TAKOTSUBO AS INITIAL MANIFESTATION OF A MITOCHONDRIAL DISORDER DUE TO A SDHB VARIANT

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Introduction

In a recent article Auriau et al. reported a 9yo female who developed Takotsubo-syndrome (TTS) presumably triggered by the presence of a paraganglioma due to a SDHB variant.1 We have the following comments and concerns.

A shortcoming of the report is that it is not mentioned that the patient obviously had a mitochondrial disorder (MID). Mutations in the SDHA, SDHB, SDHC, SDHD, genes and in genes encoding for complex-II assembly factors (SDHAF1, SDHAF2) are well-known not only for being associated with paragangliomas but also with multisystem MIDs.2 Obviously, TTS was the initial manifestation of the MID in the presented patient. However, it would be interesting to know if the patient had previously developed features of a MID. Phenotypic manifestations other than paraganglioma/pheochromocytoma include optic atrophy, polynuropathy, psychiatric disease, and cardiomyopathy.2

In a recently reported patient from India carrying a SDHA variant, myopathy, dilated cardiomyopathy, and pontine lesions on MRI were the dominant phenotypic features.3 In a study of 19 patients with succinate-dehydrogenase deficiency, leucoencephalopathy was the dominant feature.4 Other phenotypic features may be hypotonia, growth retardation, myopathy, organ failure, or metabolic derangement. Other tumours associated with SDHA-D variants include gastro-intestinal stroma tumour, renal-cell carcinoma, or pituitary neoplasm. The penetrance of SDHB variants is higher in males compared to females. Were any first-degree relatives with male gender affected in the patient’s family? Was the patient prospectively investigated for multisystem involvement or did she present with features of a multisystem disease?

Since SDHB variants are usually transmitted in an autosomal recessive mode,5 it would be interesting to know if also the parents of the index case were investigated for the presence of the variant in a heterozygous form. In this context we should be informed if the family history was positive for paragangliomas, TTS, or other clinical manifestations of a MID. Which mutation and which type of mutation was found? Did the mutation occur in the homo- or heterozygous form?

TTS resolves without therapy in the majority of the cases. Which was the rationale to treat TTS with beta-blockers and ACEI? Did the patient develop severe heart failure, or cardiogenic shock? Were there tachycardious arrhythmias or were the catecholamine levels elevated? In this respect we should be informed if blood pressure was ever measured prior to the development of the TTS and if it was ever elevated?

The trigger of TTS in the reported patient remains unclear. Usually, it is endogenous or exogenous stress. Was the history positive for a stressful event or were catecholamine levels extensively high in the index case? The authors conclude that pediatric patients with TTS and an unidentified trigger should undergo determination of the serum catecholamine levels.1 Were catecholamine levels determined during the presence of the TTS in the index patient? Which were the results?

In conclusion, this case could be more meaningful if supplementary information would have been provided about the family history, individual history, genetic findings of the index case and of first-degree relatives, and prospective investigations of the index case for multisystem disease.

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