

Iniencephaly: Radiological and pathological features of a series of three cases

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ABSTRACT

Iniencephaly is a rare form of neural tube defect with an incidence of 0.1-10 in 10,000 pregnancies. It is characterized by the presence of occipital bone defects at foramen magnum, fixed retroflexion of head, spinal dysmorphism, and lordosis of cervicothoracic vertebrae. It is usually associated with central nervous system, gastrointestinal, and cardiovascular anomalies. We present radiological and autopsy findings in a series of 3 cases of iniencephaly (gestational ages 29.3, 23, and 24 weeks) first fetus in addition showed omphalocele, pulmonary hypoplasia, two lobes in right lung, accessory spleen, atrial septal defect, bilateral clubfoot, ambiguous genitalia, and single umbilical artery. Second fetus was a classical case of iniencephaly apertus with spina bifida. Third fetus had colpocephaly and bifid spine.

Key words: Colpocephaly, iniencephaly, omphalocele, pulmonary hypoplasia, spina bifida

Introduction

Iniencephaly is a rare, fatal neural tube defect (NTD) characterized by occipital bone defects at foramen magnum, fixed retroflexion of head, spinal dysmorphism, and lordosis of cervicothoracic vertebrae.^[1] Howkin and Lawrie in 1939 classified iniencephaly into two types based on the presence or absence of encephalocele into iniencephaly clausus (without encephalocele) and iniencephaly apertus (with encephalocele).^[2] It is usually associated with central nervous system, gastrointestinal, and cardiovascular anomalies.^[3] Here we present the radiological and autopsy findings of two cases of iniencephaly clausus (29.3 and 24 weeks) and one case of iniencephaly apertus (23 weeks) with brief review of literature.

Case Reports

Case 1

A 21-year-old primigavida with 29.3 weeks of gestation was admitted in our institute for termination of pregnancy,

as her routine anomalous ultrasonogram (USG) done at a primary center revealed defective development of spine, atrial septal defect (ASD), aplasia of the right kidney, and encephalocele. The mother's routine blood and biochemical investigations were within normal limits. She was not a known diabetic or hypertensive and had a history of nonconsanguineous marriage. She gave a history of iron and folic acid tablets supplementation. A repeat USG done at our institute confirmed the above-mentioned anomalies. In view of multiple nonviable anomalies, with the informed consent of the parents, the pregnancy was terminated and abortus was sent for pathological examination.

At autopsy it was a fetus of ambiguous genitalia, weighed 900 g. The head was enlarged, severely retroflexed, and there was no neck. Head was seen directly resting on the chest and mandibular skin in continuous with chest skin surface. The ears were low set [Figure 1a] and the vertebral column was short and irregular. There was an omphalocele with partly covered membrane containing liver, bladder, and intestine as contents. Lower limbs showed bilateral clubfoot. There was overgrowth of upper limbs compared with lower limbs [Figure 1b]. Posteriorly the skin of the scalp was thick and extended up to lumbar region [Figure 1c] Radiograph of the abortus revealed hyperextension of the neck with occiput touching the cervicodorsal vertebra with soft tissue continuation on the dorsal aspect of the neck. Cervical and thoracic vertebra showed defective block vertebra with thoracolumbar

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lordosis suggestive of iniencephaly [Figure 1d]. Autopsy of the fetus revealed two lobes in the right lung with hypoplasia of both the lungs [Figure 1e]. Cardia showed ASD [Figure 1f and g]. There was an accessory spleen in the greater omentum [Figure 1h]. Both the testes were seen in the inguinal canal. On opening the cranial cavity, there was defect in the development of occipital bone, which was covered by duramater inside and thin membrane outside. The foramen magnum was enlarged and measured 5 cm at

its longest axis. Posterior fossa was small and hypoplastic cerebellar vermis [Figure 1i-k]. Cerebrum and spinal cord were normal. Umbilical cord showed single umbilical artery. Considering these features a pathological diagnosis of iniencephaly clausus was made.

