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Case Report

Radiologic Features of Anencephaly : A Serial Case Report

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Abstract

Background : Anencephaly is a lethal central nervous system anomaly characterized by absence of cerebral structures and cranial vault. It is the most common open neural tube defect that occurs in 0.5 – 2 per 1,000 live births. This anomaly can be detected as early as 11 weeks of pregnancy by transvaginal ultrasonography. Micronutrient deficiency, such as anemia and folic acid deficiency, was known to be the potential risk factor for anencephaly.
Case Report : We reported 4 cases of anencephaly diagnosed using ultrasonography during pregnancy. All patients were referred to Dr. Kariadi General Hospital from private hospitals in Central Java. There are 3 out of 4 cases were diagnosed in the first trimester and 1 case was diagnosed in the third trimester. Ultrasonography features showed typical signs of anencephaly including 'frog eyes sign', 'Mickey mouse sign' and acrania. All of the patients underwent termination of pregnancy with variable route of delivery according to condition and gestational age.
Discussion : Routine antenatal ultrasonography is recommended for early detection of fetal viability and other congenital anomalies including anencephaly. Ultrasonography is able to detect typical findings of anencephaly and therefore is able to accurately establish the diagnosis. Advanced imaging technique such as MRI is unnecessary unless diagnosis using ultrasonography is indeterminate. Enforcement of diagnosis of anencephaly is very important due to determining its definitive treatment, in which termination of pregnancy.
Conclusion : presented various radiologic features of anencephaly using ultrasonography may clinicians will be able to diagnose this anomaly in earlier age of pregnancy. So, definitive treatment can be done and complications during pregnancy can be prevented.
Keywords : Anencephaly, neural tube defect, ultrasonography

INTRODUCTION

Anencephaly is a lethal central nervous system anomaly characterized by absence of cerebral structures and cranial vault. This anomaly is a result of an open neural tube defect which occurs in 23rd to 28th days after conception.[1] Anencephaly is the most common open neural tube defect with incidence of 0.5 – 2 per 1,000 live births. Females are affected more frequently with a ratio of 4 : 1. The susceptibility of females has been suggested to result from the difference between male and female embryos in some specific aspects of the neurulation process. Anencephaly is relatively more common in Caucasian than in Asian. The etiology is unclear but there are possible risk factors including advanced maternal age, diabetes mellitus, antiepileptic drugs, radiation and chromosomal anomalies.[2]

The pathogenesis is still controversial, either a failure of closure of the neural tube or reopening after closure has been hypothesized. Other anomalies, such as vertebral anomalies, omphalocele and other systemic anomalies, are often associated with anencephaly and can be detected using ultrasonography as early as 11 weeks of pregnancy. Despite the ability to diagnose using ultrasonography, advanced imaging modality such as magnetic resonance imaging (MRI) is required in indeterminate cases.[3] Anencephaly is uniformly lethal. Fatal complications include stillbirth or death shortly after birth. Once the diagnosis is made, patients should be offered termination of pregnancy. Ability to detect anencephaly using ultrasonography is required so that definitive treatment in which termination of pregnancy can be done with minimal maternal morbidity.[4] In this serial case series, we present various radiologic features of anencephaly using ultrasonography so that clinicians will be able to diagnose this anomaly in earlier age of pregnancy. Hence, maternal complications and morbidity can be prevented.

CASE REPORTS

In this article, we presented 4 cases of pregnancy with anencephaly fetus. We present the resume of all patients' sociodemographic data is shown in Table 1. All patients were primipara with age under 30 years old and referred to Dr. Kariadi General Hospital from private hospitals in Central Java. 3 out of 4 cases were diagnosed in the first trimester and 1 case was diagnosed in the third trimester. Ultrasonography features showed typical signs of anencephaly including 'frog eyes sign', 'Mickey mouse sign' and acrania.

