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Letters to the Editor

Differentiation of early first-trimester cranial neural tube defects

Neural tube defects (NTDs) are one of the most commonly reported birth defects and are the result of failure of primary neurulation, the folding and fusion of the neural plate[1]. We report on three early first-trimester cases with different types of cranial neural tube defects (NTD) not previously reported in ultrasound studies.

Previously, it was believed that the process of neural tube closure occurred in a 'zipper-like' fashion, starting at one point and proceeding in both cranial and caudal directions. However, neural tube closure is a more complex process. More recently, Nakatsu *et al.* described three different closure initiation sites of the human neural tube after studying miscarried embryos[2]. Following from this closure model six different types of cranial NTDs were distinguished, based on location of the closure defect (Figure S1)[2]. Survival rates significantly decreased if the rhombencephalon, or fourth ventricle, was involved in the defect (Types III, IV and V) with two-thirds of cases failing to survive beyond 7 weeks' gestational age. Embryos with total dysraphism (Type VI) failed to survive at an even earlier stage. However, 70% of the embryos with a rostral defect (Types I and II) did survive beyond 7 weeks.

In Case 1 (crown–rump length (CRL), 23 mm) and Case 2 (CRL, 13 mm) a cranial defect was seen from the mesencephalon to the rhombencephalon, suggestive of Type IV (Figure 1 and Figure S2). In Case 3 (CRL, 14 mm) the neural tube did not close at the parietal region of the head and most likely represents a Type II cranial NTD (Figure 2). We concluded that some of the different types of cranial NTDs can be diagnosed *in vivo* using high-frequency two- and three-dimensional transvaginal ultrasound during the early first trimester of pregnancy.

Increasing awareness of the existence of different types of cranial NTDs is important in beginning to unravel the etiology of the development of NTDs. If good documentation exists the different types of cranial NTDs might

