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Peripheral IV Infiltration and Extravasation (PIVIE) Injuries

Developed by Alexander Perry, Dr. Chris Novak, Dr. Courtney Wilkes, and Dr. Jaret Olson for PedsCases.com.

August 5, 2022

Introduction:

Hello! My name is Alexander Perry, and I'm a fourth-year medical student from the University of Alberta and today we'll be covering the topic of peripheral IV Infiltration and Extravasation injuries or PIVIE for short.

I'd like to thank Dr. Courtney Wilkes, a plastic surgery resident at the University of Alberta as well as Dr. Jaret Olson, a pediatric plastic surgeon at the University of Alberta for helping to review develop this case. I'd also like to thank Dr. Chris Novak, a fellow in Pediatric Hospital Medicine at the University of Calgary helping to review this podcast.

Objectives:

After completing the case, the learner will be able to:

1. Recognize the risks of PIVIE injuries in the pediatric population.
2. Be able to distinguish between an extravasation injury and an infiltration injury.
3. Describe the differences in presentation, diagnosis, and management of compartment syndrome in children in comparison to adults.
4. List the risk factors associated with PIVIE injuries.
5. Formulate an appropriate management plan for different types of PIVIE injuries.

We'll use a case as well as questions throughout the podcast to hit key points about the diagnosis and management of a pediatric patient with a PIVIE injury. Let's begin:

CASE:

You are working in a neonatal intensive care unit and rounding on your patients when you are called into a room by one of the nurses to take a look at a newborn's foot.

Devin is a 3-day old infant born at 36 weeks gestational age being treated for neonatal herpes simplex virus. The dorsum of his foot appears bluish surrounding a red blister with a scab that has formed on the dorsal ankle crease. You notice smaller blisters are disseminated distal to the ankle.

The nurse by the bedside asks you, "do you think this looks like an PIVIE injury?"

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August 5, 2022



Extravasation injury Image A without caption. From Fig. 4A of Cho, Lee ¹ under the Creative Commons License: Attribution-NonCommercial 3.0 Unported. (<https://creativecommons.org/licenses/by-nc/3.0/>)

WHAT ARE PIVIE INJURIES?

Extravasation injuries are iatrogenic injuries that occur when fluid from an intravenous line is deposited into the extravascular space either by leaking from a vessel or from direct infiltration²⁻⁴. Depending on what solution is infused, these types of injuries can lead to serious functional and aesthetic deformities.

Vesicant solutions cause blister formation and tissue damage, while nonvesicants cause discomfort at the injection site, but may or may not cause inflammation⁴. Extravasation of vesicants are associated with adverse outcomes including local tissue inflammation and damage, while nonvesicants, are less likely to have adverse effects unless infused in high volumes⁴. We will discuss examples of vesicants later in the podcast.

Commonly, the terms extravasation or infiltration injuries are often applied interchangeably. Strictly speaking, extravasation injuries are caused by vesicant solutions, while infiltration injuries are caused by nonvesicant solutions⁴.

For simplicity, we will use the term PIVIE to collectively refer to both types of injuries.

SIGNS / SYMPTOMS OF AN EXTRAVASATION INJURY

Common signs/symptoms to identify if a PIVIE has occurred include:

- 1) Discomfort, pain and tenderness to the insertion site
- 2) Coolness to the touch
- 3) Blanching of the skin, where the skin becomes pale
- 4) Leak of infused fluid surrounding the insertion site
- 5) Edema at the insertion site
- 6) And, if the patient can speak, complaints of skin "tightness"

CASE CONTINUED

Based on the appearance, you suspect that this may be an extravasation injury. The nurse tells you that Devin is being treated with acyclovir via a peripheral IV for his herpes simplex virus. As per hospital protocol, the IV cannula was left in place. It has been running for several days now, however, it was only this afternoon that they noted Devin started to become increasingly agitated and inconsolable.

TYPES OF VESICANT SOLUTIONS

Acyclovir is an example of a vesicant solution. A vesicant is any solution that has the potential to cause damage to surrounding tissue. Vesicants can be categorized into vasoactive agents, electrolyte rich solutions, cytotoxic agents, and hyperosmolar solutions⁴⁻⁶.

- **Vasoactive agents** such as dopamine, epinephrine, norepinephrine, and vasopressin cause tissue necrosis secondary to ischemia.
- **Cytotoxic agents** are directly noxious to tissue and include dopamine, antineoplastic agents, (pH-related) vancomycin, and acyclovir.
- **Electrolyte rich solutions** alter the pre-/post-sphincter tone of capillaries that can cause ischemia. Solutions include extravasation of sodium bicarbonate and potassium in concentrations ≥ 60 mmol/L.
- Lastly, **hyperosmolar solutions** can cause intercompartmental pressure shifting, which can impair blood flow, induce inflammation, and cause ischemia. These agents include total parenteral nutrition (TPN), peripheral parenteral nutrition (PPN), dextrose >10%, and radiocontrast agents.

