Case: Supratherapeutic INR following warfarin ingestion
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Target Audience: Emergency Medicine Residents, Medical Students

Primary Learning Objectives

1. Generate a broad differential for an exposure to an unknown chemical
2. Detect the elevated INR
3. Treat anticoagulation overdose correctly with Vitamin K

Secondary Learning Objectives: Detailed technical/behavioral goals, didactic points

1. Describe the pathophysiology of vitamin K antagonists.
2. Discuss management priorities in the bleeding associated with a toxic ingestion from a vitamin K antagonist.
3. Describe the antidote and how it inhibits or reverses toxicity

Critical Actions Checklist

1. Recognition that GI decontamination would be ineffective
2. Give blood products for tachycardia and known bleeding.
3. Obtain workup to allow for narrowing of causative agent including PT/INR.
4. Administer IV Vitamin K following dad arriving with rat poison box or coagulation study results pointing towards an anti-coagulation agent as the cause.
5. Verbalize alternative diagnoses including Non-Accidental Trauma (NAT), poisoning, leukemia, ITP, etc.
6. Consult Poison control/Toxicology
7. Admit to PICU

Environment

1. Room Set Up - ED pediatric area

a. Manikin Set Up: Ecchymoses over extremities, demonstration of nosebleed. Two confederates in the room to act as parents.

b. Props - Standard ED equipment

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CASE SUMMARY

Synopsis of Case

This is a 4-year-old female with no significant past medical history who presents with her mother for an uncontrollable nosebleed and frank hematuria. The patient has some scattered bruises to the shins and forearms. The child appears uncomfortable, with the mother holding a towel to her nose and bruising is present under the blood pressure cuff. Dad is at home with their other kids but while cleaning the blood up in her room he finds a box of brodifacoum (a long-acting blood thinner rat poisoning) in her room. He calls the mother to inform her what he found. When asked, the child states that she found a couple of small red "candies" on the ground in the basement. The child pulls one out of her pocket and attempts to eat it before the mother stops her. The father brings the box in to compare. Approximately half of the box is empty, but mom states she did not notice the box when she was cleaning up the room a few days ago. The child may have eaten multiple pellets over several days. The father notes they found a rat in the home about a year ago and he had placed the bait out then and had forgotten about it. The child is evaluated and found to have a significant elevation of the INR but no signs of life-threatening hemorrhage. The child is treated with IV vitamin K and is subsequently admitted to the pediatric floor for 15 days as she has multiple epistaxis episodes that are difficult to control, and her INR stays elevated. The child goes on to fully recover over the next several months.

Setting is a busy community emergency department

Synopsis of Physical

Patient presents with bruising and appears pale and unwell
Mother reports the child experienced a nosebleed which was difficult to control with pinching of the nose at home.
Urine has been noted to be pink.

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Critical Actions

1. Avoid attempts at GI Decontamination
a. Activated charcoal or gastric lavage is not indicated for this type of ingestion as it has been found to be unsuccessful (1).
b. Do not give if ingestion time is greater than 1 hour before arrival.
c. Cueing guideline: The nurse can ask if the doctor really wants to attempt GI decontamination since they don't know when the child had the ingestion.
2. Consult Poison control/toxicology
a. Cue: The nursing staff asks if any consult is needed?
3. Obtain workup to allow for narrowing of causative agents including PT/INR
a. CBC, BMP + LFTs, Coagulation Studies, UA, UDS, Salicylate, acetaminophen, POC Glucose, Type and Screen, POC INR, Lactate, VBG, EKG, CXR, Abd XR
b. Cueing guideline: The nurse asks if you would like to send off any blood work?
4. Recognize the need for IV Vitamin K following dad arriving with rat poison or coagulation study results pointing towards an anti-coagulation agent as the cause.
a. Vitamin K q3-6 h, 2.5 - 5 mg. (max of 7mg/kg/24 hours), and serial INRs
b. Cueing guideline: Poison control recommends this, or the father walks in with rat poison showing anticoagulant requiring this.
5. Verbalize broad differential
a. Non-accidental trauma
b. Poisoning or ingestion including home medications, vitamin K antagonists.
c. Leukemia, ITP, TTP, lymphoma, or other blood-related cancer
d. Congenital Coagulopathies
e. Cueing guideline: The nurse can ask if the doctor has gotten a list of all medications and chemicals in the home
6. Admit to Peds/PICU
a. For serial labs to monitor hemoglobin, and INR following blood products and Vit K treatment
b. Cueing guideline: If the learner attempts to place on the floor, the pediatrician firmly refuses stating this patient requires closely monitored care and is inappropriate for the floor.

