Accidental intracranial infusion of parenteral nutrition in a preterm neonate

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Vascular access in the neonate can be challenging, especially in preterm infants. When other access is not available, superficial scalp veins can be safely used for vascular access. However, rare and potentially catastrophic complications can occur due to unique features of the neonatal skull and soft-tissue anatomy. The authors report a rare complication of vascular access in a preterm infant, which led to the direct infusion of parenteral nutrition into the intracranial space. The child had an excellent outcome after open drainage and irrigation of bilateral intracranial spaces and the spinal thecal sac. Relevant anatomy is illustrated, and an outcome-based literature review is presented on this rarely reported condition. Surgical and conservative management strategies are discussed, along with clinical and radiographic follow-up. Drainage and irrigation is advocated in patients with mass effect, viscous effusions, or declining neurological examination findings.

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KEY WORDS parenteral nutrition; preterm; neonate; subdural infusion; scalp venous access

MOST preterm infants need intravenous access for antibiotics, fluids, prostaglandin E, parenteral nutrition (PN), or other medications. Central venous catheters are often used for longer-term vascular access and administration of PN. Central venous catheter-related complications such as venous thrombosis, pulmonary embolism, retrograde flow, extravasation, and infections have been well described.^{10,12,15} Administration of intravenous products through peripherally inserted central catheters or peripherally inserted intravenous catheters reduces the inherent risks associated with central venous catheters.^{3,4} Finding an adequate peripheral vein for access in a neonate, other than the umbilical vein, can be quite difficult due to small vein caliber in the extremities. Scalp veins often offer easier access, being used in up to 50% of premature neonates in some series.⁷ Widely open fontanelles and sutures raise the possibility of inadvertent intra-

cranial infusion. In this report, we present an exceedingly rare case of accidental intracranial infusion of PN and its neurosurgical management.

Case Report

Birth History and Clinical Course in the First 10 Days of Life

A female infant was delivered by cesarean section at 31 weeks' gestation, weighing 1040 g, after a pregnancy complicated by oligohydramnios and intrauterine growth restriction. Apgar scores were 8 at both 1 and 5 minutes. The 1st week of life was complicated by mild hyperbilirubinemia, mild respiratory distress syndrome, and methicillin-sensitive *Staphylococcus aureus* sepsis. Intravenous antibiotics and parenteral nutrition were started on Day 2 of life through the umbilical vein. Due to failed venous access on Day 10 of life, a peripheral scalp intravenous

ABBREVIATIONS ICP = intracranial pressure; PN = parenteral nutrition; TPN = total PN.

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catheter was placed in the supratrochlear vein parallel to the metopic suture at the anterior-most aspect of the anterior fontanelle.

Diagnosis of Intracranial Infusion of Total Parenteral Nutrition

The child's head circumference increased by 2 cm in the 2 days following commencement of PN infusion through the scalp intravenous catheter. The fontanelle was tense and bulging, accompanied by a widely split sagittal suture. A cranial ultrasound revealed new, large bilateral subdural effusions with mass effect. A small bolus of fluid was infused through the scalp intravenous catheter during cranial ultrasonography, which revealed turbulent flow directly within the subdural space, suggesting direct infusion into the intracranial compartment. The intravenous catheter was then immediately removed, allowing egress of a milky substance from the puncture site (Fig. 1A). The patient was then transferred to our center for neurosurgical evaluation.

On arrival, milky white fluid, consistent with parenteral nutrition/intralipids, continued to ooze from the previous scalp intravenous catheter site, accompanied by clinical signs of high intracranial pressure (ICP) (Fig. 1A). During the primary evaluation the neonate was noted to be tachycardic, tachypnic, and irritable with abnormal brief extensor posturing movements. CT scanning revealed pneumocephalus in the region of the scalp intravenous catheter and a dilated subdural space (Fig. 2A). A lumbar puncture also revealed viscous, milky fluid that was difficult to drain through a spinal needle. Subsequent surgical evacuation was performed due to evidence of raised ICP, poor neurological status, and vital sign instability.

Operative Management and Hospital Course

The patient was taken emergently to the operating room for bilateral subdural and intrathecal drainage and irrigation. The dura was opened bilaterally at the coronal sutures, exposing pressurized subdural compartments filled with copious amounts of viscous milky fluid (Video 1; Fig. 1C).

VIDEO 1. Bilateral craniotomies. Bilateral craniotomies performed at the coronal suture show efflux of pressurized, viscous "milky" fluid from the subdural/subarachnoid space consistent with parental nutrition. Copyright Gerald Tuite. Published with permission. Click here to view with Media Player. Click here to view with Quicktime.