Case #1

27 y.o female was referred to Dr. Kariadi General Hospital with a suspicion of anencephaly fetus from ultrasonography examination at private hospital (Table 1). Personal history was unremarkable with no history of anemia or vaginal bleeding during pregnancy. Laboratory examination showed normal hemoglobin levels (Table 2). Ultrasonography was first performed at 12 weeks of pregnancy showing intrauterine single fetus with acrania. Examination was then repeated at 15 weeks of pregnancy showing intrauterine single fetus with normal fetal biometry, fetal heart rate and fetal movement. On sagittal plane, ultrasonography showed 'frog eyes sign' and on coronal plane, ultrasonography showed 'Mickey mouse sign' (Figure 1). Diagnosis of anencephaly was made and patients was offered termination of pregnancy (Table 2).

Case #2

28 y.o female was referred to Dr. Kariadi General Hospital with a suspicion of anencephaly fetus from ultrasonography examination at private hospital (Table 1). Personal history was unremarkable with no history of anemia or vaginal bleeding during pregnancy. Laboratory examination showed normal hemoglobin

TABLE 1
Sociodemographic data

Variable	Case 1	Case 2	Case 3	Case 4
Patient's age	27 y.o	28 y.o	27 y.o	27 y.o
Husband's age	30 y.o	29 y.o	29 y.o	30 y.o
Parity	Primipara	Primipara	Primipara	Primipara
Referral	Yes	Yes	Yes	Yes
Origin of referral	Private hospital	Private hospital	Private hospital	Private hospital
Hospital billing	Private insurance	Private insurance	Private insurance	Personal expense
Gestational age	15 weeks	13 weeks	28 weeks	14 weeks
Gestational age at timeof diagnosis	12 weeks	12 weeks	26 weeks	11 weeks

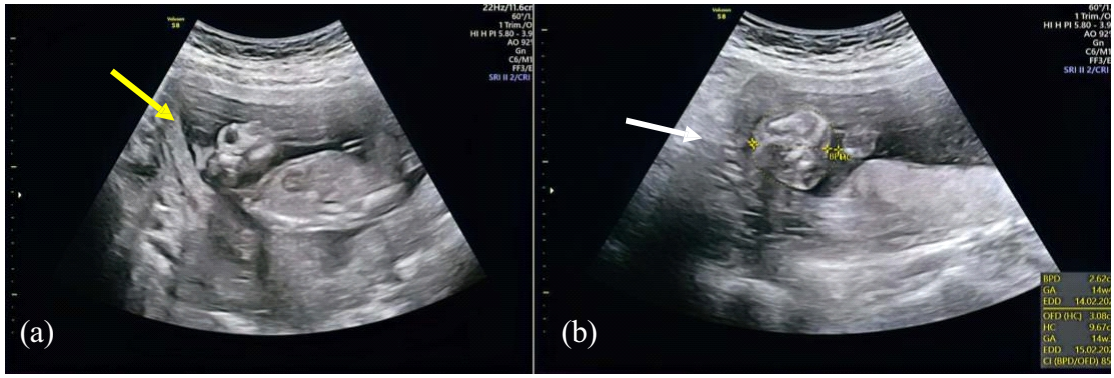

Figure 1. (a) Ultrasonography on sagittal plane showed prominent orbital structure with absence of cerebral hemisphere and cranial vault, resembling an appearance of frog eyes (yellow arrow). (b) On coronal plane, ultrasonography showed an appearance of 'Mickey mouse sign' (white arrow).

