PERINATAL JOURNAL

Original Article

Perinatal Journal 2015;23(3):175–179

Anencephaly and coexisting malformations: analysis of 35 cases

Senem Yaman Tunç, Elif Ağaçayak, Mehmet Sait İçen, Fatih Mehmet Fındık, Ahmet Yıldızbakan, Burcu Yücesoy, Ahmet Yalınkaya

Department of Gynecology and Obstetrics, Faculty of Medicine, Dicle University, Diyarbakır, Turkey

Abstract

Objective: We aimed to analyze clinical and demographic characteristics of 35 cases hospitalized in our clinic with the diagnosis of fetal anencephaly and the correlation with other anomalies.

Methods: The patients hospitalized in the Gynecology and Obstetrics Clinic of the Faculty of Medicine at Dicle University for the termination of pregnancy due to the diagnosis of fetal anencephaly between June 2013 and May 2015 were included in this retrospective study. The information of patients such as age, gravida, parity, week of gestation, ultrasonographic findings and coexisting anomalies were accessed through their medical files.

Results: A total of 35 cases were included in the study. Mean age of the patients was 27.7±7.4. Their mean week of gestation during diagnosis was 17±4.6 weeks. In our study, we found the anomaly incidence associated with anencephaly as 65.7%. Polyhydramnios was found in 14.3% (n=5) of the cases; while 22 fetuses were female, 13 fetuses were male. The most common anomalies coexisting with anencephaly were spina bifida (n=12), pes equinovarus (n=4), iniencephaly (n=2), omphalocele (n=2), gastroschisis (n=1), and cleft palate/lip (n=2), respectively.

Conclusion: Anencephaly is the most common type of neural tube defects and there is additional anomaly in most of the cases. In our study, the anomalies coexisting with anencephaly are spina bifida, pes equinovarus, iniencephaly, omphalocele, gastroschisis, and cleft palate/lip.

Keywords: Anencephaly, iniencephaly, omphalocele, spina bifida.

Özet: Anensefali ve eşlik eden malformasyonlar: 35 olgunun analizi

Amaç: Kliniğimize fetal anensefali tanısı ile yatırılan 35 olgunun klinik ve demografik özelliklerini ve diğer anomaliler ile ilişkisini değerlendirmektir.

Yöntem: Bu retrospektif çalışmaya Haziran 2013 ile Mayıs 2015 tarihleri arasında Dicle Üniversitesi Tıp Fakültesi Kadın Hastalıkları ve Doğum Anabilim Dalı Kliniğine fetal anensefali tanısı ile gebelik terminasyonu için yatırılan hastalar dahil edildi. Hastaların yaş, gravida, parite, gebelik haftası, ultrasonografik bulgular ve eşlik eden anomaliler gibi bilgilerine hasta dosyaları incelenerek ulaşıldı.

Bulgular: Çalışmaya toplam 35 olgu alındı. Hastaların yaş ortalaması 27.7±7.4 idi. Tanı esnasında ortalama gebelik haftaları 17±4.6 hafta idi. Çalışmamızda anensefali ile ilişkili anomali sıklığını %65.7 olarak bulduk. Olguların %14.3'ünde (n=5) polihidramniyos mevcuttu, 22 fetüs kız, 13 fetüs ise erkek cinsiyette idi. Anensefaliye eşlik eden en sık anomaliler sırasıyla; spina bifida (n=12), pes ekinovarus (n=4), iniensefali (n=2), omfalosel (n=2), gastroşizis (n=1), yarık damak/dudak (n=2) idi.

Sonuç: Anensefali, nöral tüp defektlerinin en yaygın tipidir ve olguların çoğunda ek anomali mevcuttur. Bizim çalışmamızda anensefaliye eşlik eden anomaliler; spina bifida, pes ekinovarus, iniensefali, omfalosel, gastroşizis ve yarık damak/dudaktır.

Anahtar sözcükler: Anensefali, spina bifida, iniensefali, omfalosel.