Critical Actions Checklist

Resident Name								
Case Description								
Skills measured **Core Competencies**: **PC** Patient Care, **MK** Medical Knowledge, **P** Professionalism, **SB** System-based Practice, **PB** Practice-based learning and improvement, **IC** Interpersonal and communication skills	**Very Unacceptable**	**Unacceptable**		**Acceptable**		**Very Acceptable**		
Data Acquisition (DA) PC, MK, IC	1	2	3	4	5	6	7	8
Problem Solving (PS) PC, MK, PB	1	2	3	4	5	6	7	8
Patient Management (PM) PC, MK, IC, P, PB, SB	1	2	3	4	5	6	7	8
Resource Utilization (RU) PC, PB, SB	1	2	3	4	5	6	7	8
Health Care Provided (HCP) PC, SB	1	2	3	4	5	6	7	8
Interpersonal Relations and Communication Skills (IRCS) IC, P	1	2	3	4	5	6	7	8
Comprehension of Pathophysiology (CP) MK, PB	1	2	3	4	5	6	7	8
Clinical Competence (CC) PC, MK, IC, P, PB, SB	1	2	3	4	5	6	7	8

Modified ABEM oral certification examination checklist and scoresheet
Modified checklist and scoresheet from the previous publication

Yes	No	Critical Actions
		Avoid attempts at GI Decontamination
		Consult Poison control/toxicology
		Obtain workup to allow for narrowing of causative agents including PT/INR
		Recognize the need for IV Vitamin K following dad arriving with rat poison or coagulation study results pointing towards an anti-coagulation agent as the cause.
		Verbalize broad differential
		Admit to Peds/PICU

Comments:

Yes	No	Dangerous Actions

Comments:

Modified ABEM oral certification examination checklist and scoresheet
Modified checklist and scoresheet from the previous publication

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History
Age: 4

Sex: Female

Name: Amelia Weasel

Method of Transportation: Personal vehicle

The person giving information: Mother

Chief Complaint: Nosebleed that won't stop

HPI: Mom is concerned because the child walked out of her room bleeding from her right nares and despite pressure and ice packs, it hasn't stopped bleeding for approximately 30 minutes. The mother denies any known recent trauma to the face but has noted new bruising to extremities over the past few days.

Allergies: No Known Drug Allergies

Past Medical History: hospitalized for RSV at age 1
Surgeries - none
Medications - none
Allergies - amoxicillin

Family Med History: The mother has a history of asthma.

Social History: lives in home with parents, only child, parents do not smoke, no marijuana use

Family Medications: multivitamins, ibuprofen, and Tylenol are in the home
No plants in the home

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Play of Case Guidelines

This is a case of a 4-year-old female with no significant past medical history who ingested brodifacoum rat poisoning and now presents with a persistent nosebleed and bruising to extremities.

