Case Report

**Iniencephaly in early gestation and accompanying ultrasonographic findings**

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**Abstract**

Based on a study of 16 fetuses that were diagnosed as having iniencephaly, we discuss the correlation between sonographic and the pathologic findings in relation to the literature. Anencephaly was the most common anomaly associated with iniencephaly in the first trimester (100%). Other associated anomalies were encephalocele, meningomyelocele, micrognathia, omphalocele, gastrochisis, kyphoscoliosis, and upper and lower extremity abnormalities. History of neural tube defect and accompanying anomalies of iniencephaly such as anencephaly should be considered as potential diagnostic indicators of iniencephaly.

**Key Words:**  
Anencephaly, encephalocele, iniencephaly

**Introduction**

Congenital anomalies are one of the major causes of perinatal mortality and morbidity. Iniencephaly is a rare and lethal neural tube defect, which was first described by Saint Hilaire [1]. It is characterized by an occipital bone defect, spinal dysraphism, and fixed retroflexion of the fetal head [2]. It may be associated with neurologic anomalies including encephalocele, anencephaly, meningomyelocele, hydrocephalus, Dandy-Walker malformation, holoprosencephaly, and non-neurologic anomalies including club foot, cardiac anomalies, omphalocele, congenital diaphragmatic hernia, polycystic kidney disease, arthrogryposis, single umbilical artery and gastrointestinal atresia [3]. Iniencephaly was classified as iniencephaly apertus and iniencephaly clausus by Lewis. Fetuses with iniencephaly apertus have an encephalocele and those with iniencephaly clausus have a spinal defect without encephalocele [3]. Howkins and Lawrie further classified iniencephaly into simple iniencephaly (iniencephalus apertus and iniencephalus clausus), and iniencephaly with anencephaly (anencephaly with spinal retroflexion) [4]. The incidence ranges from 0.1 to 10 in 10.000 births [2-3]. Most fetuses are stillborn or die soon after birth due to life threatening congenital abnormalities. Iniencephaly has a tendency for female fetuses [5]. We present 16 confirmed cases of iniencephaly in relation to the literature and discuss the correlation between the sonographic and pathologic findings.

**Case Presentation**

This study was conducted in Zeynep Kamil Women and Children’s Disease, Training and Research Hospital, İstanbul. The pathology reports of pregnancies that were termi-
nated because of fetal anomalies between April 2005 and April 2015 were reviewed using the search term iniencephaly in the hospital database. The perinatology reports of these fetuses, which were diagnosed as having iniencephaly at postmortem evaluation, were assessed (Figures 1 and 2).

![Figure 1. Postmortem appearance of a fetus with iniencephaly (Lateral view)](image1)

Sonographic diagnosis of iniencephaly had been made if there were a defect in the occipital bone involving foramen magnum, retroflexion of the neck (lordosis of cervical spine), retroflexion of the entire spine and open spinal defects of variable degrees. The parents of the fetuses were recalled and detailed histories were obtained. All of the patients gave their informed consent. Sixteen cases of iniencephaly were diagnosed based on postmortem pathologic examination. The perinatology reports of all these cases were analyzed (Table 1). None of the women declared toxic drug use and 8 of the women used folic acid supplementation before conception. The mean maternal age, gestational age at diagnosis, number of gravida and parity were 27.0±4.3 years, 15.5±2.3 weeks, 2.9±1.6, and 1.5±1.27 respectively. One of the women was married to her first cousin, one had delivered a baby with a neural tube defect in a previous pregnancy, and one another woman had a brother who had had a neural tube defect. Anencephaly was the most common anomaly associated with iniencephaly in the first trimester (100%) (Figure 3).

![Figure 2. Postmortem appearance of a fetus with iniencephaly (Posterior view)](image2)

![Figure 3. Sonographic appearance of anencephaly.](image3)
Other accompanying anomalies were encephalocele meningomyelocele, micrognathia, omphalocele, gastroschisis, kyphoscoliosis, upper and lower extremity abnormalities (club foot), bronchogenic cyst, polyhydramnios, atrioventricular septal defect, and ventricular septal defect (Figure 4). Encephalocele was sonographically diagnosed in 3 (18.7%) of the cases, spina bifida presented in 5 (31.2%) patients, and club foot was seen in 4 (25%) cases. Micrognathia, omphalocele, gastroschisis, kyphoscoliosis, bronchogenic cyst, atrioventricular septal defect and ventricular septal defect were found in one (6.2%) of the 16 fetuses.

Data were analyzed using the Statistical Package for Social Sciences, 40 v.17 (SPSS Inc, Chicago, IL, USA). Descriptive statistics are given as frequencies and percentages.