Introduction

On the 4th week of embryonic development, dorsal neural tube being unable to get closed causes abnormal vascularization of embryonic exencephalic brain.[1] Nerve tissue than degenerates and the brain becomes a spongiform vascular mass.[2] Rostral neural tube closes on 25th day after conception, and caudal neural tube closes 2 days later.[3] While anencephaly is the result of the incomplete closing of rostral neural tube on approximately postovulatory 25th day, spina bifida is the result of the incom-

Correspondence: Senem Yaman Tunç, MD. Dicle Üniversitesi Tıp Fakültesi, Kadın Hast. ve Doğum Anabilim Dalı, Diyarbakır, Turkey. e-mail: drsenemtunc@hotmail.com

Received: August 25, 2015; **Accepted:** November 10, 2015

Please cite this article as: Yaman Tunç S, Ağaçayak E, İçen MS, Fındık FM, Yıldızbakan A, Yücesoy B, Yalınkaya A. Anencephaly and coexisting malformations: analysis of 35 cases. Perinatal Journal 2015;23(3):175–179.

Available online at: www.perinataljournal.com/20150233009
doi:10.2399/prn.15.0233009
QR (Quick Response) Code:

deomed

plete closing of caudal neural tube on approximately postovulatory 27th day.[4] Anencephaly is the heavy defect of cerebrospinal development.[5,6] This malformation usually coexists with craniorachischisis (fissure in vertebral colon). Also, cleft palate/lip, and omphalocele may coexist.[7] In this study, we analyzed the clinical and demographic characteristics and coexisting anomalies of 35 anencephaly cases hospitalized in our clinic.

Methods

Approval for this retrospective study was obtained from the Ethics Committee for Non-Invasive Clinical Researches of Faculty of Medicine, Dicle University (12/06/2015; No. 269). Thirty-seven patients hospitalized in the Gynecology and Obstetrics Clinic of the Faculty of Medicine at Dicle University for the termination of pregnancy due to the diagnosis of fetal anencephaly between June 2013 and May 2015 were included in this study. The information of patients such as age, gravida, parity, week of gestation, ultrasonographic findings and coexisting anomalies were accessed through their medical files. The information such as maternal diseases, smoking habit, teratogenuos exposure, folic acid use, kin marriage, history of baby with neural tube defect were obtained from patients by phone. Two patients who could not be reached were excluded from the study. A total of 35 patients were included in the study. The analysis of the data was done by SPSS 18.0 (SPSS Inc., Chicago, IL, USA). The data was analyzed by definitive statistics. Continuous variables were given as mean±standard deviation.

Results

A total of 3621 live deliveries were carried out between June 2013 and May 2015 in the Gynecology and Obstetrics Department of the Faculty of Medicine, Dicle University, and 63 of them had neural tube defect (NTD). We found NTD incidence as 17.4 per 1000 live births in our study. Thirty-seven of 63 cases with NTD were diagnosed as anencephaly. We found anencephaly incidence as 10.2 per 1000 live births in our study. Mean age of the patients included in the study was 27.7±7.4. Mean week of gestation of the patients during hospitalization was 17±4.6 weeks. NTD history in previous pregnancies was found in 14.3% (n=5) of the patients. While no polyhydramnios was found in 85.7% (n=30) of the patients, 14.3% (n=5) of them had polyhydramnios. Fifteen (42.9%) patients were living in the city center while 20 patients (%1) were living in the district. Among the patients, 74.3% (n=26) of them were non-smokers and 25.7% (n=9) of them were smokers. Twenty-two fetuses were female and 13 fetuses were male (**Table 1**). The most common coexisting anomalies were spina bifida (n=12), pes equinovarus (n=4), iniencephaly (n=2), omphalocele (n=2), gastroschisis (n=1), and cleft palate/lip (n=2), respectively (**Table 2**).

Table 1. Demographic and clinical characteristics of the cases.