1. The patient will present with vitals normal for age.
2. Brodifacoum is the primary toxicant in this case
3. The patient presents with an active nosebleed and bruising to extremities.
4. The learner should appropriately consider NAT as part of their differential
5. If managed correctly, she will require IV Vitamin K reversal.
6. Consultation with the Poison Control Center/Toxicologist and the Intensivist will also be required
7. The participant must obtain a thorough history and physical and broad workup to uncover the possibility of an unknown ingestion until brodifacoum is identified
8. The patient requires PICU/Peds admission for continued observation and serial reassessments

Physical Exam

Vital Signs: BP 108/66, P102, T37.4, R24, SpO2 98%
Wt 17 kg, Glucose (if asked for) 83, GCS 15

General Appearance: The child appears uncomfortable, sitting in her mother's lap

HEENT: Kitchen towel to nose (saturated with blood).

Lungs: Clear to auscultation bilaterally without wheezes, rhonchi, or rales.

CV: Normal rate and rhythm without murmurs, gallops, or rubs.

Abdomen: Non-tender, non-distended, with normal bowel sounds.

Extremities: Scattered bruises to upper and lower extremities.

GU: Normal external female genitalia. No gross blood.

Back: No midline tenderness. Scattered bruising noted.

Neurological: Alert, otherwise appropriate for age

Skin: Child has ecchymosis to the right arm (under where the blood pressure cuff was), scattered bruises to arms and legs

While performing the exam, the patient takes a couple of red pieces of what look like candy out of her pocket and attempts to eat them. Mom does not recognize them when asked. Child states she "found them in the basement while playing".

Mom calls dad and describes the "candy". He states he found a bait box in her room and will bring it in for comparison.

Required Actions within the first two minutes

- Perform primary survey
- Obtain vitals
- Initial treatments: Can decide to order blood products (FFP) for concerns of active bleeding but otherwise normal physical.

You astutely decide to take a photo of the "candy" and search for similar results on google under "bait".
Rat bait is the top result.

Branch Points

- Repeat vitals.
  - If IV NS fluids given or not vitals will remain unchanged BP 105/76, P134, R22, SpO2 97%
  - If blood products given, Vitals will improve: BP 110/80, P124, R22, SpO2 98%

Required Actions over the next four minutes

- Order labs including coagulation studies, Type and Screen, Lactate, VBG, BMP, Liver Function Tests, POC glucose, and UA. =Other recommended studies include salicylates, acetaminophen, iron, and EtOH.
- Order imaging including Abd XR
- Obtain an EKG
- Apply nose clamp +/- nasal packing
- Call poison control.

Branch Points

- If poison control is called, they should be informed that the most common agents used in rat bait are "Superwarfarins". Laboratory workup and imaging of the abdomen should be conducted to help differentiate causative agents including CBC, BMP, LFTs and PT/INR. There are other agents used as rodenticides including bromethalin, strychnine, sodium phosphide, sodium monofluoroacetate, and organophosphate agents as well as heavy metals such as thallium, barium, and arsenic.

Reassessment

- The nurse comes and tells you the patient's urine was found to have frank blood
- This will not change management at this point if the learner is treating appropriately

Branch Point:

- The clinician should call poison control with updated labs to which they indicate this is likely a superwarfarin agent like brodifacoum. Poison control will note the patient requires Vitamin K q3-6 h, 2.5 - 5 mg. (max of 7mg/kg/24 hours), and serial INRs.

- If they do not call poison control, the father arrives at the hospital with the rat poison box where you see the following: See Stimulus 12

Required Actions over the next several minutes:

- Give Vitamin K q3-6 h, 2.5 - 5 mg. (max of 7mg/kg/24 hours)
- Consult to case management and consideration of report to CPS for concern for NAT
- Admit to PICU with hematology (to help guide care as Vit K1 takes effect) consultation.

