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Isolated congenital vertebral anomaly in pathogenic variant of *WBP11*, not a VCTERL syndrome : A case report

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BACKGROUND

- *WBP11* gene encodes a component of the spliceosome activating pre-messenger RNA splicing.
- The *WBP11* is known to be related to VCTERL syndrome.
- VCTERL syndrome has 3 or more clinical features of anomalies of the vertebrae, heart, trachea, esophagus, kidneys, and limbs.
- Herein, we report a boy with an isolated vertebral anomaly, and a Sprengel's deformity not a VCTERL syndrome who was found to have a pathogenic variant of the *WBP11*.

CASE REPORT

- An eight-month-old boy who showed a right 5~10-degree tilted head was referred to our institution from a local clinic. Muscular torticollis was not confirmed on ultrasound, and the vertebral anomaly was suspected on the cervical X-ray imaging study.
- Hence, Three-dimensional (3D) volume-rendered computed tomography (CT) of the cervical spine was performed, revealing the fusion state of the right C2 and C3 facet joints. (**Figure 1**)
- The right shoulder appeared to be raised, and the Sprengel's deformity was observed in a 3D chest CT. (**Figure 2**)
- Echocardiography was performed, and structural and functional problems of the heart were not found.
- In addition, a chromosome study, massive parallel panel sequencing for 185 genes related to skeletal dysplasia and chromosomal microarray tests were performed, and no pathogenic findings were found.
- Furthermore, a whole genome sequencing test was performed, and a *de novo* novel heterozygous pathogenic variant in the *WBP11* was found. The protein was terminated through frameshift (p.Arg508AlafsTer41) due to duplication (NM_016312.3:c.1521dup) at the genomic position 12-14787469-G-GC. It was a pathogenic variant because there were a null frameshift variant in the gene where LOF (loss of function) was a known mechanism of disease and also a *de novo* and novel variant. (PVS1; PS2; PM2, ACMG guideline, 2015)

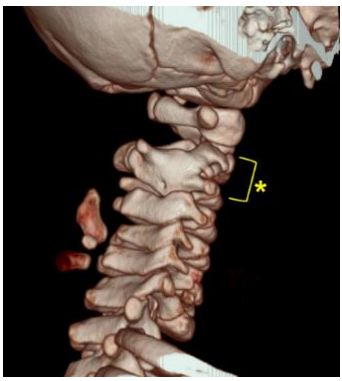

Figure 1.
- Three dimensional computed tomography (CT) scan reconstruction of cervical spine at 9 months.
- There is a fusion between right C2 and C3 facet joints.
- Asterisk (*) indicates C2 and C3 spine.

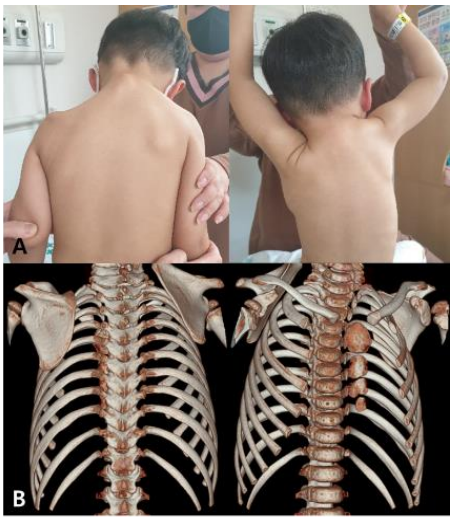

Figure 2. Sprengel's deformity at 35 months.
A. The right scapula is elevated both with the arms down (left) and with the arms raised (right).
B. Three dimensional computed tomography (CT) scan reconstruction of the chest presents right scapular elevation at posterior view (left), and no fusion between right scapula and ribs at anterior right oblique view (right).

CONCLUSION

- The *WBP11* is known to be related to VCTERL syndrome, and this was also found in animal experiments using *Wbp11* null allele mice.
- Three pathogenic variants of *WBP11* from 13 patients were first reported in 2020, and this report is the latest finding so far.
- In this report, the boy had only a vertebral anomaly among the clinical features of VCTERL syndrome, contrary to what is known.
- This suggests that phenotypes of *WBP11* may be diverse or heterogeneous and further studies with pathogenic variants of *WBP11* are needed.
- In addition, the clinician may consider the pathogenic variant of the *WBP11* when the patient showed an isolated congenital vertebral anomaly.

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