Özellikler	n
Total case number	35
Maternal age	17–44 yaş
≤20-year-old (%)	20
≥35-year-old (%)	22.8
Gravida	1–8
Mean±SD	3.5±2.4
Parity	0–6
Mean±SD	2±1.9
Week of gestation during diagnosis	11–30
Mean±SD	17±4.6
Phase of gestation during diagnosis (%)	
1st trimester	22.9
2nd trimester	68.6
3rd trimester	8.6
Preconceptional folic acid use (%)	
Yes (%)	22.9
No (%)	77.1
NTD history in previous pregnancy (%)	
Yes	85.7
No	14.3
Smoking (%)	
Yes	25.7
No	74.3
Kin marriage (%)	
Yes	22.9
No	77.1
Residential area (%)	
City center	42.9
District	51.4
Village	5.7
Polyhydramnios (%)	
Yes	14.3
No	85.7
Fetal sex (%)	
Female	62.9
Male	37.1

NTD: neural tube defect; **SD:** standard deviation

Table 2. The distribution of anomalies coexisting with anencephaly.

Anomaly	n	%	Description
Spina bifida	12	34.3	Craniospinal rachischisis in 10 cases Thoracolumbar spina bifida in 2 cases
Iniencephaly	2	5.7	
Skeletal deformity	4	11.4	Pes equinovarus in 4 cases
Cleft palate/lip	2	5.7	Cleft palate in 1 case Cleft lip in 1 case
Gastrointestinal anomalies	3	8.5	Omphalocele in 2 cases Gastroschisis in 1 case

Discussion

Neural tube defects are among the most severe congenital anomalies in Turkey and epidemiological findings show that the prevalence varies according to regional and demographical characteristics. According to the studies conducted in various cities of Turkey, NTD incidence varies between 3 and 5.8 per thousand.[8] In our study, we found NTD incidence about 17.4 per thousand, which is quite above the average of Turkey. This result is caused by the fact that our hospital is the referral hospital in the region.

Anencephaly is characterized by the outward exposure of cranial neural tube and a defect open in the calvarium. It is one of the three major neural tube defects. The other two defects are encephalocele and spina bifida. Anencephaly is a severe congenital defect incompatible with life. Babies born live usually dies within hours, or rarely may live a few days or a few weeks. In our study including 35 cases, mean maternal age was 27.7±7.4. There were 7 cases below 20-year-old and 8 cases above 35-year-old.

With the current ultrasonography technology, it is possible to identify almost all anencephaly cases. In the last decade, some papers have been published reporting that anencephaly diagnosis can be established as of 10 weeks of gestation. Anencephaly diagnosis can be established by identifying the lack of cranial dome. However, since current brain tissue may be in variable amounts, it may be difficult to establish this diagnosis in the first trimester in particular.[9,10]

In our study, mean week of gestation during diagnosis was 17±4.6 weeks. Eight cases (22.9%) were diagnosed in the first trimester, 24 cases (68.6%) were identified in the second trimester, and 3 cases (8.6%) were diagnosed in the third trimester. The reason for diagnosing most of the patients during the second trimester in our study can be associated to the fact that many of the cases (57.1%) live in small residential areas such as villages and districts. We believe that the diagnosis delayed due to the difficulties during first trimester for reaching a center capable of conducting prenatal screening. In a study carried out in Brazil, mean week of gestation during diagnosis was found as 21.3 weeks.[11] This result is consistent with the results of our study.

In the studies carried out, the rate of fetuses with anomalies coexisting with anencephaly was provided in a wide range. Tan et al. reported the rate as 9.4%[12] while David et al.[13] reported it as 84%. In another study conducted in India, the rate of coexisting anomaly in 20 patients with anencephaly was reported as 80%.[14] In our study, we found coexisting anomaly in 23 (65.7%) of 35 cases with anencephaly. It was found in various studies that anencephaly is more common among female fetuses.[13–16] In conformity with the literature, 22 (62.9%) fetuses were female and 13 (37.1%) fetuses were male in our study. About 40–50% of cases with anencephaly have polyhydramnios, and oligohydramnios is observed rarely.[17] In the analysis of 30 cases with anencephaly, Kurjak et al. reported that polyhydramnios did not develop before 25 weeks.[18] We found polyhydramnios in 14.3% (n=5) of our cases, amniotic fluid was within normal ranges in 85.7% (n=30) of them. Five cases with polyhydramnios were at 25 weeks of gestation or above.

