Cardiac pathology in 6 cases of fetal hydrops due to Noonan syndrome

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Objective
Noonan syndrome (NS) is a common, autosomal dominant, frequently de novo condition due to mutations in RAS-MAPK pathway genes. Presentation is variable, usually in infancy or early childhood, and includes poor postnatal growth, cardiac abnormalities, dysmorphic features and lymphatic dysplasia. The classic cardiac abnormalities are pulmonary valve dysplasia and hypertrophic cardiomyopathy, but other cardiac anomalies are reported. Prenatal US scan showing nuchal translucency or cystic hygroma may suggest NS, and fetal hydrops is a recognised presentation.

Methods
We present 6 cases, 5 female and 1 male, of NS presenting prenatally with fetal hydrops.

Results
In 2, NS was inherited from a parent, whilst in the other 4, mutations in PTPN11 arose de novo. 5 of 6 cases had cystic hygroma and 1 had increased nuchal translucency on early scan. In 1 case, there was a heart defect. The outcomes of the 6 cases were 2 mid-trimester intrauterine deaths, 2 terminations of pregnancy and 2 resulted in neonatal deaths. At post mortem examination, in 2 cases there was an atrioventricular septal defect and hypoplasia of the aortic arch, while in the remaining 4 cases there was, respectively, a secundum-type atrial septal defect, aortic valve dysplasia, coarctation of the aorta or no congenital heart defect. Cardiomegaly was not identified. Pulmonary lymphangiectasia was recorded in 2 cases, 2 cases had hepatomegaly and 3 increased extramedullary haemopoiesis in diverse tissues.

Conclusion
NS should be excluded in cases of fetal hydrops without a structural chromosome abnormality and with no other explanation. Cardiac valvular dysplasia is uncommon in our series and babies can have complex cardiac anomalies, isolated cardiac defects other than pulmonary stenosis or none at all.