

Prenatal MRI Findings of Polycystic Kidney Disease Associated with Holoprosencephaly

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Holoprosencephaly (HPE) and polycystic kidney disease (PKD) are genetically heterogeneous anomalies which can make up part of various syndromes or chromosomal anomalies. Due to the rapid lethality prognosis, early and precise prenatal diagnosis would be of great value. This case report describes extensive PKD involvement, already present in utero, in a patient with HPE and subdural effusion visible by MR imaging. The detailed anatomic information obtained by the MR imaging can guide the surgical planning and can aid antenatal counseling.

Index terms:

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Polycystic kidney disease (PKD) is a hereditary disease, of which, the major inherited types are autosomal dominant and autosomal recessive. The autosomal recessive type is a relatively uncommon disease that evokes its clinical symptoms at birth, with significant mortality rates within the first month of life (1). Holoprosencephaly (HPE) is a complex developmental abnormality of the brain arising from the failure to diverticulate the prosencephalon into two cerebral hemispheres (2). The association of PKD with abnormalities of the central nervous system (CNS) also occurs in diseases such as Meckel syndrome, Zellweger syndrome, Jeune syndrome is well established (3). Also, an intracranial aneurysm has been known to be associated with PKD. Although ultrasound (US) is widely used for the diagnosis of fetal anomalies, it can be unsuccessful in providing detailed imaging of fetuses with complex anomalies during the late pregnancy period. Magnetic resonance (MR) imaging is an imaging modality that has no known harmful or ionizing effect on fetuses. Before ultrafast scanning methods, MR imaging had limited benefit for prenatal diagnosis due to artifacts secondary to fetal movements (4, 5). Fetal movements can be slowed down by sedation for a fetal MR imaging examination. Moreover, ultrafast MR imaging provides image acquisition within seconds and does not require sedation. This case report describes extensive PKD involvement, already present in utero, in a patient with HPE and subdural effusion by MR imaging. To the best of our knowledge, this is the first case in the English literature simultaneously evaluating both HPE and PKD by MR imaging in utero.

CASE REPORT

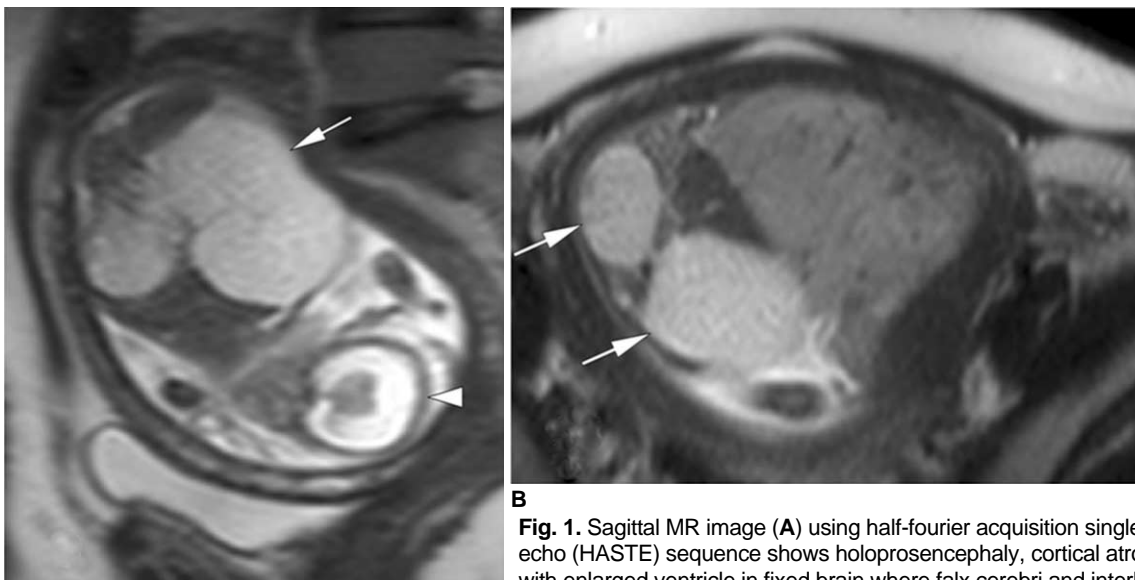
A 28-year-old woman, who had previously given birth to a boy with anomalies, including PKD and hydrocephaly, was admitted to our hospital. The pregnant mother was referred at 25 weeks of gestation. Previously she had two children; one of which was a 10-year-old boy whom was followed-up because of PKD. The patient's father had died due to PKD and renal failure. The parents did not exhibit any dysmorphic

features. An obstetric US revealed the presence of a monoventricle, hypotelorism, oligohydramnios, enlarged echogenic fetal kidneys and bilateral multiple kidney cysts. Because of oligohydramnios impaired US imaging, and in order to detect other possible accompanying anomalies, a fetal MR imaging examination was performed with a four-element phased array surface coil in a 1.5 T superconductive system (Siemens, Erlangen, Germany). Half-fourier acquisition single-shot turbo spin-echo (HASTE) MR imaging was applied at axial, coronal, and sagittal planes (TE, 60 msec; slice thickness, 4 mm; field of view, 26×35 cm; matrix, 192×256). In order to avoid radiofrequency loading, a repeat focusing pulse of 130° was used. A single study of thirteen slices was performed in only 17 seconds. Fetal MR imaging using the HASTE sequence revealed the presence of HPE, which is a wide subarachnoid space with a hugely enlarged kidney in which multiple millimetric cysts (Fig. 1A, B). Also, it was revealed that the fetus had oligohydramnios. Unfortunately, the baby died after 27 weeks of gestation. The mother delivered the deceased male baby by caesarean section. Infantile type PKD, and accompanying HPE and subdural effusion were determined in a postpartum examination of the fetus. The diagnosis of the patient's renal disease confirmed histopathologically after delivery. However, for both the MR imaging and postpartum examination, the fetus was not diagnosed with another anomaly.

