

Terminal Lucidity in a Pediatric Oncology Clinic

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Abstract: The sporadic occurrence of unusually enhanced mental clarity before death has been documented over time and cultures, and reported in patients with and without neurodegenerative diseases, psychiatric disorders, and other neurocognitive deficits, as well as those with nonterminal and terminal conditions. Using a purposive sampling method via existing professional networks, clinical presentations of terminal lucidity in pediatric populations, as witnessed by pediatric oncologists and medical personnel, were solicited. We document clinical presentations suggestive of terminal lucidity in children, which were compiled by their attending physician at two large tertiary pediatric hospitals. Unanticipated and unexplained changes in mental clarity, verbal communication, and/or physical capability in the days and hours before the death of the pediatric patients were observed. Each patient's medical condition should not have allowed for such changes. The phenomenon known as terminal lucidity provides a conceptual framework for these deviations, although more systematic documentation and clinical research is required before definitive conclusions can be drawn.

Key Words: Terminal lucidity, pediatric oncology, clinical presentations, paradoxical lucidity, end-of-life, terminal illness, children

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Unusually enhanced mental clarity in the last minutes, hours, or days before a patient's death has been intermittently documented by physicians over the past 250 years (Nahm and Greyson, 2009). Characterized by spontaneous and often animated changes in verbal and/or nonverbal behavior, such episodes are inconsistent with expectations of the patient's cognitive trajectory given their medical condition. Occurring in confused, drowsy, or otherwise nonresponsive patients, but also in patients with brain conditions such as meningitis, brain abscesses, brain tumors, strokes, neurodegenerative dementias, and psychiatric disorders such as chronic schizophrenia, these unexpected episodes have been variously referred to as “lightening up before death” (Macleod, 2009) and “terminal lucidity” (Nahm and Greyson, 2009). More recently, the term “paradoxical lucidity” has been introduced for unusual episodes of lucidity that exclusively involve patients with severe neurodegeneration who are not necessarily close to death (Eldadah et al., 2019; Mashour et al., 2019). Because little is known about lucidity episodes, consensually agreed scientific definitions are lacking, and recent attempts to develop necessary and sufficient criteria for identifying instances of terminal and paradoxical lucidity (Gilmore-Bykovskiy, 2023; Mashour et al., 2019; Nahm, 2022; Peterson et al., 2021) are welcome.

Scholarly interest in lucidity phenomena has increased over the past two decades (e.g., Batthyany and Greyson, 2021; Brayne et al., 2008; Fenwick and Brayne, 2011; Nahm, 2012; Nahm et al., 2012; Normann et al., 1998, 2006; Schreiber and Bennett, 2014) and gained recent momentum, assisted in part by a 2018 expert workshop on paradoxical lucidity and a dedicated research program, both funded by the US National Institutes of Health (NIH) (NIH Reporter, 2022). Yet, these phenomena remain little understood. Of the limited studies conducted to date, different prevalence figures have been reported, which might be attributed to different reporting mechanisms for the episodes, different clinical presentations, and different patient inclusion criteria, a consequence perhaps of the lack of definitional consensus for paradoxical lucidity and terminal lucidity. For example, 7 of 10 caregivers in a nursing home reported witnessing unconscious or confused residents unexpectedly becoming lucid just before they died (Brayne et al., 2008). In a follow-up study, 79% of 30 caregivers stated patients who had been in deep coma suddenly became alert and coherently said goodbye before dying (Fenwick et al., 2010). Others have reported much lower prevalence: 6 of 100 patients who died consecutively in a hospice displayed an episode of lightening up before death (Macleod, 2009), and only 6 cases of terminal lucidity were retrospectively identified in the medical records of 338 deaths (Lim et al., 2020). Interest in these lucidity types has centered on adult and geriatric patient populations, particularly those with neurodegenerative conditions, likely on account of the perplexing questions they raise about the assumed irreversibility of such conditions.

