

CASE REPORT

Ethical considerations about changing parental attitude towards end-of-life care in twins with lethal disease

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ABSTRACT

Advances in critical care and technology capabilities may lead to new ethical encounters in paediatrics, especially in the paediatric intensive care unit (PICU). As each patient has unique psychosocial and clinical condition interactions, paediatricians and healthcare providers must develop and adopt a suitable approach for ethical decision-making in the PICU. The healthcare provider needs to balance the four ethical domains of autonomy, beneficence, non-maleficence and justice, and apply these principles to clinical decision-making. One chief factor for ethical decision-making is to have a patient-centered and family-oriented management that is respectful of cultural background. Healthcare providers also need to observe professional ethical conduct and the applicable national laws. Applying these ethical guidelines in paediatric care ensures a more holistic approach to care, whether in the paediatric wards or the highly technical environment of the PICU. We describe two situations in which the parents of twins with a confirmed lethal disease changed their attitude towards end-of-life from full support to “do not resuscitate” and palliative care, after experiencing the palliative care of the first twin, rather than the futile effect of cardiopulmonary resuscitation in the other twin.

KEYWORDS:

Zellweger syndrome; Twins; Lethal disease; End-of-life care; Do not resuscitate; Ethics.

INTRODUCTION

Zellweger syndrome (ZS) is a peroxisomal biogenesis disorder that is caused by defects in Peroxisome Biogenesis (PEX) genes, with a phenotypic spectrum that ranges from severe to mild [1]. Patients can present in the neonatal period with severe symptoms or later in life during adolescence or adulthood with only minor features. As parents of these children are becoming better aware of their medical conditions, the decision-making processes are changing from physician-guided paternalism towards family autonomy. This situation has further enforced parent paternalism for children, with improvement in the family-centred management approach. However, parental control might bring along decisions of refusing the child's management options that are offered by the treating medical team, which may occasionally affect the health right of the child. Paternalism may also cause physicians to direct towards the defensive medicine approach and to have a tendency of avoiding legal responsibility rather than focusing on the actual benefits of the

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child. The international medical law requires maintaining the child's best interest in all cases, keeping in mind the non-maleficence principle; meaning non-harming or inflicting the least harm possible to reach a beneficial outcome [2]. In such situations, the parental decision on treatment refusal should be restricted to preserve the child's best interest and right to good health [3]. In this report of end-of-life decision in twins with a profound intellectual disability, parents and the physicians choose opposite options initially, but the progress of the first twin had influenced the parents towards joint decision-making that was initially suggested by the treating team.

CASE REPORT

A twin baby girls were born at 35 weeks' gestation and admitted to the neonatal intensive care unit (ICU) for evaluation. Parents were first cousins. Both twins had dysmorphic features suggestive of ZS (large anterior fontanelle, prominent forehead and hypotonia). Brain magnetic resonance imaging (MRI) revealed bilateral perisylvian polymicrogyria (PMG) (Figure 1), consistent with ZS in both twins, with the other parts of the brain revealing normal gyral pattern, with normal ventricles, corpus callosum, brainstem and cerebellum. Genetic testing showed that both twins had a homozygous missense mutation in *PEX5* (NM_000319.4:c.1554T > G:p.Asn518Lys), thus confirming the diagnosis of peroxisomal biogenesis disorder. Parents were tested and found to be carriers for this mutation. Genetic counselling session was conducted with both parents, informing them about the lethal nature of this disease and the future pregnancy possibilities.

During the next few months of life, both twins developed worsening clinical course, with drug-resistant epilepsy, global developmental delay, recurrent pneumonia and worsening respiratory status. Their seizures persisted despite being on phenobarbital, topiramate and lorazepam. By 10 month of life, twin A growth parameters were: weight 5.4 kg (below third centile), length 63 cm (below third centile) and head circumference 44 cm (25–50th centile), while twin B had weight of 6.8 kg (below third centile), length 70 cm

(25th centile) and head circumference 45 cm (50th centile). Their weight corresponded to the 50th percentile for 3–4-month-old infants, reflecting severe failure to thrive, despite being on continuous feeding by gastrostomy tube. As twin A had more repeated paediatric ICU (PICU) admissions than her twin sister, the parents were counselled about the fatal outcome of her disease, and they accepted the no-code status [“do not resuscitate (DNR)”] as per the hospital guidelines. When the similar counselling was offered for twin B, whose disease manifestations seemed less severe, with only one prior PICU admission, the parents were hesitant and did not accept the recommendation for DNR.