The subdural space was irrigated until clear, and bilateral subdural drains were left. Based on the preoperative lumbar puncture findings, an intrathecal lumbar drain was placed through a single-level lower lumbar laminectomy after the intrathecal space was copiously irrigated.

The subdural compartment was irrigated daily with preservative-free saline through the subdural drains, and the triglyceride level was followed serially. After 3 days of drainage, the triglyceride level improved from 1698 mmol/L to 15 mmol/L, allowing for drain removal. Due to the infant's recent methicillin-sensitive *S. aureus* sepsis and risk for fungal infection from the subdural PN infusion, she was treated with oxacillin and fluconazole for 1 week after surgery. Postoperative MRI showed a small superficial cystic area within the right frontal lobe deep to the intravenous catheter site, as well as a decompressed

FIG. 1. Intraoperative photographs. **A:** Milky discharge directly from the puncture site. **B:** Enlarged head with outlined coronal suture and anterior fontanelle. **C:** Intraoperative photograph with craniotomies at the coronal suture and evidence of milky fluid within the cranial cavity. **D:** Postoperative photograph with bilateral subdural drains.

subdural compartment (Fig. 2B and C). The parenchymal abnormality was noted on the initial diagnostic cranial ultrasound.

The infant had an uneventful recovery after surgery, with neurological examination findings consistent with her prematurity. No hydrocephalus, seizures, infection, or raised ICP developed within the 1st year of follow-up. No permanent CSF diversion was required. She made neurological gains typical for a premature child, with mild motor delay. Her head circumference paralleled the 25th percentile, similar to her weight and length. MRI performed at 1 year showed minimal focal cortical gliosis (Fig. 2C).

Discussion

Indications and Dangers of Scalp Vein Access

Prolonged venous access is necessary in the sick, premature neonate. The most common indications are the need for antibiotic therapy, PN, intravenous fluids, vitamin E infusion, or administration of other medications. Proximal extremity veins should be preserved for peripherally inserted central catheter or central line placement, and distal sites can be difficult to manage due to neighboring joints and extremity mobility. Umbilical access may be available up to several days after parturition, but this is not a good option for long-term access. For these reasons, the scalp has often been the site of choice for long-term intravenous access in a premature infant.

The scalp of the neonate provides 4 reasonable options for venous access: the supratrochlear, anterior facial, superficial temporal, and posterior auricular veins (Fig. 3). The absence of bone at the sutures and fontanelles creates unique anatomy in the neonate. Identifying a "danger zone" related to the vein of interest is crucial for complication avoidance (Fig. 3). A danger zone includes a superficial scalp vein, its associated underlying suture and fontanelle, and the underlying dural venous sinus. Insertion techniques for venous access should be directed away from the suture with blood return to confirm intravenous

FIG. 2. CT and MRI radiographic evaluation. **A:** CT scan of the head (bone window) obtained at the time of initial evaluation, showing right frontal hypodensity consistent with pneumocephalus. **B:** Coronal T2-weighted MR image obtained during the initial hospitalization, showing right frontal intraparenchymal cystic area. **C:** Axial T2-weighted MR image obtained 1 year postoperatively with evidence of mild right frontal gliosis and focal atrophy.

placement. Ultrasound can be used to confirm catheter placement within the superficial vein as opposed to dural venous sinus.⁵ We propose that one way to avoid intracranial placement may be to place a scalp intravenous catheter only over bone and not over a fontanelle or an open suture line. Despite these efforts, inadvertent intracranial infusion may be unavoidable in some circumstances.

Possible Mechanisms for Intracranial Infusion

Inadvertent intracranial infusion of intravenous fluids, blood products, and PN can be related to direct infusion of a misplaced catheter or due to retrograde flow through thrombosed, valveless scalp veins that communicate with the intracranial compartment.^{1,2,9,11–13} Tuthill et al. showed a transudative ultrafiltrate of total PN (TPN) in the subdural space rather than pure intralipid,¹⁴ supporting the notion of intracranial infusion even in the presence of a correctly placed subcutaneous venous catheter. In our case, pure unfiltered TPN and intralipids were found in the subdural space, suggesting direct infusion.

Management Strategies and Literature Review

Many complications have been associated with scalp intravenous access, including air embolism, retrograde flow, inadvertent subdural placement, and subdural infusion of packed red blood cells.^{2,6,8} Intracranial infusion of PN has been rarely reported, with variable consequences, including fungal infection, seizures, hydrocephalus, and death.¹ Separating poor outcomes related to intracranial infusion of PN from other complications of prematurity is difficult because of limited detail available in previous case reports (Table 1).

