Integration of imaging and pathological studies in Meckel–Gruber syndrome

INTRODUCTION

Meckel–Gruber syndrome (MGS) was first described and illustrated in the literature in 1684 (Kompanje, 2003). The combination of additional fingers and toes, a large saclike hood behind the head, a large tail and the prune-belly were originally depicted for a baby with MGS. Meckel (Meckel, 1822) and Gruber (Gruber, 1934) associated the findings, and Opitz and Howe (Opitz and Howe, 1969) named the complex of these findings as Meckel syndrome. Today, the diagnosis of the MGS is usually accomplished by prenatal ultrasonography with described fetal anomalies of encephalocele, renal dysplasia and polydactyly (Nyberg *et al*., 1990). Prenatal magnetic resonance imaging (MRI) describing anomalous fetus was sparingly used in obstetrics, and only one other case of MRI-studied MGS has been reported (Williamson *et al*., 1989). Three centuries after the oldest described case, herein, we compile a comprehensive description of MGS with prenatal ultrasonography and MRI together with clinicopathologic findings.

CASE REPORT

A 25-year-old woman, gravida 2, para 1, was referred to our clinics because a suspected abnormal fetus was detected with ultrasonography at 18 weeks of gestation. The parents were not consanguineous with a negative family history. At 14th week of the present pregnancy, the maternal serum levels of alpha-fetoprotein and beta human chorionic gonadotrophin were within normal range. Ultrasonography revealed severe oligohydramnios with an occipital encephalocele, polydactyly (Figure 1a) and large echogenic kidneys (Figure 2a). Prenatal MRI (Philips 1.5-T Gyroscan Intera; Netherlands) using a balanced fact-field-echo T2-weighted sequence (TR, 4.5 ms; TE, 2.2 ms; time of acquisition, 18 s; flip angle, 60°; field of view, 270 × 270 mm; matrix, 256 × 256) showed herniation of the left occipital brain and the left occipital horn through a skull defect to the amniotic cavity. MRI also demonstrated bilateral enlarged kidneys with the renal parenchyma replaced by numerous tiny cysts, suggesting polycystic kidneys (Figures 1b and 2b). The patient and her family were informed that the most likely diagnosis was MGS and it was usually lethal. After extensive parental counseling, the decision of terminating the pregnancy was made.

The prenatal imaging diagnosis was confirmed by gross and histopathological studies. Physical examination after birth demonstrated a visible skull defect with tissues protruding through the occiput (Figure 1c), the distended abdomen and polydactyly of both hands and both feet. At autopsy, the abdomen was mostly occupied by bilateral enlarged kidneys that contained a cystic structure ranging from one to several millimeters (Figure 2c). The cerebral hemispheres were asymmetrical without obvious gyri or sulci seen grossly (Figure 1d). Histopathologically, the encephalocele contained disorganized glial tissue with ependymal-like epithelium and thickened meninges with many congested blood vessels (Figure 1e). The kidneys were occupied by numerous cysts that were lined with single-layered cuboidal epithelium (Figure 2d). No abnormalities were seen in the lung and liver.

DISCUSSION

MGS is a rare disorder often resulting in neonatal death. This condition is usually diagnosed by ultrasonography in the second trimester and earlier diagnosis has been made possible to those women with a previous pregnancy of a MGS (Nyberg *et al*., 1990). Our case showed typical sonographic features of MGS before 20 weeks, including the occipital encephalocele, multicystic kidneys and polydactyly. Ultrasonographic visualization of fetal central nervous system anomalies is often hampered by severe oligohydramnios. Transabdominal embryofetoscopy (Quintero *et al*., 1993) and transcervical embryoscopy (Dumez *et al*., 1994) during early trimester had been used to circumvent the limitation of ultrasound resolution, but the benefits were weighted against the risk of these invasive procedures, not to mention its inaccessibility of some aspects of the fetus.

MRI has the major advantage of clearly visualizing the fetus in the circumstances of maternal aortic pulsation and fetal movement, despite the oligohydramnios (Williamson *et al*., 1989). In our case, MRI not only identified the encephalocele and the skull defect but also excluded the possibility of severe cortical and callosal dysgenesis or posterior fossa anomalies by showing clearer images of the intracranial structures than ultrasonography. The combined use of MRI and ultrasound imaging provided sufficient information for prenatal counseling in this case, facilitating the patient's decision to terminate the pregnancy.

