Case Report

Iniencephaly: radiologic and pathomorphologic perinatal observation

Alexandra Korostyshevskaya, MD, PhD\(^a\), Alyona Gornostaeva, MD\(^a,b,*\), Rem Volkov, MD\(^c\), Vasily Yarnykh, PhD\(^d,e\)

\(^a\)Institute “International Tomography Center” of the Siberian Branch of the Russian Academy of Sciences, Novosibirsk, Russian Federation
\(^b\)Novosibirsk State Medical University, Novosibirsk, Russian Federation
\(^c\)National Medical Research Center, Novosibirsk, Russian Federation
\(^d\)Department of Radiology, University of Washington, Seattle, WA, USA
\(^e\)Research Institute of Biology and Biophysics, Tomsk State University, Tomsk, Russian Federation

ABSTRACT

Iniencephaly (IE) is a rare neural tube malformation involving severe head retroflexion and deformity of the spine. IE is typically accompanied with other congenital abnormalities and carrying a poor fetal prognosis. This report presents radiological findings in a rare case of IE associated with multiple malformations of the skull, spine, face, heart, and body. A 44-year-old pregnant female underwent an obstetric ultrasound examination on the 26th week of gestation followed by fetal magnetic resonance imaging on the 36th week. Imaging revealed complex developmental anomalies, which led to the diagnosis of IE with a large cervical meningocele, occipital bone defect, spina bifida of the cervical vertebrae, multiple malformed vertebra, deformed face, coarctation of the aortic arch, and hypoplastic lungs. Based on these findings, a decision to terminate pregnancy was made. Pathological examination of the fetus showed close agreement with imaging. The presented case underscores the importance of multimodal imaging for clinical decision making in the management of complex neural tube malformations.

© 2020 The Authors. Published by Elsevier Inc. on behalf of University of Washington. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/)

Acknowledgments: The authors thank Dr. Tamara Feygin, MD (Children Hospital of Philadelphia, Department of Neuroradiology) for helpful discussion.

Funding: This work was supported by the Russian Science Foundation Project No. 19-75-20142. Access to the MRI equipment was partially funded by the Ministry of Science and Higher Education of the Russian Federation. V. Yarnykh received partial salary support from the National Institutes of Health grants R21NS109727 and R24NS104098.

Conflicts of Interest: The authors declare no conflict of interest.

* Corresponding author at Institute “International Tomography Center” of the Siberian Branch of the Russian Academy of Sciences, Institutetskaya St., Bldg. 3a, 630090, Novosibirsk, Russian Federation.

E-mail address: am.popkova@yandex.ru (A. Gornostaeva).
https://doi.org/10.1016/j.radcr.2020.11.003

1930-0433/© 2020 The Authors. Published by Elsevier Inc. on behalf of University of Washington. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/)
Introduction

Iniencephaly (IE) is a rare neural tube defect [1,2] involving dysmorphic spine and abnormal fusion of the portion of the occipital skull with the back. It results in extreme fixed head retroflexion. This condition accounts for approximately 1% of all fetal malformations and has been described in scattered case reports [2,4–8]. We present a case of the iniencephaly aperture variant (characterized by the presence of cervical encephalocele) accompanied with numerous additional neural axis and body malformations.

Case report

A 44-year-old woman (gravida 2, para 1) living in a rural area of the mountain Altay region of Siberia appeared at the first obstetric appointment on the 25th week of pregnancy. No obvious risk factors were noticed. The mother was on iron and folic acid supplementation during the second trimester due to mild anemia.

Ultrasoundography and magnetic resonance imaging

The routine ultrasonogram performed at 26 weeks of pregnancy revealed a live single female fetus with multiple congenital anomalies including cervical meningocele, neck hyperextension, and abnormally short and deformed spine (Fig. 1a and b). In addition, a congenital heart defect, coarctation of the aortic arch with a transposition of the great vessels was detected.

Fetal 3 T magnetic resonance imaging (MRI) was performed on the 36th week of pregnancy. The delay was due to limited availability of advanced care at the patient’s place of residence. MRI revealed complex developmental anomalies, which led to the diagnosis of iniencephaly aperture variant (with cervical encephalocele) accompanied with face and body malformations (Fig. 2a and b). An exramidine exophytic cystic lesion filled with cerebrospinal fluid with the size of 7.7 × 7.1 × 3.1 cm and overlying skin was identified in the occipital neck region. The finding was impressive of a closed cervical meningocele (Figs. 2b, and 3a). A small soft tissue component was present within the proximal part of the cyst (Fig. 2a). The occipital bone defect, spina bifida of the cervical vertebrae, enlarged foramen magnum, and herniation of the brainstem and cerebellum beyond the cervicomedullary junction were also seen (Figs. 2a, and 3d). The spinal canal in this region was widened (Fig. 2a). The malformed cervicothoracic spine appeared thin and curved due to hyperextension and shortening of the spinal column. The supratentorial brain parenchyma was normal. The lateral and third ventricles were normal in size and shape, except for mild colpocephaly (Fig. 3a–d). The fourth ventricle and cisterna magna were moderately compressed (Fig. 3a and d). T1- and T2-weighted images demonstrated no signs of cerebral hemorrhage. On the screening fetal body MRI, the small round trunk was seen (Figs. 1a, and 3b, d). Lungs were hypoplastic and dehydrated with a reduced thoracic volume.