At 10 months of age, twin A developed episodes of apnoea and desaturations, so she was transferred to the PICU for palliative care, with a non-breathing oxygen mask and intravenous fluids. Her comfort was ensured throughout her brief PICU admission, and she died peacefully within 24 hours of PICU transfer.

The next day, twin B was coded in the paediatric ward for frequent episodes of seizures with apnoeas and desaturations and was intubated after a brief cardiopulmonary resuscitation (CPR). As she was transferred to the PICU and connected to mechanical ventilation (MV), the father requested not to perform any further active invasive interventions for their baby. The primary treating consultant re-discussed the issue with the parents and agreed to sign the consent forms for DNR with no escalation of therapy (no chest compression, no inotropic support; and if extubated, to use noninvasive ventilation and no reintubation). The baby was kept on same MV settings, with no escalation of life-sustaining therapy. On day 3 of PICU admission, while on MV, the patient had a sudden desaturation down to 6%, with bradycardia and then asystole. CPR was not performed. The parents were counselled and provided with a support through social services and the medical team.

DISCUSSION

ZS usually manifests in the neonatal age, with severe hypotonia, distinctive facies, gyral malformations, seizures, feeding

difficulties, renal cysts, hepatic dysfunction and chondrodysplasia punctata. Infants with ZS commonly die in the first year of life, and this is usually due to worsening respiratory failure with apnoea or respiratory compromise from chest infections [1]. The twins in this report were genetically diagnosed with the same lethal disease; however, the worsening of their clinical pictures during the first few months of life varied slightly, with one twin having more severe manifestations as compared to the other.

Parents of children with lethal disease undergo many difficulties. When coping with difficult circumstances, most parents have one thing in common: their inability to process and understand all the information that they need when they become aware of their child's condition [4]. Therefore, parents may not fully understand that while a child with the irreversible or progressively terminal disease may benefit temporarily from CPR, this painful and invasive experience could be unnecessary and the child may be left in a worse condition [4]. Appropriate