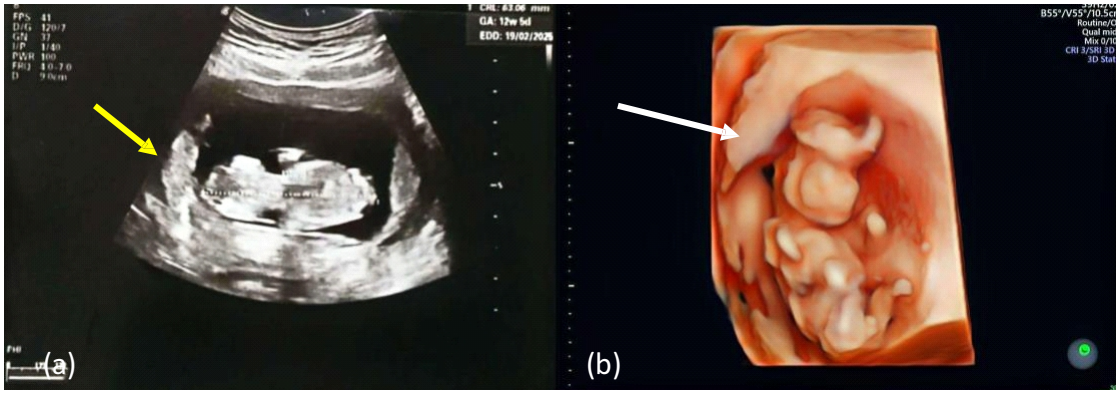

Figure 2. (a) Ultrasonography on coronal plane showed prominent orbital structure with absence of cerebral hemisphere and cranial vault, resembling an appearance of frog eyes (yellow arrow). (b) On 3D ultrasonography examination, absence of cranial vault was clearly shown (white arrow).

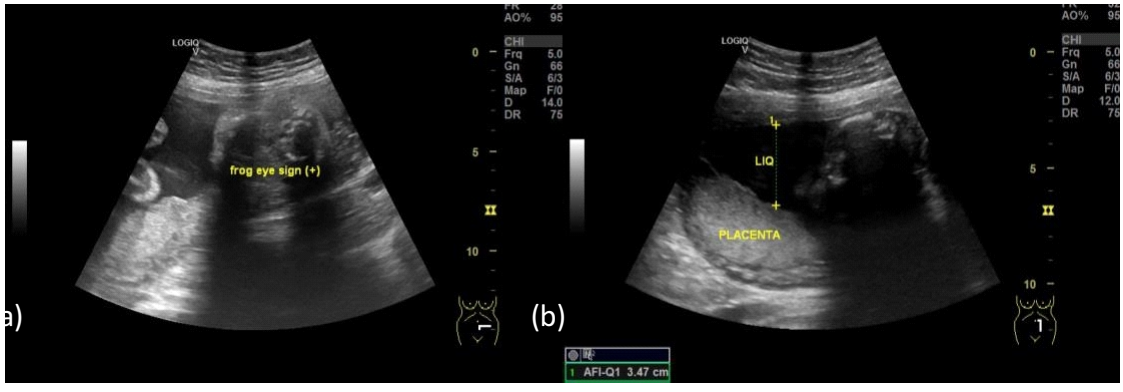

Figure 3. (a) Ultrasonography on coronal plane showed prominent orbital structure with absence of cerebral hemisphere and cranial vault, resembling an appearance of frog eyes. (b) No signs of polyhydramnios showed by normal AFI and single pocket depth.

levels (Table 2). Ultrasonography was first performed at 12 weeks of pregnancy showing intrauterine single fetus with acrania. Examination was then repeated at 13 weeks of pregnancy showing intrauterine single fetus with normal fetal biometry, fetal heart rate and fetal movement. On coronal plane, ultrasonography showed 'frog eyes sign' and 3D ultrasonography showed absence of cranial vault (Figure 2). Diagnosis of anencephaly was made and patients was offered termination of pregnancy. (Table 2).