In our study, the most common anomalies coexisting with anencephaly were spina bifida (craniospinal rachischisis in 10 cases, thoracolumbar spina bifida in 2

cases), pes equinovarus (4 cases), cleft palate/lip (2 cases), iniencephaly (2 cases) and gastrointestinal anomalies (3 cases). Craniospinal rachischisis is the most severe form of spina bifida, and it is observed more in anencephalic fetuses compared to general population.[19,20] In the study of Gole et al., spida bifida was observed in 9 of 20 anencephalic cases, and while 8 of them had cervical craniorachischisis, only one case had lumbar spina bifida.[14] Similarly, we identified spina bifida in 12 of 35 cases in our study; of these cases, 10 cases had craniospinal rachischisis and 2 cases had lumbar spina bifida (**Figs. 1a** and **b**).

Among our cases, 4 (11.4%) cases had pes equinovarus as skeletal deformity. David et al. reported the anencephaly + skeletal deformity incidence as 1.7%,[13] Gole et al. reported as 35%,[14] and Tan et al. reported as 20%.[12]

In our study, 2 (5.7%) cases had iniencephaly. Iniencephaly is characterized with the distinct dorsiflexion of the head and cervical rachischisis. The head is on

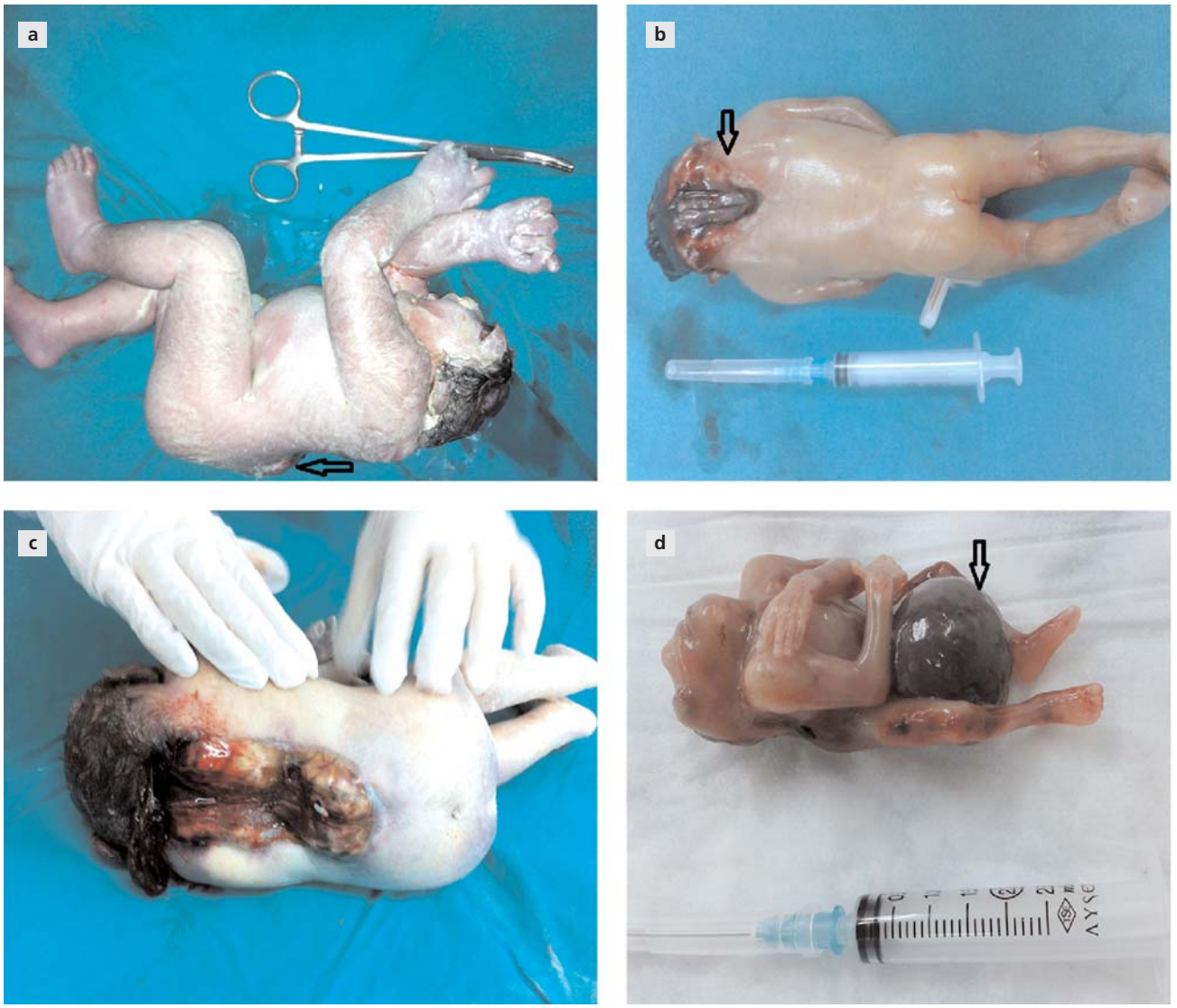

Fig. 1. Anencephaly case (**a**) with spina bifida (**arrow**) in lumbar area. The anencephaly (**arrow**) case (**b**) with craniospinal rachischisis. Craniospinal rachischisis is observed in the case with iniencephaly (**c**). The case (**d**) with iniencephaly and omphalocele (**arrow**).