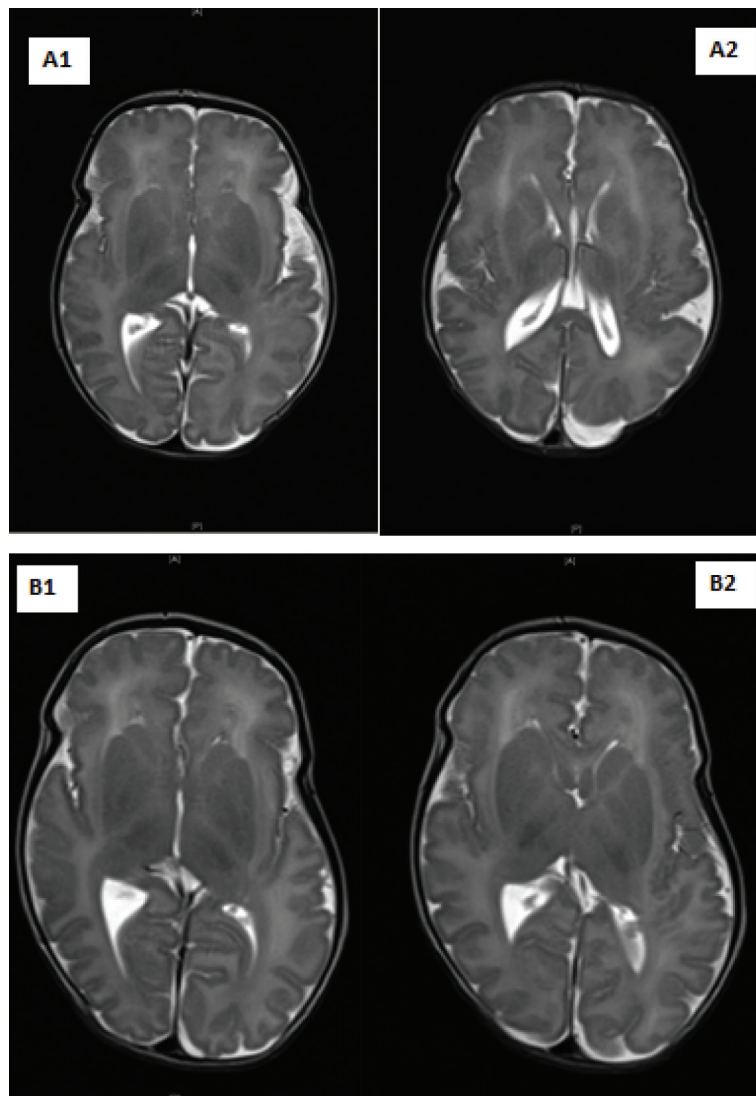


Figure 1 - Axial T2-weighted brain MRI for twins A (A1 and A2) and B (B1 and B2) revealing bilateral perisylvian PMG. The sylvian fissures show an abnormal development, with a lack of proper operculisation. The anterior and posterior opercula of the sylvian fissures and the insular cortex demonstrate abnormal small gyri with shallow sulci and remarkably irregular gray–white matter interface indicating PMG. PMG is also noted bilaterally in the frontoparietal region.

Table 1 - Summary of ethical principles with paediatric examples.

Ethical principal	Summary	Example from paediatrics
Autonomy	Self-determination; includes reliability, disclosure, informed consent, confidentiality and promise observance	Obtaining consent from parents for a medical procedure (such as lumbar puncture), with assent from older children about the same procedure
Beneficence	Acting from the essence of sympathy and kindness to benefit others	Providing a broad-spectrum antimicrobial therapy to a child with bacterial meningitis
Nonmaleficence	Non-harming or inflicting the least harm possible to reach a beneficial outcome	Changing the broad-spectrum antimicrobial therapy to penicillin in a child with <i>Streptococcus</i> group B bacterial meningitis after obtaining antibiotic susceptibility testing results
Justice	Acting out of fairness for individuals, groups and society, with fair allocation of health-care resources	Having the optimal treatment available for all children who present with meningitis in any hospital in the community
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actions and understanding from healthcare providers are essential, as well as the emotional support for the parents in stressful situations [5]. Therefore, research by healthcare professionals (HCPs) on what parents need and expect from HCPs has mostly focused on parents who lost a child due to cancer [6]. Although much can be extrapolated and learned from such studies, parents of children with other lethal diseases may yield additional special needs, as was shown in our case of these parents of twins with a fatal disease. Up to knowledge, this is the first case reported in the literature of twins with ZS who had different code status initially (i.e., one with DNR and the other with full resuscitation status).

Our case report of twins and their parents' change in attitude towards end-of-life care in lethal disease demonstrated that parental perceptions and judgment are ongoing processes. The ability of HCPs to track and appropriately address the evolving parental needs would ensure optimal family-centred medical care in these critical times. Yuen et al. [6] reported that parents who lost a child to fatal epidermolysis bullosa indicated the following needs: quick and accurate referral to an expert clinical service, honesty about the diagnosis and fatal prognosis, need for an organised network of caregivers for palliative care, involvement in their child's care and medical decisions, information about the end-of-life process, guidance and memories of their child and genetic counselling. Therefore, HCPs need to

communicate with parents, addressing such needs and concerns appropriately. Surveys about factors that influence resuscitation preferences for young patients with severe developmental disabilities revealed that personal relationships, such as with family, religious leaders and physicians, were more significant for families who indicated a preference for full resuscitation than those with no code preference [7]. Other points to consider include each family's unique background in mind. Hileli et al. [8] reported that parental DNR consent was associated with educational level of parents and the family income. When communication is clear and appropriate, change of parental attitude towards resuscitation preferences is possible. When families of 60 young patients with severe developmental disabilities were provided with information that explained the resuscitation in a non-acute, paediatric nursing home site, the request for DNR significantly increased (from 18% to 43%, $P < 0.001$) [9].

