

DOI: 10.4274/tpa.507



The role of anencephalic neonates in organ transplantation: A case report

Mehmet Yekta Öncel¹, Erhan Çalışıcı¹, Hatice Tatar Aksoy¹, Ramazan Özdemir¹, Şerife Suna Oğuz¹,
Ömer Erdeve², Nurdan Uraş¹, Uğur Dilmen^{1,3}

¹Zekai Tahir Burak Women's Health Education and Research Hospital, Neonatology Clinic, Ankara, Turkey

²Ankara University Medical Faculty, Department of Pediatrics, Division of Neonatology, Ankara, Turkey

³Yıldırım Beyazıt University Medical Faculty, Department of Pediatrics, Ankara, Turkey

Summary

Currently, a large number of patients are waiting for organ transplantation and newborns with anencephaly are thought to be potential candidates for organ transplantation. A male baby was born to a 30-year-old mother after 38 weeks of gestation with a birth weight of 2430 g. Antenatal ultrasonography performed during the last months of the pregnancy revealed the presence of anencephaly. The parents were asked for organ donation from the infant and informed consent was obtained. The infant died at the 24th hours of his life. Therefore the diagnosis of the brain death which required two clinical examinations and two electroencephalographic examinations with an interval of 48 hours could not be achieved. It is not a practical approach in such cases to make a diagnosis of brain death with electroencephalography. Therefore, new approaches should be developed for anencephalic newborns. Ethical and legal issues on this subject are still controversial. Here we present the challenges posed by this case and also discuss the difficulty involved in choosing anencephalic neonates as candidate organ donors. (*Turk Arch Ped* 2013; 48: 165-168)

Key words: Anencephaly, ethic, newborn, organ transplantation

Introduction

Neural tube defects (NTD) are the most common congenital anomaly following cardiac anomalies. This anomaly has been screened since 1970s with the development of ultrasonography (USG) during regular follow-up of pregnant women (1). Anencephaly which is one of the neural tube defects occurs as a result of failure of closure of the cephalic part of the neural tube until the 6th week. Anencephaly may be defined ultrasonographically with absence of the cranial bones above the cranial base (especially frontal) and both hemispheres in the second and third months (2). Anencephaly is observed in 0.03% of all births. It occurs with a 3-4-fold higher rate in the female fetus compared to the male fetus. The frequency of anencephalic birth is being gradually decreasing with the widespread use of prenatal USG and maternal serum screenings (3).

Since anencephalic newborns have a brain stem, they can also have spontaneous breathing. When cardiac and respiratory functions stop in these newborns, they are considered exitus (4). Because of small number of compatible organs for infants for transplantation worldwide use of anencephalic newborns as donors has come to the fore. Despite initiations in many countries ethical and legal issues have not been solved yet (5). In this article, use of an anencephalic patient as donor for organ transplantation and the problems which can be faced in this process were emphasized.

Case

The APGAR scores in the 1st and 5th minutes of a male baby born with a gestational age of 32 weeks by the vaginal route from the third pregnancy of a 33-year old mother as the third living child with a birth weight of 2430 g were found

Address for Correspondence: Mehmet Yekta Öncel MD, Zekai Tahir Burak Women's Health Education and Research Hospital, Neonatology Clinic, Ankara, Turkey

E-mail: dryekta@gmail.com **Received:** 03.02.2011 **Accepted:** 09.05.2011

Turkish Archives of Pediatrics, published by Galenos Publishing

to be 2 and 4. Maternal history revealed that the pregnancy follow-up was not done regularly and anencephaly was found on USG performed in the last months prenatally. There was no consanguineous marriage between the mother and the father. The patient had two healthy siblings aged 7 and 10 years.

On physical examination of the newborn performed just after the delivery, an ancephalocel covered with scalp with leakage of blood and cerebrospinal fluid (CSF) in places was found (Picture 1). Cranium bones could not be palpated. The pupils were anisocoric and light reflex was negative. Breathing was superficial and intercostal-subcostal retractions were observed. A II/VI pansystolic murmur was heard in the 3-4th intercostal space in the left side of the sternum. The newborn who had respiratory distress was intubated and mechanical ventilation was started. Intravenous fluid and inotropic support were started. Laboratory tests revealed that complete blood count, blood gases, serum electrolytes and hepatic and renal functions were normal. On superficial USG performed on the ancephalocel in the posterior part of the head, brain tissue was not observed and CSF was present in this area. Association of anencephaly and ancephalocel was considered. On abdominal USG performed in terms of additional anomaly, only the left kidney was found to be localized ectopically in the pelvis. On echocardiography, patent foramen ovale (PFO), patent ductus arteriosus (PDA) and perimembraneous wide ventricular septal defect (VSD) were found. The family was interviewed about the baby being a donor for transplantation and consent was obtained. In pediatric neurology consultation which was necessary for a diagnosis of brain death, it was stated that two clinical examinations and two electroencephalograms (EEG) 48 hours apart were required and this diagnosis could not be made, since the patient was younger than 7 days. Inotropic support was increased in the patient who had intermittent bradycardia. In the follow-up, his general state deteriorated and bradycardia continued. He did not respond to interventions and was lost in the 24th hour after birth.

