. This may exert strong anti-angiogenic and pro-apoptotic effects on cardiovascular system.[5–7]

On the other hand, enhanced oxidative stress, due to various internal or external sources, has been recently suggested as an important contributory factor in the evolution of TTS.[1,8] Based on this notion,[1,8] the pathogenetic mechanisms of oxidative stress in TTS evolution, may, in part, be based on the increased generation of 16 kDa prolactin fragment during periods of physiological (during breastfeeding) or pathological (in case of prolactin-secreting tumors) hyperprolactinemia, particularly in susceptible women (those who are vulnerable to oxidative stress).[5–7,9] Significant levels of 16 kDa prolactin fragment may significantly reduce the threshold for TTS evolution in a similar manner to estrogen deficiency[1,2,9] in response to various stressful triggers. In the context of TTS evolution, the adverse impact of 16 kDa prolactin fragment might be even stronger and more persistent compared with prolactin-related estrogen depletion due to the association of this fragment with apoptosis and impaired angiogenesis[5–7] leading to residual myocardial abnormalities (subclinical myocardial dysfunction, persistent diastolic dysfunction) following TTS recovery.[3,4]

The report by Brás et al.[1] may have important implications: first, the patient may have further TTS recurrences along with an increased risk for PCMP and/or PE evolution, particularly during breastfeeding in future pregnancies. Therefore, the patient may be strongly discouraged from future breastfeeding, including the prophylactic initiation of certain dopaminergic agents including bromocriptine and cabergoline to suppress prolactin secretion may also be considered during puerperium, where necessary.[5] It is noteworthy that even after emergence of overt myocardial disease associated with prolactin (in the form of TTS or PCMP), initiation of anti-prolactin agents, on top of conventional heart failure medications, might significantly speed up myocardial recovery and hence improve the overall prognosis.[5–7] Accordingly, the use of bromocriptine in the patient, possibly based on the presumption of an existing PCMP, may have significantly improved the prognosis of her TTS episode.[1] Second, the patient might have suffered a subclinical form of myocardial dysfunction that might present with exercise intolerance following her discharge.[1,3] This could be diagnosed with advanced echocardiographic parameters including strain and strain rate as well as diastolic stress testing.[3] We wonder about the results of these tests (if any). Finally, the patient might have an increased risk for future cardiovascular events possibly due to the generalized endothelial dysfunction that might be induced by toxic prolactin fragments,[6] and needs close monitoring. We also wonder about the surveillance schedule for the patient.[1]

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In conclusion, prolactin may have important implications in TTS evolution during breastfeeding.[1,2,5–7,9] However, the adverse impact of prolactin in the general context of cardiovascular disease might not be exclusively attributable to estrogen depletion,[1,2] but might also be due to toxic prolactin fragments in susceptible females.[5–7,9] In general, the primary goal should be to combat hyperprolactinemia with the implementation of certain strategies (discouragement from breastfeeding and/or future pregnancies, use of antiprolactin agents during puerperium, etc.) for the prevention or management of prolactin-associated cardiovascular conditions (including TTS associated with breastfeeding and PCMP, etc.).[5–7] However, further aspects related to prolactin in the setting of cardiovascular disease still need to be established.

Conflict of interest

None declared.

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