Published reports of lucidity in children do exist but are rare. Here we describe four behavioral observations that would qualify as terminal lucidity in children, on the grounds mental clarity and physical movement improved suddenly just before death. The first known report, from the 13th century, concerns an infant near death and in seemingly painful distress, who suddenly became very alert, started to laugh, and lifted his arms, but died soon after (Cantipratanus, 1605). From the 17th century, an 18-month-old girl who lay convulsing, suddenly stopped, opened her eyes, became alert, smiled, lifted her arms, and called “Ei, beautiful, ei beautiful!” [Ei schön, ei schön!], before dying (Scriver, 1681). Contemporaneously, two cases of terminal lucidity were documented in children younger than 8 years. Lerma (2007) describes a 2-year-old boy in the final stage of disease, unable to speak or move his muscles including facial muscles and eyelids, who opened his eyes, smiled brightly, raised his arms, and then died. In a previous publication, we summarized a case described by Morse and Perry concerning a 5-year-old boy dying from a malignant brain tumor, who unexpectedly awoke from a coma to lucid awareness, but died the next day (Morse and Perry, 1990; Nahm et al., 2012).

Enhanced understandings of these phenomena in pediatric populations, particularly through systematic investigation, are vitally important, having implications for patients, caregivers, medical professionals, and systems of care at the end of life. For example, in medical settings, attending medical staff who recognize lucidity episodes and differentiate them from other phenomena will be better able to make evidence-based assessments of whether an escalation or transition of treatment is necessary. Caregivers and family members could make more informed decisions about what aspects of treatment may or may not be useful at a particular stage of care, as these episodes often represent the

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last chance to connect with a dying child. Because these patients are hospitalized and receive treatment by health care providers at the end of life, documenting and reporting by medical staff of lucidity episodes is necessary to increase understanding of prevalence, potential triggers, and possible neurobiological mechanisms, as well as the neuropathology and psychopathology of cognitive impairment in pediatric populations during the last phase of life.

Finally, pediatric oncology patients are mostly treated by institutions involved in national and international research/translational consortiums, making collaborative investigative efforts into lucidity episodes in pediatric populations highly feasible. This includes the potential for access to biological (blood/imaging/tissue samples) correlates from treatment related studies, where these samples and clinical data could be readily accessible for further research. Systematic investigation of these events occurring while in the hospital setting may facilitate neurobiological insights that have implications for new/developing technology (e.g., less invasive electroencephalograms), more formalized neurocognitive evaluations, and obtaining “real-time” blood samples/clinical data during and after these events. For these reasons, this brief report is intended to draw attention to and facilitate systematic enquiry concerning the occurrence of terminal lucidity in pediatric patient populations.

METHODS

We report clinical presentations of terminal lucidity in a pediatric oncology clinic between 2012 and 2018. Although these were not the only presentations witnessed by the physician, he described them as the “most memorable.” Both the attending physician and other members of his respective teams over time have witnessed presentations beyond these three patients, of what they would now consider to be terminal lucidity. The medical records of each patient reported herein were compiled and reviewed by their attending physician, who also completed a questionnaire designed to capture the clinical presentation and impact of the lucidity episodes for each patient. The questionnaire was developed as a pilot version of an online questionnaire that is being used in a multicountry study the authors have recently launched. The descriptions of the presentations below are based on the retrospective recall of the attending physician and are given in his own words. The responses to the questionnaire are not reported here, as they will be provided in a follow-up article.

PATIENT REPORTS

All patient information was provided anonymously by the attending physician, and no data are presented that could identify the patient or their family. All three patients were described as having severe mental impairment immediately before their period of lucidity. Asked if there were any possible changes in their condition, medication, or treatment before the lucid event that could be responsible for the experience, the attending physician responded “no,” and for two of the patients, a decision had been made before the lucidity event not to escalate medical care.