extreme dorsiflexion due to the lack of foramen magnum and cervical vertebra. Extreme lordosis of cervical spine causes the face to look upward (star observer) (**Fig. 1c**). Forty-eight percent of the fetuses with iniencephaly have coexisting anomalies such as anencephaly, holoprosencephaly, vermian agenesis, cleft palate and lip, abdominal wall defects, anal atresia, and diaphragmatic hernia.[13] In our study, one case with iniencephaly had anencephaly and omphalocele additionally (**Fig. 1d**).

Two cases in our study had cleft palate/lip as facial anomalies. In the studies conducted, cleft palate and lip was reported as facial anomaly in addition to the anencephaly.[13–16] As gastrointestinal anomalies, two cases had omphalocele, and one case had gastroschisis. We found no genital anomaly in our cases. While Nielsen et al.[21] and Golalipour et al.[22] reported no genital anomaly in fetuses with anencephaly, Gole et al.[14] reported hypospadias in two anencephalic male cases.

Conclusion

Anencephaly develops due to the incomplete closing of rostral neural tube; however, its etiology is still controversial. Many studies have been conducted to understand the association between anencephaly and neural tube defects. However, the genetic association of neural tube defects could not be fully explained.[23,24] In anencephaly which is the most common type of neural tube defects, there is an additional anomaly coexisting with anencephaly. In our study, the anomalies coexisting with anencephaly are spina bifida, pes equinovarus, iniencephaly, omphalocele, gastroschisis, and cleft palate/lip.

Conflicts of Interest: No conflicts declared.