Case 2

A 27-year-old female gravida 2, para 1 living 1 with 23 weeks of gestation presented to obstetrics department



Figure 1: (a) Gross photograph of iniencephaly showing low-set ears, absence of neck, and club foot. (b) Gross photograph of lateral view of iniencephaly showing omphalocele (arrow). Note the overgrowth of the upper limbs compared with lower limbs. (c) Posterior view of iniencephaly showing thick scalp skin extending up to lumbar region. Omphalocele contents are also seen (arrow). (d) X-ray lateral view reveals short vertebral column, fused cervical vertebrae, malformed thoracic and lumbar vertebrae, and overcrowding of the ribs. (e) Gross photograph of hypoplastic lungs with right lung showing two lobes. (f) Gross photograph of opened left atrium showing atrial septal defect (ASD). (g) Probe demonstrating the ASD. (h) Gross photo showing accessory spleen. (i) Gross photograph after scalp skin reflexion showing defective development of occipital bone (arrow). Also note bilateral club foot. (j) Gross photograph of sagittal section of the fetus. (k) Closer view of the sagittal section showing shallow posterior fossa (black arrow), defective occipital bone development, fused cervical vertebrae, and malformed thoracic and lumbar vertebrae with lordosis. (Case 1)

with a history of abdominal pain since a day. She gave a history of nonconsanguineous marriage. She was a booked case and received iron and folic tablets supplementation. Perabdominal examination revealed uterus of 22 weeks size and pervaginuum showed cervix unaffaced. Serum alpha-feto protein was significantly raised. USG revealed features of intrauterine growth retardation (IUGR) with multiple congenital anomalies and malformed spine and skull. With informed consent, the pregnancy was terminated and abortus was subjected

for pathological examination. At autopsy, it was a female fetus and weighed 510 g. On external examination, the head was retroflexed with no neck. Small occipital encephalocele, low-set ears, and lordotic short spinal column [Figures 2a-c]. Umbilical cord was unremarkable.

Computed tomography (CT) scan revealed defective development of endochondral portion of occipital bone, rachischisis of cervical spine, and club foot. Head was hyperextended and foramen magnum was enlarged



Figure 2: Gross photograph of lateral (a), anterior (b), posterior (c) view of iniencephaly showing hyperextended head with encephalocele (*) (d) Computed tomography (CT) scan showing fusion of occipital bone with cervicothoracic vertebrae, spina bifida, and malformed ribs. (Case 2) Gross photograph of iniencephaly showing hyperextended head, low-set ears. (e&f) CT scan (g) and magnetic resonance imaging (MRI) (h) showing defective development of occipital bone with fusion to the cervicothoracic vertebrae. Note in MRI image colpocephaly. (i) Coronal section of MRI showing colpocephaly. (Case 3)

with fusion of occiput to upper cervical vertebrae. Ribs were less in number and fused [Figure 2d]. Magnetic resonance imaging (MRI) in addition to CT scan findings revealed an encephalocele from the occipital defect. Configurations of infratentorial structures were highly distorted. Visceral organs were unremarkable. Autopsy confirmed all the above findings, and final pathological diagnosis of iniencephaly apertus was constructed.

Case 3

A 24-year-old primigravida with 24 weeks of gestation arrived at casualty with complains of pain in the abdomen and bleeding pervaginuum since 2 days. She gave a history of nonconsanguineous marriage. She has not taken antenatal checkups. Her routine investigations were within normal limits. USG revealed anomalous fetus with absent cardiac activity. With the informed consent, the pregnancy was terminated and abortus was sent for pathological examination. At autopsy, it was a male fetus and weighed 580 g. On external examination, the head was severely retroflexed and no neck. Ears were low set and short lordotic spinal column [Figure 2e and f]. Umbilical cord was unremarkable.

CT scan revealed defective development of endochondral portion of occipital bone. Retroflexed head was seen in fusion with fused upper cervicothoracic vertebrae. Enlarged foramen magnum, short irregular vertebral column, and mild club foot were noted [Figure 2g]. MRI in addition to CT findings, showed bifid spine. Corpus callosum was not visualized. Lateral ventricles were dilated in the posterior horn (colpocephaly) and configurations of the infratentorial structures were distorted [Figure 2h and i]. Autopsy confirmed all the above findings. All other visceral organs were normal. With the above features, a pathological diagnosis of iniencephaly clauses was made.

Discussion

Iniencephaly is an uncommon NTD. The word inion is derived from Greek meaning occiput.^[4] The first description of iniencephaly is attributed to Saint-Hilare in 1836.^[5] Incidence of this rare anomaly is 0.1-10 in 10,000 pregnancies. In this condition, posterior most part of the head (occiput) is fused with the back leading to severe retroflexion of the head.^[4] Till date approximately 250 such cases have been reported in the literature.^[6]

The exact etiology of this condition is not known. Environmental factors such as poor socioeconomic conditions, lack of folic acid supplementation, obesity, drugs (sulfonamides, tetracycline, antihistaminic),

genetic factors such as monosomy X, trisomy 13, trisomy 18, and chromosomal abnormalities are implicated in the etiology of this condition.^[4] Balci *et al.*^[1] in their study observed mutation in methyl tetrahydrofolate reductase gene (677C→T) in parents of iniencephaly indicating possible etiology.