Inadvertent PN subdural infusion has been managed with supportive care, subdural aspiration, or subdural drain placement in previously published cases. Initial reports of supportive care described over 30 years ago resulted in death in both patients,^{1,2} but a good outcome was described in a 2004 report of a patient treated with only supportive care.⁶ Similarly, subdural aspiration has result-

ed in disparate results; 2 patients died and 2 others had a good outcome.^{10–12,14,16}

Rare postmortem studies after intracranial PN infusion have provided conflicting results. One autopsy showed lipid-laden macrophages with gliosis,³ another showed marked pleocytosis,¹ and a third case showed no inflammatory change.² We cannot make any definite conclusions about the inflammatory response in our patient because a brain biopsy was not performed at the time of drainage.

We considered observation, aspiration, and drainage in the management of our patient. The initial lumbar puncture revealed viscous, milky fluid. The presence of PN in the spinal subdural space from a hemispheric convexity infusion indicated a global intracranial and spinal space involvement rather than a focal collection. The patient's increasing head circumference, deteriorating neurological examination findings, the viscosity of the fluid obtained on lumbar puncture, and associated poor outcomes previously reported in the literature prompted surgical intervention. We chose to perform an open procedure instead

FIG. 3. Illustration of safe zones for venous access. v. = vein. Artist: Devon Truong. Published with permission from Jennifer Clare Truong.

TABLE 1. Literature review of intracranial infusion and outcomes

Authors & Year	Adjusted Age/Sex	Follow-Up Interval	Outcome	Management	Notes
Black et al., 1978	30 wks, F	100 days	Death	Stopped infusion, removed catheter, supportive	Died of severe PNA unresponsive to treatment at 100 days of age
Beaumont et al., 1982	Term, M	6 wks	Death	Stopped infusion, removal of catheter, osmotic diuretics, hyperventilation, steroids	Omphalocele; infusion of PN & ampicillin in subdural space led to seizures; immediate diffuse cerebral edema, stroke; HCP developed by 6 wks; withdrawal of care
Stine & Harris, 1985	32 wks, F	5 mos	Good	Stopped infusion, removal of catheter, subdural tap, placement of subdural drain	NEC led to PICC line through scalp vein; normal neurological exam at 5 mos adjusted age
Young et al., 1989	30.5 wks, M	8 mos	Good	Stopped infusion, subdural tap, then removal of catheter, supportive	8-mo follow-up HC 75th percentile; 4-mo development at 5-mo adjusted exam
Rushforth et al., 1991	36 wks, F	17 wks	Death	Stopped infusion, subdural tap, then removal of catheter, supportive	Died of respiratory failure; seizure led to US showing subdural collection
Tuthill et al., 1998	28 wks, F	103 days	Death	Stopped infusion, removal of catheter, subdural tap, supportive	NEC led to PIV for PN; died of bronchopulmonary dysplasia, sepsis
Gazdik et al., 2003	Term, M	2 yrs	Good	Stopped infusion, removal of catheter, supportive	Gastroschisis; PN infusion associated w/ seizure, unresponsive to AEDs; normal development at 2-yr follow-up
Rosales et al., 2004	33 wks, F	86 days	Death	Stopped infusion, unknown if catheter removed, subdural tap	23-wk EGA; death at 86 days due to withdrawal of care due to <i>Malassezia furfur</i> meningitis & hydrocephalus
Present study	31 wks, F	1 yr	Good	Open drainage & irrigation of bilateral intracranial subdural spaces & lumbar thecal sac	Clinical development appropriate for age, MRI shows only minimal gliosis

AED = antiepileptic drug; EGA = estimated gestational age; HC = head circumference; HCP = hydrocephalus; NEC = necrotizing enterocolitis; PICC = peripherally inserted central catheter; PIV = peripheral intravenous line; PNA = pneumonia; US = ultrasound.

of aspiration to maximize effective drainage and irrigation of the intracranial and intraspinal spaces.

Conclusions

In the rare event of an inadvertent symptomatic subdural infusion of PN, we propose that drainage of the offending agent should be considered. Open drainage and irrigation of the intracranial and spinal compartments resulted in a good outcome in this child.

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Author Contributions

Conception and design: Tuite, Ahmadian. Acquisition of data: Tuite, Ahmadian, Manwaring, Truong. Analysis and interpretation of data: Truong. Drafting the article: Tuite, Ahmadian, Manwaring. Critically revising the article: Tuite, Ahmadian, Manwaring, McCarthy, Rodriguez, Carey. Reviewed submitted version

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Supplemental Information

Videos

Video 1, Media Player. http://mfile.akamai.com/21490/wmv/digitalwbc.download.akamai.com/21492/wm.digitalsource-na-regional/peds13-34_video_1.asx.

Video 1, Quicktime. http://mfile.akamai.com/21488/mov/digitalwbc.download.akamai.com/21492/qt.digitalsource-global/peds13-34_video_1.mov.

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