DISCUSSION

Knowledge of the embryologic development is necessary to understand the link between malformations of the CNS and kidneys. One explanation commonly offered for the association is the coincident development within the gestation period. Also, development of both the kidney and the CNS depends upon inductive intercellular interactions. The observation that contact with embryonic spinal cord induces early differentiation of the metanephrogenic mesenchyme prompted an investigation of the specific factors present in the CNS that may stimulate mesenchymal differentiation (3).

Holoprosencephaly is a developmental field defect characterized by the impaired midline cleavage of the embryonic forebrain (6). This malformation sequence is graded as lobar, semilobar and lobar forms based on the degree of cleavage impairment, but there is a continuum between the milder and the worse forms (2, 7). In the most severe alobar type, which is usually lethal, the interhemispheric fissure, corpus callosum, septum, falx cerebri, optic tracts and olfactory bulbs are absent. The thalami are fused and there is a single ventricle. In the semilobar type, the two cerebral hemispheres are partially separated posteriorly, but there is still a single ventricular cavity. Lobar HPE is the mildest form. The interhemispheric fissure is well developed anteriorly and posteriorly, but there is a little fusion (2). In general, forebrain malformations are associated with facial anomalies, ranging from anophthalmia, cyclopia or proboscis in the most severe



B

Fig. 1. Sagittal MR image (A) using half-fourier acquisition single-shot turbo spin-echo (HASTE) sequence shows holoprosencephaly, cortical atrophy hydrocephaly with enlarged ventricle in fixed brain where falx cerebri and interhemispheric fissure were absent (arrowhead) along with enlarged fetal kidneys (white arrow). Axial MR image (B) using same sequence reveals enlarged fetal kidneys with increased intensity and multiple millimetric renal cysts (white arrows).

A

cases, as opposed to a midline cleft lip, a simple hypotelorism or even no anomalies in the less severe HPE forms (8, 9). HPE has an estimated prevalence of 1:16,000 live births (8).

Autosomal dominant and recessive PKD are the best known of the inherited diseases characterized by the development of renal cysts from tubular epithelial cells (10). Autosomal recessive PKD, previously termed infantile polycystic kidney disease, is an inherited disorder characterized by bilateral symmetrical enlargement of the kidneys and cystic dilation of the renal tubules, often with hepatic fibrosis. The clinical situation is variable, depending on the degree of renal and hepatic involvement (11), and has an estimated prevalence of 1:20,000 live births (10). The disease is most commonly observed during the perinatal period and usually produces renal failure in utero or at birth, and eventual death from pulmonary hypoplasia secondary to the oligohydramnios (11, 12). HPE and PKD are genetically heterogeneous anomalies and can make up part of different syndromes or chromosomal anomalies (8, 13). To the best of our knowledge, this is the first case in the English literature simultaneously evaluating both HPE and PKD by MR imaging in utero.

Because of the rapid lethality prognosis, early diagnosis would be of great value. US has a wide use and it provides good results in the detection of cranial and kidney anomalies, despite some limitations. The limitations of US are mostly due to an inability to visualize fetal intracranial anomalies secondary to the reverberation artifacts of the calvarium and a low sensitivity for the detection of cerebral cortical malformations and small destructive lesions of the cerebrum and cerebellum. In addition to these, the imaging quality of US can be diminished if the mother is obese, suffers from oligohydramnios, and if the engagement of fetal head occurs in the late pregnancy (4).

In fetal MR imaging, patients are not exposed to ionizing radiation and there is no evidence for any teratogenic side effects, however because of the significantly low image quality due to motion artifacts during long examination times, the diagnostic value of routine intrauterine MR imaging for fetuses is limited (4, 14). Technical developments in ultrafast MR imaging, especially the HASTE and single-shot fast spin-echo sequences led to an increased use of MR imaging in prenatal diagnosis. HASTE MR imaging sequences are now used for the detection of CNS anomalies as they provide a perfect contrast between the cerebral spinal fluid, brain and spinal cord. Additionally, some investigators successfully used the ultrafast MR imaging for the evaluation of abdominal pathologies. As in

our case, MR imaging clearly detected HPE, PKD and oligohydramnios. The differential diagnosis should include trisomy 13, Zellweger syndrome, Jeune syndrome, Joubert syndrome, Meckel syndrome for PKD, hydranencephaly, massive hydrocephalus and callosal dysgenesis for HPE.

In conclusion, because of the lethal prognosis, and the risk of recurrence in future pregnancies, an early and precise prenatal diagnosis is quite important. MR imaging can be a perfect complement to the US in complex anomalies, as it was in the presented case. The detailed anatomic information obtained by the method can guide the surgical planning and can provide aid in antenatal counseling.

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