When applying the ethical principles (Table 1) in paediatrics, it is crucial to recognise that children are not just "small adults." The fundamental principles that were stated in the Belmont report (1979), specifically, respect for persons, beneficence and justice, have affected the thinking of bioethicists in a wide range of subjects [10]. However, an early development of bioethical reasoning was mainly focused on issues of adults with decisional capacity and compliance with the principle of respect for autonomy [11].

Parents are not expected to speak for their child but rather to address their child's "best interests" [11]. This parental judgment is more difficult when parents are facing major end-of-life decisions, which may be multifactorial, including conflicting parental emotions between the parental instinct for preserving their child's life and the parent's hope for the child to have no suffering from the lethal medical condition. This situation may have occurred in our reported case of twins, as the parents initially felt that the DNR decision was suitable for one twin only who apparently had a more severe disease course, on the basis of the parents' understanding of her illness severity, as compared to the other twin. Later on, as they experienced palliative care for ZS, which was more "gentle" than CPR, along with repeated

counselling, their attitude toward end-of-life care changed remarkably. They eventually agreed with the medical team to assign DNR for both siblings as part of a palliative care.

Paediatric care classically contains a default assumption of parental decision-making, which is often phrased as a parental right to make decisions. However, ethically, it might be better described as "parental responsibility" [11]. While rights can be exercised as desired, responsibilities have a stronger moral claim on those who have them. Parents should demonstrate that they are responsible for making good decisions for their child. Usually, to act responsibly, parents are expected to decide for their child based on what is in the child's "best interest" [12]. However, what "best interest" means for each particular child and family might vary significantly. Parental decision-making may be impaired in some complex medical situations. Therefore, shared medical decision between the parents and the medical team may seem the better alternative. However, when addressing moral decisions, for example, when it is uncertain if life support treatment or non-treatment will have a child's best interests, the shared decision-making may be disputed because the agreement does not guarantee moral validity [13].

To clarify the ethical principles of medical decisions about minors, two standards have been proposed: the "best interests" standard and the "harm" principle. The best interest standard requires decision-making aimed at the care that is in the best interest of the patient [14]. Parents are required to pursue the "best interests" of their child, but so are HCPs. When parents and HCPs have different ideas of what is "best," the best interest standard becomes the problem rather than the solution. This disagreement led to another balancing standard: the harm principle. As parents have more authority over their children's care, the use of the harm principle would attempt to guide parental decision-making parameters to help define not what parents should be trying to achieve when they make decisions but, instead, when others should step in to process the decision-making instead of the parents. The question changes from "what is best for this child?" to "how can we identify when decisions

exceed parental authority to avoid harming the child?" Therefore, the best ethical approach to paediatric decision-making is combining the best interest standard with the harm principle. Especially when confronted with challenging paediatric cases that raise the question of what is best for a specific patient, it is crucial to carefully pursue the medical, personal, familial, cultural and legal facts and interests. Determining what interests are involved represents a significant task, but the target of providing the best care for such patient requires a full understanding of what benefits are relevant in determining what is "best" [15]. At the same time, the balance is needed between the limited authority of HCPs and the broader parental authority. Given that no one for sure has the hold on "truth," it may be necessary to allow parental decision-making to hold dominance even when doubts remain about whether those decisions are, in fact, best for the child. Here is where the harm principle plays a role, setting a threshold for harm below which parents are not allowed to go. Above that threshold, however, the most that HCPs can do ethically is to attempt to convince parents; by giving reasons and explanations why they think a given treatment choice is the best.

CONCLUSION

Holistic management of children with lethal diseases, such as severe ZS, should be expanded to include ethical considerations with a tailored patient-centered and family-oriented approach. End-of-life care should be provided with appropriate counselling and psychological support. When addressing complex paediatric medical conditions, one ethical approach to decision-making is combining the "best interest standard" with the "harm principle."

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