Patient 1

The patient was a 3-year-old Hispanic female patient with prolonged medical treatment history for her diagnosis of hemophagocytic lymphohistiocytosis (HLH), a complex and often life-threatening medical condition resulting from an uncontrolled and ineffective immune response, leading to extreme inflammation in many organs/tissues. After over a year of intense treatments, she underwent an umbilical cord blood transplant, which is the only known cure for this condition. Unfortunately, the transplant was rejected, and although attempts were made to find another option for a second transplant, she had a reemergence of her HLH and was admitted to the hospital for chemotherapy and immunotherapy. Despite some initial improvements, she developed progressive organ damage and deterioration over the next several weeks, prompting transfer to the intensive care unit (ICU), with worsening liver

and pulmonary failure. She became severely jaundiced and encephalopathic, and was no longer speaking, eating, or responding to parents/providers. The ICU physicians were worried that she was an aspiration risk, prompting intensification of do not resuscitate (DNR)/do not intubate (DNI) conversations with her parents. As all the known treatments available were exhausted and her condition worsened, the focus shifted to providing palliative care. Although initially resistant, after nearly 2 weeks of intense conversations with parents (including family members and a Catholic priest) and further deterioration in their daughter's condition, a DNI and modified DNR status change was agreed. That evening, the patient awoke and asked for her usual comfort items (i.e., Lion King movie, parents, toys) and food. She showed no indication of mental impairment and regained the ability to sit up in bed and participate in coloring and other simple age-appropriate tasks. She spoke using logical, organized full sentences, and had multiple conversations with her parents that evening, which they and the bedside nurse described as “like a miracle.” During the conversations with her parents, she reviewed all the important people in her life and prayed for them. She indicated awareness of transitioning to death and reassured loved ones of the need not to be concerned about her. She also seemed to be communicating with people who were not visible to others. After several hours, she asked to “go to bed” and returned to her comatose state. Over the next 24–48 hours, she never awoke again, and she ultimately died peacefully of cardiac arrest in her parents' arms.

Patient 2

The patient was a 12-year-old girl with relapsed acute lymphoblastic leukemia status post haploidentical marrow transplant (half-matched from her father) admitted with worsening weakness, lethargy, and new-onset diabetes. She was eventually found to have developed antihypertensive antibodies as a complication from her transplant, and she had progressive neurological decline and new-onset status epilepticus. She was noted to be encephalopathic after her seizures were controlled with antiepileptics and was unresponsive on examination with diffuse slowing on an electroencephalogram. She became minimally responsive to her surroundings despite the initiation of rituximab; however, she had acute worsening of her medical condition with acute abdominal distension and bleeding with loss of blood pressure/pulses. She was declared dead after 20–30 minutes of resuscitative measures. Just before this event, her mother noted that the patient opened her eyes, and mouthed “I love you” and “I'm ready to go home,” and blinked her eyes to answer yes/no questions. Her mother commented that she had not “seen her eyes” in several months and appeared to consider these moments as signs of life, despite her daughter's medical condition. This information was provided to the attending physician by the patient's mother in a debrief within 48 hours after her daughter's death. This lucidity event likely explained the mother's desires for further resuscitation, despite such attempts being regarded as futile by medical providers.

Patient 3

The patient was a 19-month-old boy who underwent a bone marrow transplant at 16 months of age for ill-defined immune deficiency. He was recovering with typical transplant complications until he developed fevers and progressive neurologic symptoms with loss of ability to communicate, loss of motor function, and loss of cognition. He was found to have human herpesvirus 6 (HHV-6) infection in his blood and spinal fluid, which was refractory to treatment with three antivirals. He was hospitalized for the last 3 months of his life, as he had waxing/waning symptoms, which were attributed to inflammation from the immune response to HHV-6 infection, and he would temporarily improve after receiving steroids or another immune suppressant. However, HHV-6 levels would increase again, leading to further inflammatory responses in his central nervous system, heart, and bowel. Before the lucid event, he was not responding to health care providers and was giving

parents only minimal response/eye contact. Three days before his death, he became much more alert and interactive, in stark contrast to his steady decline of the prior 3 months, which was preceded by his parents having decided they would not proceed with further life-saving medical interventions (*i.e.*, surgeries, intubation, etc.). He was noted to be able to move, talk, eat, and communicate for 24–48 hours before a rapid decline and death. On the night before his death, he communicated with his parents that he “was ready to go home” and that “he and parents would be OK” using verbal and sign language. They talked about joining his brother who was a stillbirth, and he told his parents he was going to be fine. Subsequently, he returned to severe mental impairment and died within 24 hours.

