RArEST Rare Disease Awareness, Education, Support, and Training

Key learnings from Rare Disease Project ECHO®

Series 1: Session 5 - Genomics

Opening presentation

Dr Emma Palmer, Clinical Geneticist at Sydney Children's Hospitals Network, spoke on prenatal genomic screening and Bronwyn Terrill, Australian Genomics, spoke on direct to consumer testing.

You can find a recording of the presentation here.

For more on genomics, check out Lesson 6 in our **Rare Disease 101 Australia module**. You can register for this short, free CPD on the Medics for Rare Disease website.

Opening presentation discussion

Discussion was extensive and included:

- The difference between genetic testing (single genes) and genomic testing (multiple genes or entire genome).
- That non-invasive prenatal testing (NIPT) could more accurately be called non-invasive prenatal screening (NIPS).
- That the evidence does not support routine use of extended NIPT/NIPS, where companies offer screening for genetic changes beyond what the test was originally designed for (Down Syndrome and some other large chromosomal changes). As more conditions are added, the chance of false negatives increases.
- Genomic tests that can be done after a child is born and are often required to see a clinical geneticist, including:
    - Chromosomal microarray (CMA) and Fragile X screening for children with multiple congenital conditions.
    - Urine metabolic screening when there is a reason to suspect a metabolic condition, such as developmental regression.
- That karyotype testing is now an older technology and done less frequently, but can still be very useful. For example, for couples with recurrent miscarriages to screen for translocations, as CMA can't detect neutral chromosomal changes (i.e. where the change does not result in missing or additional genetic material, such as a section of DNA being flipped/inverted).

Case presentation

A GP presented on a case of a woman who is pregnant with her second child. She had gestational diabetes and perinatal anxiety in her first pregnancy. There are no known genetic disorders in her family. Her first NIPT/NIPS had insufficient foetal DNA in the sample. She did a second NIPT/NIPS a week later, which also had a technical failure. The GP referred her to an obstetric ultrasound service and amniocentesis was performed, which the patient informed the GP had normal results.

Case discussion

The case discussion covered:

- Reasons why a NIPT/NIPS might fail, including insufficient foetal DNA and 'vanishing twin syndrome' where one twin dies in utero.
- The role of surveillance as well as further testing such as CVS and amniocentesis (more reliable as it tests foetal rather than placental cells) after abnormal test results.
- The importance of ultrasound in the prenatal setting.
- The stress and anxiety involved in prenatal tests, including because there is time pressure.
- That screening tests can have incidental findings, such as detecting cancer in the pregnant person.
- That continuity of care is challenging, as most GPs will not see their patient from about 20 weeks to 6 weeks after birth. There is fear that their knowledge about their patient will not be properly conveyed to the rest of the healthcare team, and they often don't get information about their patient during this gap.

Key recommendations that the Project ECHO® participants and experts shared at the end of this case-based discussion were:

- That clearly explaining the role and limitations of screening tests often falls onto the GP, decision aids would help with this.
- That counselling around uncertainty is beneficial, including discussing how screening tests are only part of the picture.
- That there is a need for additional care coordination and better transitions of care between GPs and antenatal teams.
- That expanding NIPT/NIPS screening is not necessarily beneficial due to the increased risk of false positives and negatives.

Useful resources for clinicians and patients include:

- RACGP Genomics in General Practice
- RArEST Rare Disease 101 Australia module (Lesson 6)
- Australian Genomics
- The Centre for Genetics Education
- GeneEQUAL (resources for people with an intellectual disability)

Thank you to all who attended. Please do not forget to let us know how we did so we can continue to improve via this link.

Send us questions, discuss presenting a cae, or let us know your 'go to' resources by emailing us at rarest@unsw.edu.au