Genetic Assessments for Clinical Courses of Left Ventricle Noncompaction

64

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Left ventricle noncompaction (LVNC) is a clinically heterogeneous disorder. Although several genetic mutations have been reported, only a little is known about its genotype–phenotype correlation. We report two cases of LVNC with different mutations and different clinical courses for each. Case 1 was a 15-year-old boy with atrial septum defect and pulmonary valve stenosis. He was diagnosed as LVNC when he was 3 years old, but his cardiac function was maintained and no medication was necessary. A 432 kb deletion in chromosome 8p 23.1, including *GATA4*, was found. Case 2 was a boy who was referred to our hospital at the age 6 for apparent right ventricle hypertrophy in electrocardiogram carried out for screening. We recognized severe pulmonary hypertension (PH) and LVNC with attenuated cardiac diastolic function and fair systolic function. In spite of medications for both heart failure and PH, the response was poor. A genetic investigation revealed a point mutation at exon 6 of *TBX20*, c.655-2A>G.

Both *GATA4* and *TBX20* have been reported to cause LVNC, but their clinical courses are not well known. Blinder et al. reported a case with *GATA4* mutation [1], presenting a normal cardiac function. While Wang et al. reported genetic pathogenic variants to be independent risk factors for adverse events [2], there may be some relatively favorable mutations as our case 1 and the report by Blinder et al. *GATA4* is known as one of the earliest-expressed transcriptional factors in cardiac progenitor

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cells, and the expression continues throughout life in cardiomyocytes. It concerns to differentiation of myocardium together with *TBX5*, but how and when it affects myocardium compaction is unknown. In case 2, the severe PH could not be explained only by passive etiology, and pulmonary arterial hypertension also existed. *TBX20* is related to various cardiac disorders including cardiomyopathy, intracardiac septal defects and abnormal valvulogenesis. Although the relation between the *TBX20* mutation and PH was not clear in our case, it is interesting that Edwin et al. reported a familial case of dilated cardiomyopathy (DCM) with *TBX20* mutation with primary PH [3]. Provided that both DCM and LVNC fall in a spectrum of cardiomyopathy, association of PH might be a key to find the function of *TBX20* in these similar cases.

In summary, we report two cases of LVNC, one with *GATA4* deletion and slight symptoms and the other with *TBX20* mutation with severe PH and diastolic dysfunction, which were resistant to treatments.

References

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