Despite being put into these categories, there can be crossover in their effects. For example, electrolyte rich solutions such as sodium bicarbonate and hyperosmolar solutions such as TPN may also induce direct cell death through the rupture of cellular membranes.

On the other hand, nonvesicant solutions are typically benign in small volumes, do not cause adverse reactions, and are eventually absorbed by the body; however, they can have serious consequences if large volumes are infused into the interstitial space. As such, other factors that contribute to the severity of a peripheral infiltration injury includes flow rate, and the volume infused⁷.

RISK FACTORS FOR DEVELOPING PERIPHERAL INFILTRATION INJURIES

There are a number of different risk factors involved in developing a peripheral infiltration injury; of which, the number one risk factor is age⁷.

Pediatric patients and the elderly are more likely acquire a peripheral infiltration injury secondary to fragile vascularity. Infants and non-verbal children are at higher risk because they have less capacity to vocalize their concerns.

Neonatal vasculature is also more fragile as the skin is immature and lacks substantial subdermal fat. In combination with poor patient cooperation, constant movement, and the inability to communicate, line placement is also more challenging for providers^{7, 8}.

Additionally, solutions that are continuously running (such as TPN or PPN) provide more opportunities for an IV to become interstitial. Vesicants and infusions that are intended to run continuously are recommended be put through a central line and should be monitored closely⁹. For the safety of the patient, many institutions ensure that IV sites are checked regularly every hour. Even 10-20 minutes of extravasation of a vesicant fluid can cause serious harm.

The NICU is known to be one of the most common places for peripheral interstitial injuries due to their patients and their needs⁸.

CASE CONTINUED

After you've done a quick initial assessment of the area in question, you take a better look at Devin. Devin is visibly distressed, and his face is beet red from crying.

You ask the nurse for Devin's vitals:

BP 65/40, HR 155, RR 45, 98% on room air, 36.5°C (All normal).

Devin's IV site was being checked regularly every hour, which is when the changes to Devin's foot were noticed. On suspicion for an extravasation injury, the infusion was stopped.

Examining Devin's left foot: it has a capillary refill of ~3 seconds and palpable but diminished pedal pulses in comparison to his right foot. Overall, Devin's left foot appears swollen, and is cold to the touch. You also notice a small area that is whiter in color towards the tip of his big toe.

COMPARTMENT SYNDROME SECONDARY TO EXTRAVASATION

One serious complication of PIVIEs that should always be considered in compartment syndrome.

Compartment syndrome is defined as a rise in the interstitial pressure within a closed fascial compartment, or simply put, when the compartment pressure exceeds the perfusion pressure preventing adequate tissue oxygenation. The most common causes of compartment syndrome in adults and children are after fractures from traumatic injury; however, compartment syndrome secondary to a vascular insult or infection is more prevalent in children <10 years old¹⁰.

Compartment syndrome can happen with extravasation of vesicant or non-vesicant solutions in high volumes; however, hyperosmolar solutions such as TPN are more likely to cause compartment syndrome due to the acute edema caused by reaction to the solution⁷.

Classically, there are the **6 Ps of compartment syndrome**¹¹:

- 1) Pain (early finding, worse with passive stretch)
- 2) Pallor
- 3) Poikilothermia (coldness)
- 4) Pressure
- 5) Paralysis/ paresthesias (early nerve ischemia)
- 6) Pulselessness (late finding)

However, some of the literature suggests the presentation of compartment in children is different than adults and some studies have found the six Ps to be less reliable in pediatric population particularly if they are non-verbal⁷. Therefore, in combination with the six Ps, you can also consider the **three As**¹²:

- 1) Increasing analgesic requirement
- 2) Agitation
- 3) Anxiety

Increased analgesic requirement is perhaps the most sensitive but may also be difficult to distinguish in neonates. Notably, the six Ps may still manifest in children but as later signs.

CASE CONTINUED

You are concerned that Devin could be developing a compartment syndrome. You check with his nurse and are reassured Devin hasn't required any additional analgesics, although he has been agitated and anxious for the last 30 minutes.

As Devin is a 3-day old infant, he is unable to verbalize that he is feeling any increased pressures or paresthesias in his foot, but you can tell that he is actively moving his leg. Devin still has palpable, though diminished pulses to his left foot.

You wish you had a more definitive way of figuring out if this was compartment syndrome. You recall something about some sort of needle. You also think, what is the conservative and definitive management of a compartment syndrome?