References

1. Botto LD, Moore CA, Khoury MJ, Erickson JD. Neural-tube defects. N Engl J Med 1999;341(20):1509–19.
2. Trenouth MJ. Craniofacial shape in the anencephalic human fetus. J Anat 1989;165:215–24.
3. Sadler TW. Langman's medical embryology. Philadelphia, PA: Lippincott Williams & Wilkins: 1990. p. 352.
4. O'Rahilly M, Muller F. Human embryology & teratology. New York, NY: Wiley-Liss, Inc.: 1992. p. 253.
5. Lemire RJ, Beckwith JB, Warkuny J. Anencephaly. New York, NY: Raven Press; 1978.
6. Stone DH. The declining prevalence of anencephalus and spina bifida: its nature, causes and implications. Dev Med Child Neurol 1987;29:541.
7. Merz E. Obstetrik ve jinekolojide ultrasonografi. Çeviri editörü: Özden S. İstanbul: Doğan Tıp Kitabevi; 2009. s. 212.
8. Tunçbilek E. Türkiye'deki yüksek nöral tüp defekti sıklığı ve önlemek için yapılabilecekler. Çocuk Sağlığı ve Hastalıkları Dergisi 2004;47:79–84.
9. Johnson SP, Sebire NJ, Snijders RJ, Tunkel S, Nicolaides KH. Ultrasound screening for anencephaly at 10–14 weeks of gestation. Ultrasound Obstet Gynecol 1997;9:14–6.
10. Becker R, Mende B, Stiemer B, Entezami M. Sonographic markers of exencephaly at 9 + 3 weeks of gestation. Ultrasound Obstet Gynecol. 2000;16:582–4.
11. Pelizzari E, Valdez CM, Picetti Jdos S, Cunha AC, Dietrich C, Fell PR, et al. Characteristics of fetuses evaluated due to suspected anencephaly: a population-based cohort study in southern Brazil. Sao Paulo Med J 2015;133:101–8.
12. Tan KB, Tan SH, Tan KH, Yeo GS. Anencephaly in Singapore: a ten-year series 1993 -2002. Singapore Med J 2007;48:12–15.
13. David TJ, Nixon A. Congenital malformation associated with anencephaly and inencephaly. J Med Gen 1976;13:263–65.
14. Gole RA, Meshram PM, Hattangdi SS. Anencephaly and its associated malformations. J Clin Diagn Res 2014;8:7–9.
15. Panduranga C, Kangle R, Suranagi W, Pilli GS, Patil PV. Anencephaly: a pathological study of 41 cases. J Sci Soc 2012; 39:81–4.
16. Aruna E, Diddi RR, Vallabhaneni KC. Anencephaly: a 3 years study. IOSR Journal of Dental and Medical Sciences (IOSR-JDMS) 2013;12:12–5.
17. Fiske CE, Filly RA. Ultrasound evaluation of the normal and abnormal fetal neural axis. Radiol Clin N Am 1982;20:285–96.
18. Kurjak A. Direct ultrasonic diagnosis of fetal malformations and abnormalities. In: Murken JD, Stengel-Rutkowski S, Schwinger E, editors. Prenatal diagnosis: Proceedings of the Third European Conference on Prenatal Diagnosis of Genetic Disorders. Stuttgart: Enke; 1979. p. 22–23.
19. Horowitz I, Mc Donald AD. Anencephaly and spina bifida in the province of Quebec. Can Med Assoc J 1969;100:748–55.
20. Sadlerr TW. Langman's medical embryology. Central nervous system. 11th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2010. p. 302–16.
21. Nielsen LA, Maroun LL, Broholm H, Laursen H, Graem N. Neural tube defects and associated anomaliesin a fetal and perinatal autopsy series. APMIS 2006;114:239–46.
22. Golalipour MJ, Najafi L, Keshtkar AA. Prevalence of anencephaly in Gorgan, northern Iran. Arch Iran Med 2010;13:34–7.
23. Botto LD, Yang Q. 5,10-Methylenetetrahydrofolate reductase gene variants and congenital anomalies: a HuGE review. Am J Epidemiol 2000;151(9):862–77.
24. Melvin EC, George TM, Worley G, Franklin A, Mackey J, Viles K, et al. Genetic studies in neural tube defects. Pediatr Neurosurg 2000;32:1–9.