Discussion

Brain death is defined as a clinical condition characterized with stopping of the intracranial circulation and irreversible loss of all brain functions (6). In our country, approximately 11 932 patients are waiting for organ transplantation and 5-13% of these patients are in the pediatric age group. The diagnosis of brain death is substantially important in terms of providing organ donors for these patients (7). Brain death criteria which can be used for children were defined in 1987 by the International Study Group (Table 1). In addition, electrolyte, acid-base and endocrin disorders

which can mimic the clinical picture of brain death should be excluded for a diagnosis of brain death. Since anencephalic newborns have no brain cortex, brain blood flow and EEG which are used to determine brain death are meaningless. It is known that 5% of these patients who do not have a brain parenchyma live only up to one week. Since the diagnosis of brain death can not be made in the first 7 days according to the diagnostic criteria of brain death, new approaches have been developed for anencephalic newborns (4). In our patient, EEG was ordered in accordance with the diagnostic criteria established in 1987 by the International Study Group to make a diagnosis of brain death. However, it is not possible to make a diagnosis of brain death by EEG in selected patients like our patient. Difficulties were also experienced in making the diagnosis of brain death in our patient and the patient was lost before he could be a donor for transplantation. Therefore, we think that a common decision should be made for these cases by establishing a committee by related divisions.

In one of the autopsy studies performed in anencephalic newborns, cardiac histologies of 10 anencephalic newborns and 10 normal newborns were compared and the right heart wall was found to be thinner in the anencephalic newborns (8). However, this result was not found to be statistically significant. In another autopsy study, renal macroscopic and microscopic histopathologies in 5 anencephalic and 5 normal newborns were compared and no significant difference was found and it was emphasized that anencephalic newborns could be compatible donors for transplantation (9). Therefore, it may be recommended that anencephalic subjects be evaluated as donors.

Transplantation is the only efficient treatment for some renal, hepatic and cardiac diseases. Many patients who are waiting for the appropriate organ lose their lives in this process. Newborns who have anencephaly are significant



Picture 1. Lateral view of the patient

Table 1. Diagnostic criteria for brain death in children (1987)**1. The possible cause of coma could not be determined****2. Physical examination**

- a. Coma and apnea should be present
- b. Brain stem reflexes should be absent
- c. Hypothermia and hypotension should be absent
- d. Flaccid tonus, spontaneous movement other than spinal chord movements should be absent
- e. Clinical findings should not change throughout the observation

3. Duration of observation and laboratory tests

- a. Seven days-2 months: Two clinical examinations and 2 EEGs 48 hours apart
- b. Two months-1 year: Two clinical examinations and 2 EEGs at least 24 hours apart or one clinical examination (a second clinical examination is not necessary if the initial EEG shows electrocerebral inactivity with a cerebral angiography revealing stopping of the cerebral blood flow).
- c. > 12 months: Two clinical examinations 12-24 hours apart. Electroencephalography and isotope angiography are optional. The duration of observation should be increased to 24 hours in hypoxic ischemic encephalopathy

candidates for organ transplantation. Renal transplantation in which an anencephalic newborn was used as donor was performed for the first time in 1961. Anencephalic newborns with low birth weight and anomaly or who do not have regular vital functions are not appropriate as donors (4,5,10,11). There are four basic approaches for determining these anencephalic newborns for organ transplantation. These include:

1) In the subjects in this group, life support was given immediately after delivery and the organs were removed in an appropriate way whether or not brain death occurred. In a study, the kidneys taken from three anencephalic subjects were transplanted to four patients and renal functions were found to be normal in the third year after transplantation (12).

2) In the subjects in this group, life support was given immediately after delivery and occurrence of brain death was waited. In a series applying this approach, brain death occurred only in one of 6 babies who were monitored for 7 days and the patient was lost before transplantation, since no appropriate receiver was present (13).

3) Very little support was given to the subjects in this group and resuscitation was performed after cardiac arrest and full life support was given. These subjects lost their brain functions and the risk of damage to the other organs was increased (13).

4) Very little support was given to the subjects in this group and full life support was not given after development

of cardiac arrest. The organs were taken after the patients were lost and transplantation was performed. The organs which can be used for transplantation in this approach include the cornea, heart valves and kidneys (4).

In a meta-analysis including 25 centers, one of the above-mentioned four approaches was applied in 33 of 80 anencephalic newborns. The first approach was applied in 4 newborns, the second approach was applied in 8 newborns, the third approach was applied in 12 newborns and the fourth approach was applied in 9 newborns. The success rates in organ transplantation vary according to the approach applied. The success rate was found to be 100% in the first approach, 0% in the second approach, 8% in the third approach and 11% in the fourth approach (4). Our patients were lost in the first day of life, though consent was obtained from the family to use the patient as donor for transplantation. Transplantation could not be performed, since it was necessary to wait for 7 days according to the criteria of brain death. Especially, if the first approach was used, some organs of the patients could be used for transplantation.