DISCUSSION

These behavioral observations reflect unanticipated and unexplained changes in mental clarity, verbal communication, and/or physical capability in the days and hours before the death of three pediatric patients. Supporting the descriptions, the attending physician's responses to our questionnaire indicated that each patient was diagnosed as having severe mental impairment before the lucidity episode, yet the average degree of mental impairment was substantially decreased during the lucidity episode, such that each patient was more calm, energetic, smiling, and cheerful during the event, compared with their state beforehand. The attending physician also noted their respective medical conditions, medications, or treatments before the lucidity event could not be considered responsible for the experience. Like older aged populations with and without substantial neurodegenerative conditions (*e.g.*, Fenwick et al., 2010; Macleod, 2009; Nahm, 2009, 2012; Nahm and Greyson, 2009; Nahm et al., 2012; Schreiber and Bennett, 2014), children with severe medical conditions and associated mental impairments can, at least in some instances, regain cognitive lucidity, communicative ability, and dynamic physical activity, just before death.

Yet, key considerations remain. Could a spontaneous return to lucidity have been possible or expected given the medical conditions of the patients, or was their decline considered irreversible? Two of the children (patients 1 and 2) were encephalopathic after all treatment options were exhausted, suggesting that medical intervention was no longer effective in managing symptoms, and implying the associated cognitive decline was deemed irreversible. The attending physician also indicated that, to the best of his knowledge, the medication regime could not have been responsible for the lucidity episodes. Consequently, the expectation of regaining mental clarity would have been minimal for these children and raises intriguing questions about how the lucidity episodes could have been possible.

An equally important consideration is whether there is a need to differentiate between verbal and nonverbal behaviors when assessing these lucidity episodes. Patients 2 and 3 were both described as using nonverbal indicators (*i.e.*, sign language and mouthing words) as a form of communication. Yet, we acknowledge the possibility that such behaviors may be confounded with other reactions related to their medical conditions, including responses to treatment. Notwithstanding this, we also note that the nonverbal behaviors were considered as meaningful communication from the children by their parents, including the mother of patient 2 who regarded the communication to be “signs of life” that went beyond what her daughter's medical condition could support, and the attending medical providers thought possible. In the absence of definitional criteria and associated neurobiological explanatory models, for now, the above considerations remain open to interpretation.

The observations of these patients also raise interesting questions from a psychological perspective about cognitive development in childhood. All three individuals indicated an awareness of their approaching death, and a simultaneous reassurance to their parents that they (the parents) would “be OK.” Although this may not seem unusual for a 12-year-old who likely had been exposed to sociocultural conditioning

about death (patient 2), children aged 3 years and nearly 2 years (patients 1 and 3, respectively) would not be expected to have the cultural conditioning or developmental capacity to understand the concepts of death and dying—particularly their permanent nature—nor be aware of the emotional impact of their impending death upon their parents. Yet, this understanding is evident in all three patients. Also of note is the communication by patient 3 of joining his stillborn brother. It is possible the parents had communicated to the child he had a brother who had died, but this should not imply the child understood the concept of a dead brother, nor does it explain why the child would be inclined to communicate he would soon be joining him. This aspect of the patient's experience may instead point to the child having an awareness of death that would not be common at this developmental stage. Similar accounts of unusual understandings about the nature of death and dying that seem to challenge understandings of child development on this topic have also been recorded from pediatric near-death experiences (Morse, 1994; Morse et al., 1986) seemingly lending further support for the need to revise current understandings about death concepts and cognitive and social development in young children. Yet, in the absence of neurobiological explanations to indicate otherwise, they suggest children with specific medical conditions may have more advanced cognitive capabilities relative to age, than is often assumed.