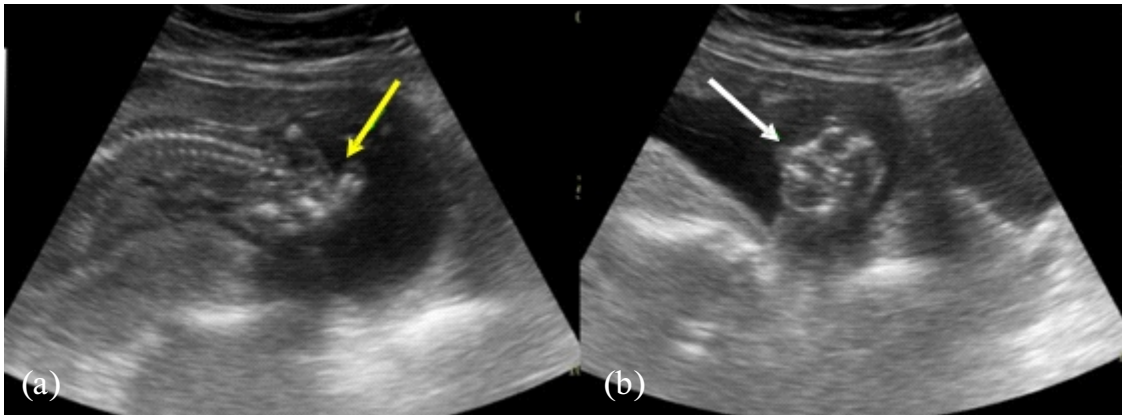

Figure 4. (a) Ultrasonography on sagittal plane showed absence of cranial vault (yellow arrow). (b) On coronal plane, prominent orbits were clearly shown (white arrow).

TABLE 2
Clinical data

Variable	Case 1	Case 2	Case 3	Case 4
Laboratory (hemoglobin)	12.3g/dL (normal)	12.5g/dL (normal)	10g/dL (low)	9.1 g/dL (low)
Treatment	Termination of pregnancy	Termination of pregnancy	Vaginal delivery	Spontaneous vaginal delivery
Length of stay	n/a	n/a	3 days	3 days

Case #3
27 y.o female was referred to Dr. Kariadi General Hospital with a suspicion of anencephaly fetus from ultrasonography examination at private hospital (Table 1). Personal history was unremarkable. Laboratory examination showed low hemoglobin level (Table 2). Ultrasonography was first performed at 11 weeks of pregnancy showing intrauterine single fetus with no congenital anomalies. Examination was then repeated at 26 weeks of pregnancy showing intrauterine single fetus with normal fetal biometry, fetal heart rate and fetal movement. On coronal plane, ultrasonography showed 'frog eyes sign' and normal amniotic fluid index (AFI) with no signs of polyhydramnios (Figure 3). Diagnosis of anencephaly was made and patients was offered termination of pregnancy. Prior to the planned termination date, patient felt periodic contraction with reduced fetal movement. Physical examination showed no fetal heart rate and diagnosis of intrauterine fetal death was made. Vaginal delivery was done to reduce maternal complications and morbidity (Table 2).

Case #4
27 y.o female was referred to Dr. Kariadi General Hospital with a suspicion of anencephaly fetus from ultrasonography examination at private hospital (Table 1). Personal history was unremarkable. Laboratory examination showed low level of hemoglobin (Table 2). Ultrasonography was first performed at 11 weeks of pregnancy showing intrauterine single fetus with acrania. Examination was then repeated at 14 weeks of pregnancy showing intrauterine single fetus with normal fetal biometry, fetal heart rate and fetal movement. 'Frog eyes sign' and acrania was discovered and diagnosis of anencephaly was made (Figure 4). Patient was offered termination of pregnancy but prior to the planned termination date, patientcame to emergency department with complaint of vaginal bleeding. Patient was having a spontaneous vaginal delivery and no additional curettage therapy was needed (Table 2).

We present the resume of all patients' clinical data is shown in Table 2. 2 out of 4 patients were present with anemia with low level of hemoglobin below 10 g/dL. Two patients underwent termination of pregnancy using curettage method and two other patients underwent vaginal delivery as the method of pregnancy termination.

DISCUSSION

The neural tube closes within the first 28 days of development. Fusion starts in the mid region and then extends in both directions to form the neural tube. The ends of the tube, called the anterior and posterior

neuropores, close later. Failed closure of the anterior neuropore results in anencephaly, whereas failed closure of the posterior neuropore results in spina bifida. Both pathology was classified as open neural tube defect in which anencephaly is the most common and the most lethal congenital anomaly with worst prognosis. The etiology is still unknown andvarious factors known to play a role in increasing the risk of anencephaly. Among those factors, folate deficiency is known to be the most important in neural tube fusion process. [5,6]