Discussion

Iniencephaly is characterized by a variable defect in the occipital bone that results in an enlarged foramen magnum. Total or partial absence of cervical and thoracic vertebrae is accompanied by incomplete closure of the vertebral arches and/or bodies. Shortening of the spinal column due to hyperextension of the malformed cervicothoracic spine results in an upward-turned face [6]; affected fetuses have a characteristic “star gazing” appearance because of their upturned faces (Figure 5). There is a discrepancy

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Table 1. Sonographic findings, management, and outcomes of iniencephaly cases

<table>
<thead>
<tr>
<th>Case</th>
<th>Age</th>
<th>Gravida</th>
<th>Parity</th>
<th>Intermarriage</th>
<th>Gestational age at diagnosis</th>
<th>Sonographic findings</th>
<th>Management</th>
<th>Pathologic findings</th>
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<td>1</td>
<td>37</td>
<td>5</td>
<td>4</td>
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<td>Termination</td>
<td>Iniencephaly</td>
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<tr>
<td>2</td>
<td>26</td>
<td>5</td>
<td>3</td>
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<td>14</td>
<td>Acrania</td>
<td>Missed abortion</td>
<td>Iniencephaly</td>
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<tr>
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<td>28</td>
<td>3</td>
<td>2</td>
<td>-</td>
<td>13</td>
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<td>Termination</td>
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<td>17</td>
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<td>1</td>
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<td>Missed abortion</td>
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<td>3</td>
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<tr>
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<tr>
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<td>18</td>
<td>Iniencephaly/Acrania/Encephalocele/Polyhydramnios/ClubFoot</td>
<td>Termination</td>
<td>Iniencephaly</td>
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in the incidence of disease. The incidence may be higher than previously reported due to the failure of recognizing the entity. On the other hand, conditions including nuchal tumors, fetal guatr, lymphangioma, cervical meningomyelocele, encephalocele, Klippel-Feil and Jarcho-Levin syndrome, which cause cervical hyperextension, should be kept in mind in the differential diagnosis [7].

Cervical vertebrae are abnormal in iniencephaly and they are almost normal in anencephaly. Anencephaly shows absence of cranium and a retroflexed head, which is not covered with skin; the retroflexed head is completely covered with skin in iniencephaly. Klippel-Feil syndrome (KFS) is caused by a segmentation failure of the cervical vertebrae. Retroflexion of the head is usually not seen in KFS and its presence should raise suspicion of iniencephaly. The differential diagnosis of these two may be quite difficult; however, it is important to separate the two because KFS is not lethal and can be corrected surgically [8]. The exact etiopathogenesis of the disease is still unknown. Diabetes, obesity, low socioeconomic conditions, low parity, exposure to toxic drugs, lack of folic acid supplementation, chromosomal abnormalities including trisomy 18, trisomy 13, and Turner’s syndrome have been associated with iniencephaly [1]. Dogan et al. reported that urinary tract infection in the first 28 days of gestation and taking antihistamines for the common cold might be some possible causes [9]. In animal experiments, treating pregnant rats with streptonigrin can result in iniencephaly [10]. Iniencephaly is encountered in families with a history of neural tube defects and recurrence risk is reported as 5% [4]. It is known that not all cases of neural-tube defect can be prevented by increasing the intake of folic acid [11]. In our study, despite the use of folic acid supplementation prior to conception, 8 of the women had fetuses with neural tube defect. All women had neither systemic illness nor exposure to toxic drugs. A review of the obstetric and gynecologic history revealed no common etiologic factors. Neural tube defect history was present in 2 of our case series (13.3%). One woman reported having delivered a child with a neural tube defect in a previous pregnancy and another woman had a brother who had had a neural tube defect. Although most fetuses with iniencephaly are stillborn or die soon after birth due to life threatening congenital abnormalities, a few cases with long-term survival have been reported in the literature, such as a male newborn who underwent surgery to correct his cervical deformity and survived postnatally [12-15]. In our study, 3 women spontaneously aborted and 13 of the 16 women accepted the choice of therapeutic abortion after counselling; none of the women gave live birth. Diagnosis of iniencephaly has become feasible in the first and early second trimester due to advances in the field of ultrasonography [16]. Cuilier et al. reported a diagnosis of iniencephaly in a fetus at 9 weeks using transvaginal ultrasound. Acrania, cervical encephalocele, and short distorted spine accompanied the ultrasonographic findings [17]. Marton et al. made the diagnosis in a fetus aged 10 weeks with accompanying findings that included short neck, short crown-rump length, retroflexion of the head, and cervical myelocele [18]. In our case series, prenatal diagnosis was possible at the end of their first trimester (13th week) through transabdominal ultrasound, and only 6 (37%) of the cases were prenatally diagnosed as having inienceph-
Anencephaly was the major ultrasonographic finding. As mentioned in the studies of Cuillier and Marton, diagnosis of iniencephaly can be made as early as 9 to 10 weeks of pregnancy using transvaginal sonography, which can be made in risk groups for neural tube defects. In our study, due to the lack of exact diagnosis of iniencephaly in early gestation, we think that proper and meticulous evaluation of accompanying anomalies or transvaginal sonographic examination of suspected cases may aid diagnosis. The diagnosis rate of iniencephaly was 94.7% in the case series of Dogan et al. [9], but the gestational week of diagnosis was ≥ 24 weeks in all but 2 cases. In our case series, the gestational weeks of the fetuses were between 13 and 19 weeks.

In conclusion, whenever the above mentioned anomalies are detected and there is a history of neural tube defect, iniencephaly must be kept in mind as a potential diagnosis.

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Conflict of Interest Statement
None

References