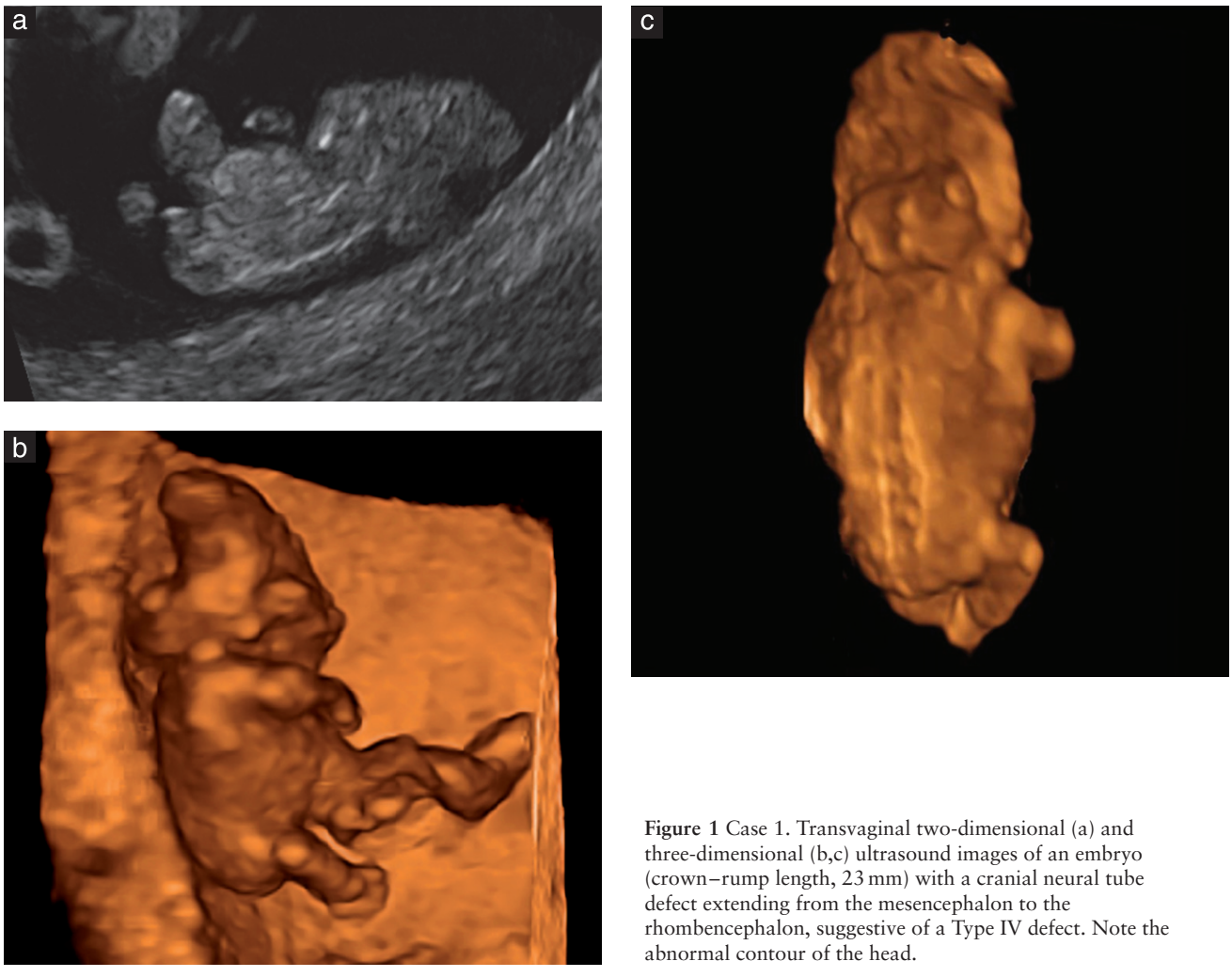

Figure 1 Case 1. Transvaginal two-dimensional (a) and three-dimensional (b,c) ultrasound images of an embryo (crown–rump length, 23 mm) with a cranial neural tube defect extending from the mesencephalon to the rhombencephalon, suggestive of a Type IV defect. Note the abnormal contour of the head.

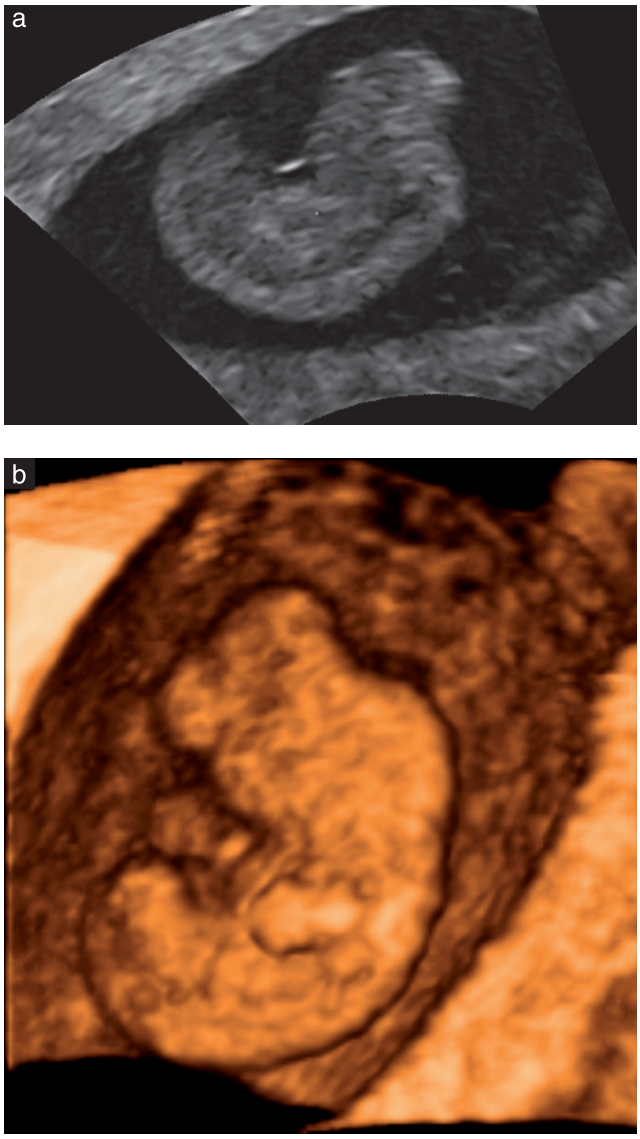

Figure 2 Case 3. Transvaginal two-dimensional (a) and three-dimensional (b) ultrasound images of an embryo (crown–rump length, 14 mm) with a cranial neural tube defect visible at the partietal region of the head, suggestive of a Type II defect.

be linked to different genetic pathways or environmental factors[3]. However, since the moment of demise in the majority of cases appears to be before 10 weeks' gestation, detection remains a challenge.

The existence of different types of cranial NTDs is a rather recent insight and the implications for counseling are not yet well understood. Understanding the cause of these malformations might contribute to determination of increased risks in couples and development of new prevention strategies. The *in vivo* detection of cranial NTDs raises the question whether these women are at increased risk for recurrence of NTD. If so, in a subsequent pregnancy, an increased dosage of supplemental folic acid is indicated and additional ultrasound examinations are recommended.

In conclusion, different types of cranial NTDs can be diagnosed using transvaginal ultrasound examination in early pregnancy. Detection of these NTDs is of particular importance in beginning to understand etiology, in developing prevention strategies, in counseling patients and in initiating new research projects.

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SUPPORTING INFORMATION ON THE INTERNET

The following supporting information may be found in the online version of this article:

Figure S1 Different types of cranial neural tube defects in human embryos (as reported by Nakatsu *et al.*[2]).

Figure S2 Transvaginal two-dimensional and three-dimensional ultrasound images of an embryo (at crown–rump lengths 13 mm and 17 mm) with a cranial neural tube defect extending from the mesencephalon to the rhombencephalon (suggestive of Type IV neural tube defect).