We reported 4 cases of primipara patients with age range below 30 years old and present with anencephaly fetus. The age of these patients is still considered as optimal age for risk-free pregnancy in which below 35 years old. Therefore, primipara conditions are not a risk factor for anencephaly, but primiparas with reproductive age tend to have micronutrient deficiencies such as anemia, vitamin B12 deficiency and folate deficiency. In this case report, we found 2 patients with anemia characterized by low level of hemoglobin. Anemia and folate deficiency are two related conditions in which folate deficiency can cause normochromic macrocytic anemia and both can be major risk factors for anencephaly. Providing iron and folate supplements to pregnant women is recommended and able to reduce the risk of neural tube defect. The recommended dose is 400 µg per day for 1 month before pregnancy and for patients with a history of anencephaly the recommended dose is 4 mg per day. [7,8]

The first line modality in diagnosing anencephaly is using ultrasonography examination. Ultrasonography will be able to discover typical signs of anencephaly such as 'frog eyes sign', 'Mickey mouse sign' and acrania. These typical signs are due to defects in the scalp and calvarium and the absence of both cerebral hemispheres. In addition to these signs, polyhydramnios can also be found in anencephaly as an indirect sign due to impaired swallowing ability in fetus. These ultrasonography features can be detected at as early as 11 weeks of pregnancy using transvaginal ultrasonography.[9] We reported 4 patients in which 3 of them were diagnosed with anencephaly in first trimester, whereas 1 of them were diagnosed in third trimester. Ultrasonography of the 4 patients in this case report showed the absence of cerebral hemispheres and cranial vault making an appearance of 'Mickey mouse sign' and prominent orbital structures making an appearance of 'frog eyes sign'. Both features support the diagnosis of anencephaly using ultrasonography examination. Although ultrasonography examination can diagnose anencephaly accurately, there are still some exceptions that require more advanced imaging modalities, such as MRI. MRI is used in indeterminate case where ultrasonography is not be able to confirm anencephaly and to rule out other possible differential diagnosis. Absence of cerebral hemisphere can accurately depicted using MRI and presence of differential diagnosis such as exencephaly can be ruled out using this modality (Figure 4). In this case report, all four patients could be diagnosed accurately using ultrasonography examination so that MRI examination was no longer needed. [10,11]

Anencephaly can also be diagnosed using alpha fetoprotein (AFP) level examination in amniotic fluid and maternal blood serum as additional examination. In pregnancies with anencephaly and other open neural tube defects, there is an increase in AFP due to AFP produced in liver and fetal yolk sac can easily escape into the amniotic fluid and maternal circulation through defect. But due to its invasiveness measuring AFP levels in amniotic fluid, the examination was not done in our patients. [14,15]

Reinforcement of diagnosis of anencephaly is very important due to determining its definitive treatment, in which termination of pregnancy. In this case report, all 4 patients underwent termination of pregnancy with variable route of delivery according to each patients' condition and gestational age. The third case underwent vaginal delivery due to intrauterine fetal death and the fourth case underwent spontaneous vaginal delivery with no additionalcurettage therapy needed. The first two cases were planned to have termination of pregnancy. The route of delivery is chosen according to the patient's gestational age with the least maternal complications and morbidity rate, in which vaginal delivery. The very low life expectancy with a mortality rate of 100% in anencephaly makes termination of pregnancy the definitive management. However, there are also several cases of anencephaly that are born alive with the longest life expectancy being 28 days. This is due to an intact brain stem in anencephaly so that the baby can breathe spontaneously, respond to light and move its extremities. In cases of babies with anencephaly who are born alive, supportive therapy is still given according to the baby's condition. [16]

CONCLUSION

Ultrasonography is the first line modality in diagnosing anencephaly. Routine antenatal ultrasonography is recommended for early detection of fetal viability and other congenital anomalies. Ultrasonography is required to detect anencephaly. Hence, complications and mortality during pregnancy can be prevented.

ABBREVIATIONS

AFP = amniotic fluid index ; AFP = alpha feto protein ; MRI = magnetic resonance imaging.

ETHICAL APPROVAL AND INFORMED CONSENT

Written informed consents were already taken and signed by all patients and their family members . All data collection tools were used anonymously to maintain confidentiality of data. Participation in the study was on a fully voluntary basis.

DISCLOSURE

All authors declare that they have no conflicts of interest.

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