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Diagnostic value of chromosomal microarray in fetuses with isolated hypoplastic nasal bone

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We read with interest the paper by Lostchuck et al.[1] reporting on a population-based series of prenatal diagnostic procedures performed from 18 weeks following the diagnosis of fetal hypoplastic nasal bone (NB) on ultrasound.

Eighty of the 127 amniocenteses were performed for isolated hypoplastic nasal bone and there were no cases of pathogenic copy number variant in the 47 cases analysed by chromosomal microarray (0%; 95% CI, 0-7.1%). We note that the upper limit of this confidence interval for the yield of a chromosomal microarray (CMA) is similar to the overall CMA yield for a fetus with any ultrasound abnormality[2].

We have recently reported our tertiary centre experience with isolated hypoplastic nasal bone including newborn follow-up and postnatal microarray results[3]. We have found two non-trisomy 21 abnormalities, resulting in a frequency of pathogenic CNV in isolated hypoplastic NB of 5.1% (2/39). One fetus had Wolf-Hirshhorn syndrome presenting as isolated hypoplastic nasal bone at 19 weeks, with amniocentesis performed at 24 weeks for subsequent early-onset fetal growth restriction. The second case had a CVS for advanced maternal age which detected de novo microdeletions (1p31.3 [1.2Mb]; 6p21q22.1 [2.2 Mb]) but normal first trimester anatomy. Subsequent ultrasounds showed isolated hypoplastic nasal bone at 20 weeks and then mild ventriculomegaly and fetal growth restriction in the

third trimester; the newborn had minor dysmorphisms, a hypoplastic corpus callosum and paraventricular cysts on postnatal MRI[3].

Our results are not dissimilar to those of Lostchuck et al, with a frequency of pathogenic results within their reported confidence interval. However, our results highlight the limitations of conclusions based on a cross-sectional prenatal dataset only.

It is important to keep in mind that timing of invasive testing may not necessarily align with the exact time of the initial detection of a hypoplastic nasal bone. Invasive testing could be undertaken after additional ultrasound findings arise.

The data captured by Lostchuck et al only included amniocenteses from 18 weeks and would not have included those cases returning at 16 weeks for review of uncertain findings such as a nasal bone that could not be confidently assessed at 12-13 weeks.

Until larger population-based series are available, including prenatal and postnatal data, we caution against considering a hypoplastic nasal bone as a marker for trisomy 21 only. Fetuses with isolated hypoplastic nasal bone and a low-risk cfDNA result should have detailed tertiary-level follow-up ultrasound and genetic counselling, including consideration to the risks of atypical chromosomal abnormalities detectable by CMA.

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