Malformations of the central nervous system in MGS include prosencephalic dysgenesis, occipital exencephalocele through the posterior fontanelle and rhombic roof dysgenesis (Ahdab-Barmada and Claassen, 1990). Our ultrasound and MRI findings demonstrate occipital exencephalocele through the posterior fontanelle, distinguishing this case from trisomy 13 that may be complicated with holoprosencephaly or other midline central nervous system anomalies. Other anomalies associated with MGS are microcephaly, absence of olfactory lobes, cerebral and cerebellar dysgenesis, cleft palate or lip, ocular malformations, short limbs, syndactyly, clinodactyly, clubbed foot, congenital heart malformations, hypoplasia of lungs, hepatic cysts and anomalies of the external genitalia. Various combinations of these anomalies have been observed in individual cases (Nyberg *et al*., 1990).

This report reflects the evolving detection techniques and descriptions of MGS since 1684. We again stress the importance of various prenatal imaging techniques, such as, ultrasonography as the primary screening and MRI as a confirmatory imaging for the aforementioned

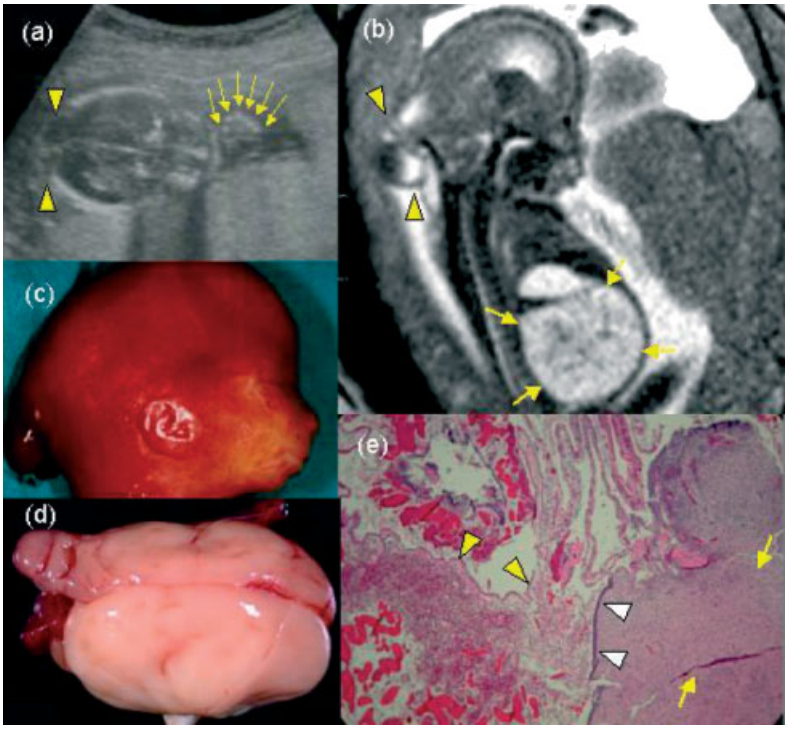

Figure 1—(a) Ultrasonography of occipital encephalocele (arrowheads), polydactyly (arrows) and severe oligohydramnios. (b) T2-weighted sagittal scan of MRI revealed left occipital encephalocele (arrowheads) and polycystic kidneys (arrows). (c) Head defect at the occiput. (d) Protruding tissues from the left occipital lobe of brain. (e) The encephaloceled mass contained disorganized glial tissues (arrows) with ependymal-like epithelium (white arrowheads) and thickened meninges (yellow arrowheads) with congested blood vessels (H & E stains, original magnification ×40)

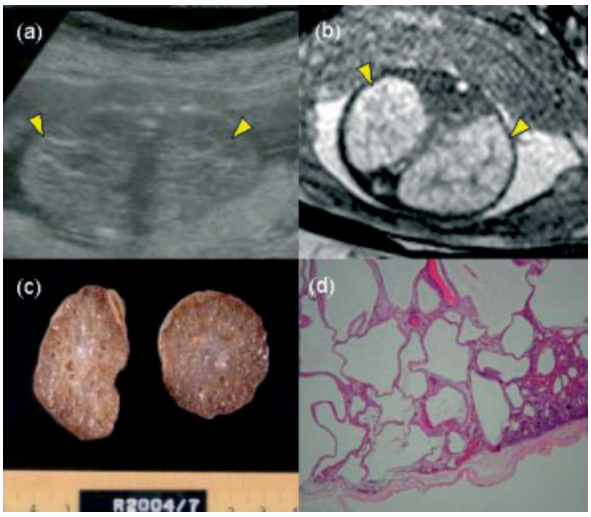

Figure 2—Bilateral, polycystic kidneys shown by (a) ultrasonography (arrowheads), (b) MRI (arrowheads), (c) gross examination and (d) histopathology (H & E stains, original magnification ×40)

anomalies in the affected fetus, so that the diagnosis of this syndrome can be made and the counseling of the subsequent recurrence risk will be conducted.

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