FUTURE CONSIDERATIONS

Although we have presented only three instances of lucidity in pediatric patients and recognize the limitations of retrospective recall by the attending physician, anecdotal evidence indicates that terminal lucidity does occur in pediatric populations and may do so more frequently than previously believed, perhaps because they are underreported by medical professionals and caregivers. This interpretation is consistent with literature suggesting medical professionals are reluctant to report anomalous phenomena, due to concerns that a willingness to describe such experiences would be considered a sign of uncritical credulity or dismissed as lacking scientific validation (Brayne et al., 2008; Fenwick et al., 2010). Limited understanding of a phenomenon should not equate to lack of engagement with that phenomenon, particularly because unusual episodes of lucidity close to dying have been discussed by physicians since at least the 19th century in the contexts of mental disorders, dementias, brain diseases, or *Spes phthisica*, the elated mental clarity commonly observed in the terminal stage of tuberculosis (Breathnach, 1998; Nahm, 2012; Nahm and Greyson, 2009). Our observations reported here instead point to a need for further investigation of terminal lucidity episodes in pediatric patient populations to complement ongoing work with older aged populations with neurodegenerative conditions (*e.g.*, NIH Reporter, 2022).

Beyond their potential for enhancing understandings about prevalence, the immediate imperative for further research into terminal lucidity in children is to explore their potential for advancing pediatric palliative care and intellectual understandings of cognitive function in children at the end of life. To this end, we suggest future research should prioritize identifying any covariation between features of pediatric patients' specific medical conditions and treatment regimens and features of the terminal lucidity episodes that are reported. Such investigation would enable a more definitive analysis of the likelihood of terminal lucidity episodes occurring, as well as confidence in being able to differentiate lucidity episodes from the spectrum of features that are particular to the child's medical condition. Research could also provide more clarity around the irreversibility (or not) of specific medical conditions.

Equally, future research could investigate whether and in what ways the features of terminal lucidity correlate with childhood developmental expectations. This could provide more direct evidence of whether current psychological models of child development, intelligence, and cognizance may need to be revisited in light of terminal lucidity episodes. It could also provide much needed information about the reversibility or not of medically related cognitive decline in children, which has direct

implications for, among others, resuscitation protocols (as implied by the mother of patient 2).

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DISCLOSURE

Author Statement and Contributions: P.R. provided the descriptions of the patient clinical presentations, and critically reviewed and revised the article. P.F. read and commented on the draft article. B.G. wrote the initial draft of the introductory text of the article, verified details of the patient clinical presentations, critically reviewed, and revised the article for important intellectual content, and had final responsibility (with M.W.) for the decision to submit the article. A.K. provided essential historical medical information to include in the article, and critically reviewed and revised the article. K.K. analyzed quantitative findings of the survey that was completed by the attending physician, and critically reviewed and revised the article. M.N. wrote the initial draft of the introductory text of the article, refined, and completed the reference list, and critically reviewed and revised the article for important intellectual content. C.R. wrote the initial draft of the methods and findings sections of the article, developed the survey that was completed by the attending physician, and critically reviewed and revised the article for important intellectual content. N.T.-M. wrote the initial draft of the discussion section and abstract of the article, conducted the PRISMA review that helped inform the article, critically reviewed, and revised the article, and prepared the final version of the article for submission. M.W. is the overall lead of the research team and facilitated the article writing process, analyzed the quantitative findings of the survey that was completed by the attending physician, critically reviewed, and revised the article, and had final responsibility (with B.G.) for the decision to submit the article.

The authorship of this article is provided according to alphabetical order of the surname of each contributing author, except for P.R. who is named as first author due to his contribution in the patient clinical presentations.

All authors approved the final article and agreed to be accountable for all aspects of the work.

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