MANAGING COMPARTMENT SYNDROME

Classically, the diagnosis of compartment syndrome in adults is determined clinically, but in more difficult cases, objective tests in the form of using a Stryker needle or arterial line transducer may be used; however, these tools are less reliable in pediatrics. Young adults may demonstrate compartmental pressures similar to adults; however, there is no well-established normal intracompartmental pressures in infants and children¹¹. Therefore, diagnosis in neonates are based on clinical judgement alone¹⁰. In combination with difficulty in expressing oneself and poor patient cooperation, a high level of suspicion should always be maintained with a potential presentation of compartment syndrome in children.

The definitive management in adults and children is a wide decompressive fasciotomy and should not be delayed if the suspicion of compartment syndrome is high. Ischemia may begin as early as 4 hours after a rise in intracompartmental pressure. After 8 hours there may be lasting tissue necrosis¹⁰. Tight external dressings or splints can worsen compartment syndrome. Elevating the extremity can also help compartment syndrome by reducing the amount of edema.

CASE CONTINUED

You double check that Devin does not have any circumferential dressings and elevate his leg. At this time, you believe the degree of edema and is keeping in line with the inflammation caused by the acyclovir.

Concerned about Devin, you call your preceptor to tell them about what has happened. They ask you if you can describe the severity of Devin's injury?

PEDIATRIC PIV INFILTRATION SCALE

There are different grading scales between different hospital sites, but one way of grading PIVIEs in pediatrics is called the Pediatric PIV Infiltration Scale¹³.

The scale ranges from grade 0 to grade 4, where 0 is the least severe 4 is the most severe.

- In a grade 0, there are no signs of a PIVIE injury and the IV flushes with ease
- In a grade 1, there is some localized swelling, tenderness at the IV site and it is difficult to flush the IV.
- In a grade 2 the swelling can encompass up to 25% above or below the extremity, there are signs of erythema, and ongoing tenderness at the IV site.
- In a grade 3, 50% of the extremity is swollen, the tenderness is still present; however, the skin starts to feel cool as more of the fluid leaks out into the tissues. The skin can

start to blanch, and pulses may start to become diminished below the site of the PIVIE injury.

- Lastly, a grade 4 encompasses much of a grade 3 but the swelling is now >50%, and there are now signs of skin breakdown/ necrosis, blistering occurring, and when elicits, the capillary refill is >4 seconds.

To note, PIVIE injuries involving any amount of blood products or vesicants are typically considered a grade 4 considering how quickly they can cause damage.

CASE CONTINUED

You convey to your preceptor that Devin's injury is consistent with a grade 3-4 injury according to the Pediatric PIV infiltration scale and that acyclovir was being infused through his IV. His skin is cool to the touch, is blanched, blistering is present, and he has diminished distal pulses. His foot is swollen >50% compared to his right, and the non-blanching portions of his foot have a capillary refill is ~5 seconds.

Your preceptor agrees and tells you they are headed there now but asks you to begin some of the management before they get there.

MANAGEMENT OF PERIPHERAL INFILTRATION INJURIES

There are non-pharmacologic management options and reversal agents that can be used in certain scenarios of peripheral infiltration injuries. Protocol for handling peripheral infiltration injuries may vary between hospitals.

For the management of PIVIE injuries, the Stollery and the Alberta Children's hospital use the **SLAAPP mnemonic**. SLAAPP (with two As and two Ps) stands for:

- S: Stop the infusion immediately
- L: Leave the cannula in place
- A: Aspirate as much as possible with a 3-cc syringe.
- A: Assess site and measure using assessment criteria including capillary refill, skin color, skin integrity, distal limb pulse, and estimation of swelling.
- P: Pull the cannula.
- P: Provider notification (most responsible physician) of a stage 3 or 4 PIVIE injury.

To note: Much of the non-pharmacologic management using thermal compresses lacks substantial data but if nothing else, comforts the patient. The extremity should be elevated for at least 12 hours if possible, and a cold compress may be applied to the site; however, extravasations involving vasopressors and phenytoin should instead use a warm dry compress. Methods of manual extraction via multiple puncture sites to further aspirate infused solutions have been quoted in the literature but should be avoided⁴.

Reversal agents:

Prior to pulling the cannula, a reversal agent can be used for severe injuries. Two types of reversal agents can be used depending on the type of vesicant^{7,9}:

- 1) **Hyaluronidase**: Destabilizes the interstitial tissue barrier increasing distribution and absorption of the injected solution. Used as an antidote for hyperosmolar agents, some antibiotics, electrolyte rich solutions, and cytotoxic agents including acyclovir).
- 2) **Phentolamine**: Nonspecific α -receptor blocker. Useful for vasoconstrictive substances (e.g. dopamine, epinephrine, norepinephrine, dobutamine).