The defects in iniencephaly occur in the early pregnancy prior to the closure of cephalic neural fold at 24 days of gestational age. The paravertebral mesoderm differentiates into two parts wherein ventral mass forms the vertebral bodies, pedicles, and cranial homologues. Dorsal mass forms the neural arches and bones of the cranial vault. In iniencephaly, one or both of these masses are malformed. Initially it was believed that neural tube closure begins in the cervical region and extends rostrally and caudally, but now evidences suggest that neural tube closure is a multisite initiation process and five closure sites are proposed (Site 1: Mid cervical, 2: Between prosencephalon and mesencephalon, site 3: Stomodeum, site 4: Caudal end of rhombencephalon, and site 5: Caudal end of neural tube). Iniencephaly occurs due to the defect at site 1 and 4.^[7]

Iniencephaly is usually associated with systemic anomalies. The observed central nervous system anomalies include anencephaly, encephalocele, cyclopia, hydrocephalus, and holoprosencephaly. Other systemic anomalies reported in the literature are cardiac septal defects, cleft lip and palate, pulmonary hypoplasia, right lung with two lobes, omphalocele, congenital diaphragmatic hernia (CDH), intestinal atresia, imperforate anus, horseshoe kidney, bronchogenic cysts, genital malformations, and skeletal abnormalities such as club foot and overgrowth of upper limbs compared with lower limbs.^[1,5-8] In the present case series, pulmonary hypoplasia, omphalocele, disproportionate limbs, accessory spleen, ASD, spina bifida, colpocephaly, and club foot were noted. Accessory spleen association with iniencephaly observed in the present case is previously not reported in the literature. Pulmonary hypoplasia, CDH, and omphalocele occur due to increased pressure in the thoracic and abdominal cavity due to exaggerated spinal retroflexion.^[7] Halder *et al.*,^[7] in their large series on iniencephaly of 19 cases, observed 3 cases of cardiac septal defects, 5 cases of pulmonary hypoplasia, 1 case of horseshoe kidney, 2 cases each of omphalocele, gastrointestinal malformation and dandy walker malformations, 3 cases of adrenal hypoplasia, and 1 case of thymic hypoplasia.

Congenital retroflexion of spine is seen in conditions such as iniencephaly, anencephaly, Klippel-Feil syndrome (KFS) and nuchal tumors. Iniencephaly apertus needs to be differentiated from anencephaly. In anencephaly there

will be partial or complete absence of cranial vault with retroflexed head, which is not covered by skin, and cervical vertebrae are normal. In contrast, in iniencephaly, the head retroflexed and covered by skin and cervical vertebrae is abnormal. Iniencephaly clausus needs to be differentiated from KFS. KFS is a surgically treatable condition, which is due to the failure of segmentation of cervical vertebrae leading to fusion, but retroflexion of head is not seen, which is a feature of iniencephaly.^[4]

Iniencephaly can be diagnosed antenatally by USG, the fetus typically shows “star-gazing” appearance. A detailed examination of the spine and cranial bones is possible with CT and MRI, but fetal autopsy is gold standard to document the associated anomalies.^[4] MRI is safe in pregnancy as there is no radiation exposure and gives better detailed visualization of organs.^[9]

Iniencephaly carries a bad prognosis and is incompatible with survival. Most of the patients are still born or die soon after birth. Till date there are only six fetuses recorded in the literature with long-term survival.^[6] Of the six fetuses, two required surgery. Gartman *et al.*^[10] suggested that the fibrosed trapezius muscle is the cause for the retroflexion but Edinçler *et al.*^[11] suggested craniocervical junction abnormality. It is the associated nonviable congenital anomalies that determine the longevity of the patient. It also carries a risk of recurrence in subsequent pregnancies (1%-5%).^[4,8]

Conclusion

Iniencephaly is a rare fatal NTD, which occurs due to the defect in the neural tube closure at sites 1 and 4. Because

the condition is incompatible with life, careful and early USG diagnosis is required so that termination can be offered for willing parents. CT and MRI are equally sensitive as autopsy in diagnosis of iniencephaly.

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