Fig. 1 – Transabdominal ultrasound images at 26 weeks of pregnancy. (a) Excessive thickening of the fetal neck with subcutaneous craniothoracic lipoma (arrow). (b) Cystic lesion in the neck.

Fig. 2 – T2-weighted MRI of the fetal head at 36 weeks of pregnancy. Axial (a) and sagittal (b) images show meningocele with a small soft tissue component in the proximal part (arrow), low-set and malformed ears, posterior fossa defect with the cerebellum herniation, polyhydramnios, neck hyperextension, and fusion of fatty tissue at the neck level.
Pathology

Due to hopeless fetal prognosis, the pregnancy was terminated on the 38th week of gestation by induction of labor upon the mother's informed consent. The fetus was delivered vaginally after induced fetal demise and intrauterine meningocele puncture (Fig. 4a and d). On autopsy, the fetus weighed 2110 g and showed delayed and discordant development according to the anthropometric indicators, which approximately corresponded to 33 weeks of gestation. The retroflexed head (30 cm in circumference) and body were small relative to the enlarged extremities. The abortus had the short and thickened hyper-extended neck covered with hair. The ears were low-set (Fig. 4b and c). Pathologic examination confirmed the diagnosis of IE. The occipital bone had a pronounced defect adjacent to the enlarged foramen magnum (Fig. 5a). Posterior fossa was small. The meningocele was covered from inside with the dura mater, which extended from the cranial cavity. (Fig. 5a).

Discussion

The embryologic basis of the clinical variations in the neural-tube defects is poorly understood. Different cellular mechanisms and various sites of neural tube closure might underlie clinical manifestations, as they could have different sensitivity to various pathogenic factors, such as the type and time of exposure to teratogenic agents [1]. The advanced maternal age is a known risk factor for neural tube defects [1,2]. A female preponderance (90%) of IE has been noted in the literature [4]. Both these factors were present in our case. Occasionally IE is seen in families with a history of neural tube defects, and the recurrence risk is about 5% [4]. The exact etiology and pathogenesis are not clear, and both genetic and environmental causes have been implicated. Various factors, such as poor socioeconomic status, obesity, certain medica-
tions (sulphonamide, tetracycline, antihistamines, and cytotoxic agents), and the lack of folic acid supplementation were shown to increase the risk [5]. However, in the present case there were no relevant family history or abovementioned risk factors. The first child in the family has no congenital abnormalities.

From the radiological point of view, we can emphasize that only comprehensive multimodal imaging can prevent the delay in the diagnosis of IE and convince the mother to terminate the pregnancy. Congenital retroflexion of the spine and accompanying heart defects are mainly seen on ultrasound images. Ultrasound findings might be surely confirmed by MRI in most cases, as additional information can be acquired about the precise diagnosis, severity and location of the neural tube anomaly. Thus, further clinical management can be guided with regard to terminating pregnancy or providing adequate postnatal care. IE carries a poor prognosis [3-5,8]. There are some cases of long-term survival [6,7], but most neonates die antenatally or soon after birth. Prevention is still problematic due to poorly understood pathogenesis.

In conclusion, accurate MRI diagnosis is required in addition to ultrasonography to demonstrate the inevitability of pregnancy termination in IE to obstetricians and parents. The comparison between imaging and pathological findings in IE revealed the benefits of both ultrasound for the cardiac and great vessel malformation diagnosis and MRI for the detection of the brain and spine abnormalities. Both modalities demonstrated high concordance with pathology and should be complimentary used in evaluation of complex neural tube malformations.

**Patient Consent Statement**

Written informed consent for publication of this case report was obtained from the patient. All images were anonymized and contain no personally identifiable information.

**REFERENCES**

[1] Sadler TW. Mechanisms of neural tube closure and defects. Ment Retard Dev Disabil Res Rev 1998;4:247–53 Google Scholar.
[2] Botto LD, Moore CA, Khoury MJ, Erickson JD. Neural-tube defects. N Engl J Med 1999;341:1509–19 PubMed.
[3] Cimmino CV, Painter JW. Iniencephaly. Radiology 1962;79:942–94 PubMed.
[4] Jayant K, Mehta A, Sanghvi LD. A study of congenital malformations in Mumbai. J Obstet Gynaecol India 1961;11:280–94.
[5] Tugrul S, Uludogan M, Pekin O, Uslu H, Celik C, Ersan F. Iniencephaly: prenatal diagnosis with postmortem findings. J Obstet Gynecol 2007;33:566–9 PubMed.
[6] Katz VL, Aylsworth AS, Albright SG. Iniencephaly is not uniformly fatal. Prenat Diagn 1989;9:595–9 PubMed.
[7] Ayter MH, Dogulu F, Cemil B, Ergun G, Kurt G, Baykaner K. Iniencephaly and long-term survival: a rare case report. Childs Nerv Syst 2007;23:719–21 PubMed.
[8] Meizner I, Levi A, Katz M, Maor E. Iniencephaly. A case report. J Reprod Med. 1992;37:885–8 PubMed.