CASE CONTINUED

As the IV was already stopped, the cannula was left in place to aspirate as much of the extravasated acyclovir as possible using the 3-cc syringe. A cold compress is applied, and the foot is propped up using a rolled towel. Plastic surgery was consulted to examine the blistering of the foot and for concerns of diminished pulses in the distal extremity. Devin was closely monitored for the rest of the day to ensure no further acute changes took place.

COMPLICATIONS

One main concern after a PIVIE is to ensure the site does not get infected. With blistering, skin breakdown, and possible necrosis, this can serve as a site for bacterial infection. Keeping the wound clean and dry. Partial thickness wounds and wounds that penetrate into the dermis should have a wound care specialist see the wound for management. Wounds that show evidence of vascular impairment or concerns about tissue viability, plastic surgery should be consulted. Similarly, plastics should be consulted if there are any concerns about diminished pulses, impaired limb function <48 hours or any severe PIVIE injuries. Acutely after the injury, it is not uncommon for an abscess or ulcer to develop. Ultrasound is one modality that can be used to follow any suspicious fluid collections. PIVIEs over joint surfaces have the potential for developing contractures that can prevent functional limb movement.

In the long term, unrecognized extravasation and infiltration injuries can have lasting negative outcomes on patients including tissue necrosis and loss of limb. However, if identified early, as in Devin's case, most outcomes are good without any lasting sequelae.

PREVENTION

Keeping both the healthcare team as well as the patient's family informed about the potential of a PIVIE is important. This ensures there is close observation of the IV site and any signs of an early PIVIE are picked up. All peripheral IVs should be assessed hourly for any signs of an early PIVIE. A safer alternative to a peripheral IV is using a central venous catheter when possible. These are less likely to extravasate when vesicant solutions are being used. As mentioned above, the younger the patient the higher the likelihood of a potential PIVIE due to the immaturity of their skin.

CASE CONCLUSION

It has been 18 months since you last worked in the NICU. Since then, you have started work in an outpatient pediatrics clinic and you just so happen to run into Devin and Debbie who are here for Devin's regular checkup.

"It's great you see you again!", says Debbie. "Devin has been doing well. The injury on his foot, it has healed so nicely! It's like nothing even happened!"

Pulling out her phone, Devin's mom shows you a photo of how his foot looked 18 days after the injury, 2 months after, and today in clinic:



August 3, 2022

Extravasation injury Image A without caption. From Fig. 4B, 4C, 4D of Cho, Lee ¹ under the Creative Commons License: Attribution-NonCommercial 3.0 Unported. (<https://creativecommons.org/licenses/by-nc/3.0/>)

(Take a look at the Pedscases website for this podcast to see sample images of a healing extravasation injury in a neonate.

WOUND HEALING

Neonatal healing is quite exceptional. In adults and the elderly who are more prone to extravasation injuries are unlikely to heal as well. Would healing in the elderly population may impair wound healing due to co-morbid factors of systemic disease. This should also be considered when dealing with pediatric patients that may have congenital co-morbidities such as prematurity, immune conditions, or nutrition deficiencies. Issues such as these can complicate management, and instead of resulting in a fully healed wound, can develop into a longstanding ulcer

SUMMARY

Thank you very much for listening to this episode. We've covered a lot of information but hopefully you are now more informed about PIVIE's and how to manage them. Some take home points about PIVIEs are:

1. PIVIEs or Peripheral IV infiltration and extravasation injuries are iatrogenic injuries that occur when fluid from an intravenous line is deposited into the extravascular space.
2. Extravasation injuries involve vesicant fluids while infiltration injuries involve non-vesicant fluids.
3. Compartment syndrome should always be on the differential in the setting of a PIVIE injury, particularly if high volumes of fluid have been infused or if the infusing fluid is a vesicant.
4. Remember compartment syndrome by recalling the six Ps: Pain, pallor, poikilothermia, pressure, paralysis/paresthesias and pulseless as well as the three As for children: increasing analgesic requirements, agitation, and anxiety.
5. To prevent PIVIEs, a central venous catheter should be considered in long-term lines and the peripheral IV sites should be checked regularly for signs of a PIVIE.
6. Early signs of a PIVIE include difficulty to flush and localized edema or erythema, while late signs can include blistering, tissue necrosis, and diminished limb pulses secondary to swelling.
7. Lastly remember SLAAPP for the management of PIVIEs: stop the infusion, leave the cannula in place, aspirate as much as possible with a 3cc syringe, assess the site, pull the cannula, and provider notification.

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