Sonographic soft markers in the second trimester: Subtle indicators or significant findings?

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Abstract
Advances in ultrasound technology over recent times, mean that the once controversial area of aneuploidy detection is becoming a popular topic for sonographers worldwide. Improved resolutions from high end machines mean that very subtle anatomic variants may have a part to play in the detection of chromosomal abnormalities. When combined with laboratory testing and risk assessment tools, early detection of these soft markers can provide a rationale for the diagnosis and management of fetal chromosomal defects.

Introduction
The second trimester detailed anomaly scan remains a highly effective screening tool for the assessment of structural normality and recognition of fetal abnormalities (Liu et al, 2014). Improvements in ultrasound resolution now mean that subtle anatomic variations referred to as “soft markers” are more detectable, often leaving practitioners in a dilemma regarding referral for further testing and follow up care pathways. The National Institute for Health and Care Excellence recommend early screening for aneuploidy and that all women are offered a detailed anomaly scan between 18 weeks and 20+6 weeks (NICE, 2012).

The literature is abundant with information defining these soft markers and the inclusion criteria varies throughout institutions; however the majority of sources have a classification list comprising of: chord plexus cyst, intracardiac focus, echogenic bowel, pylectasis, shortened femur, single umbilical artery and mild ventriculomegaly. This paper highlights the ultrasound image analysis of the most relevant soft markers and discusses the recent developments in the field.

Ultrasound Findings

Figure 1: Choroid plexus cyst

Figure 2: Echogenic intracardiac focus

Figure 3: Echogenic bowel/ normal bowel

Figure 4: Pyelectasis

Figure 5: Single umbilical artery

Figure 6: Mild ventriculomegaly

Figure 7: Graph summarising data from Agathokleous et al (2013).

Discussion

On review of the current literature the significance of specific soft markers has changed considerably over the years. In relation to single umbilical artery as an isolated finding, Voskamp et al (2013) undertook a large systematic review and meta-analysis and found no evidence that fetuses with isolated single umbilical artery have an increased risk of aneuploidy compared to a 10% risk mentioned in past studies.

On the other hand the diagnosis of an isolated fetal pylectasis >4mm as a soft marker for Down syndrome showed a notable positive and negative likelihood ratio of 2.78 respectively (Orzechowski and Berghella, 2013). In turn a more extended study carried out by Agathokleous et al (2013) looked at the various different soft markers and their correlation with Down syndrome. The positive likelihood ratios are shown in the chart below to demonstrate the significance of each individual marker. Statistics showed that ventriculomegaly, increased nuchal fold, aberrant right subclavian artery and hypoplastic nasal bone yielded the highest positive likelihood results.

Follow up and further investigations

Referral for further management will depend on institutional guidelines and client preference, however the majority of settings advocate further investigations if two or more anatomic variations are noted on ultrasound. The number of soft markers detected can have a significant bearing on the risk for aneuploidy. Finding one soft marker determines a risk of 2%, it rises to 11% in the presence of two softmarkers and up to 66% with five and in turn 92% with eight (Zelit, 2013).

Figure 8: Image of amniocentesis from births injury Justice.org.

Although CVS and amniocentesis remain the definitive diagnostic tests in the detection of aneuploidy, recent advances in the field of non-invasive prenatal screening of maternal cell free DNA boast significant detection results without the added risks to the fetus. Analysis of cell free fetal DNA has detection rates of 99.2% for T21, 96.3% for T18, 91.0% for T13 and 93.0% for sex chromosome aneuploidy (Gil et al, 2015).

Amniocentesis carries a 1% risk for miscarriage and should be carried out after 15 weeks gestation (RGO, 2010).

In relation to ultrasound the inclusion of the nasal bone length as part of the detailed anomaly scan is also recommended, particularly in the diagnosis of T21. Zelit et al (2013) reviewed studies linking nasal bone hypoplasia (NBH) to aneuploidy in the second trimester. Findings suggested that NBH was present in 61.8% of fetuses with Down syndrome, 12.1% of normal fetuses and 3.3% with other chromosomal abnormalities, strengthening its significance as an additional soft marker.

Figure 9: Nasal bone

Figure 9: Demonstrates a sagittal profile view ideal for nasal bone measurements in the second trimester.

Conclusion

Currently in Ireland there is no standardized policy for second trimester aneuploidy screening. The detailed anomaly scan is usually the first screening tool applied to determine structural normally, exposing abnormal anatomic variants as possible warning signs. Referral for follow up and further investigation often poses dilemmas due to the lack of a set classification critique and a universal perception of the specific soft markers and follow up care advancements, sonographers can strive to improve client care in this much debated field of sonography.

References