However, there are still ethical and legal issues about this subjects. The issue of anencephaly and organ transplantation was discussed by the Committee for the Ethical Aspects of Human Reproduction and Women's Health (FIGO) and a declaration was published (11). In this report, it was stated that there was a conflict between the ethical principle of utility and the protection of the vulnerable. In the light of the publications in this area, the following principles were developed by the committee:

1) It should be accepted that selection of organ donation by the mother who accepts to continue an anencephalic pregnancy after receiving full information by consultancy service given to the family is based on ethical grounds.

2) If an anencephalic newborn is born with life signs and only if there is no expectation for survival, brain death can be declared in this baby. The baby can be prepared for organ transplantation with the permission of the family.

Since the difficulties about the diagnosis of brain death can not be solved in many countries, discussions about this subject continue (14). Committees including the related divisions for the subject of anencephalic newborns being transplantation donors should also be established in our country and a common decision should be made.

30-50% of all subjects who are recorded in the transplantation list below the age of two are lost before transplantation can be performed (15). Since the success of transplantation in young children were considered to be low in previous years, sufficient importance was not given to this age group. However, successful outcomes can also be obtained even in infants because of development of current transplantation techniques (7). Therefore, anencephalic newborns should be more carefully evaluated as important

transplantation donors especially for children below the age of two. Special committees should be established in this area by related divisions and lawyers. These committees should provide a common approach by solving the ethical and legal issues.

Conflict of interest: None declared.

References

1. Tunçbilek E. Türkiye'deki yüksek nöral tüp defekti sıklığı ve önlemek için yapılabilecekler. *Çocuk Sağlığı ve Hastalıkları Dergisi* 2004; 47(2): 79-84.
2. Jaquier M, Klein A, Boltshauser E. Spontaneous pregnancy outcome after prenatal diagnosis of anencephaly. *BJOG* 2006; 113(8): 951-953.
3. Sadler TW. Embryology of neural tube development. *Am J Med Genet C Semin Med Genet* 2005; 135: 2-8.
4. Stumpf DA, Ronald E, Fost NC, McQuillen MP. The infant with anencephaly. The medical task force on anencephaly. *N Eng J Med* 1990; 322(10): 669-674.
5. Ashwal S. Determining brain death in newborn. *Clin Perinatol* 1989; 16: 501-518.
6. Banasiak KJ, Lister G. Brain death in children. *Curr Opin Pediatr* 2003; 15(3): 288-293.
7. Akyıldız BN. Beyin ölümü. İçinde: Karaböcüoğlu M, Köroğlu TF, (yazarlar). *Çocuk yoğun bakım esaslar ve uygulamalar. Birinci baskı. İstanbul: İstanbul Medikal Yayıncılık, 2008: 557-563.*
8. Öztürk AH, Kurtoğlu Z, Tuncel M, Uluutku H, Aktekin M, Camdeviren H. Comparison of thicknesses of the myocardial fibers of anencephalic and normal human fetuses. *Turk J Pediatr* 2002; 44(4): 330-333.
9. Kalaycıoğlu A, Karaca M, Can I, Keleş ON, Uçuncü Y, Gündoğdu C, Uyanık A, Unal B. Anencephalic fetuses can be an alternative for kidney transplantation: a stereological and histological investigation. *Histol Histopathol* 2010; 25(4): 413-422.
10. Leclerc R, Watts JL, Kaiser S. Transplantation of organs from newborns with anencephaly. Bioethics Committee, Canadian Paediatric Society). *CMAJ* 1990; 142(7): 715-717.
11. FIGO Committee for the Ethical Aspects of Human Reproduction and Women's Health. Anencephaly and organ transplantation. *Int J Gynaecol Obstet* 2008; 102(1): 99.
12. Holzgreve W, Beller FK, Buchholz B, Hansmann M, Köhler K. Kidney transplantation from anencephalic donors. *N Eng J Med* 1987; 316(17): 1069-1070.
13. Peabody JL, Emery JR, Ashwal S. Experience with anencephalic infants as prospective organ donors. *N Engl J Med* 1989; 321(6): 344-350.
14. Kohrman FA, Clayton EW, Frader JE, Grodin MA. American Academy of Pediatrics Committee on Bioethics: Infants with anencephaly as organ sources: ethical considerations. *Pediatrics* 1992; 89: 1116-1119.
15. Soysal DD. Beyin ölümü ve donör seçimi. İçinde: Karaböcüoğlu M, Uzel N, Yılmaz L, (yazarlar). *Çocuk acil tıp kitabı. Birinci baskı. İstanbul: Çapa Tıp Kitabevi, 2004: 639-660.*