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STIMULUS INVENTORY

1. BMP with LFTs
2. CBC
3. Coagulation Studies
4. CPK
5. UA
6. UDS
7. Co-ingestions: Salicylate, acetaminophen, ETOH
8. 12-lead EKG
9. Abd XR
10. Rat poisoning/Broadificum packaging

Labs and imaging results

Stimulus #1:

BMP with LFTs	
Sodium	142
Potassium	3.6
Chloride	110
Bicarb	16
Glucose	110
BUN	17
Creatinine	1.2
AST	45
ALT	31
ALP	103
T. Bili	1.2
D. Bili	0.2
Albumin	4.3

Stimulus #2:

Complete Blood Count (CBC)	
WBC	8.000/mm3
Hg	9.4 g/dL
Hct	40%
Plts	249,000/mm
Differential	
PMNs	55%
Lymph	27%
Mono	12%
Eosin	4.5%
Baso	1.5%

Stimulus #3:

Coagulation studies	
PT	80 (10-12)
INR	102 (<1)
APTT	32 (30-40)

Stimulus #4:

CPK	47

Stimulus #5:

Urinalysis	
Color	Yellow
Specific gravity	1.017
glucose	Negative
protein	Negative
ketones	Trace
LE/Nitrites	Negative
Blood	Large
WBC	0
RBC	Many
Crystals/Bacteria	Negative

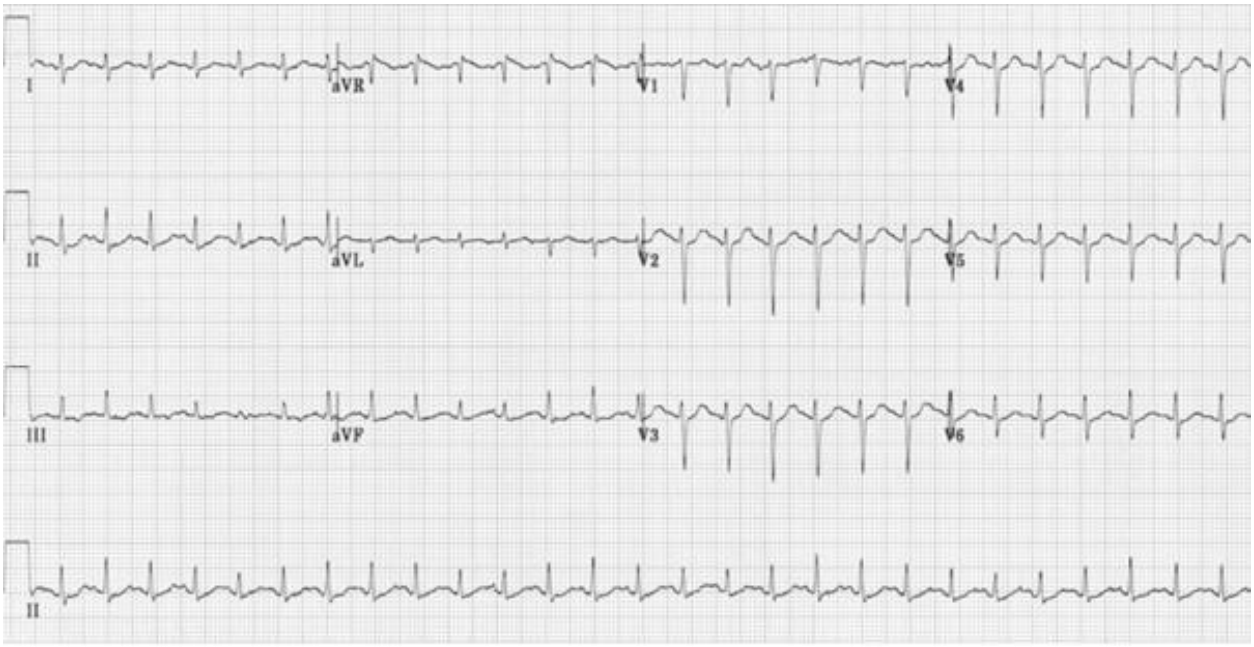
Stimulus #6:

Urine Drug Screen	
Benzodiazepines	Negative
THC	Negative
Cocaine	Negative
Opiates	Negative
TCAs	Negative
THC	Negative
Amphetamines	Negative

Stimulus #7:

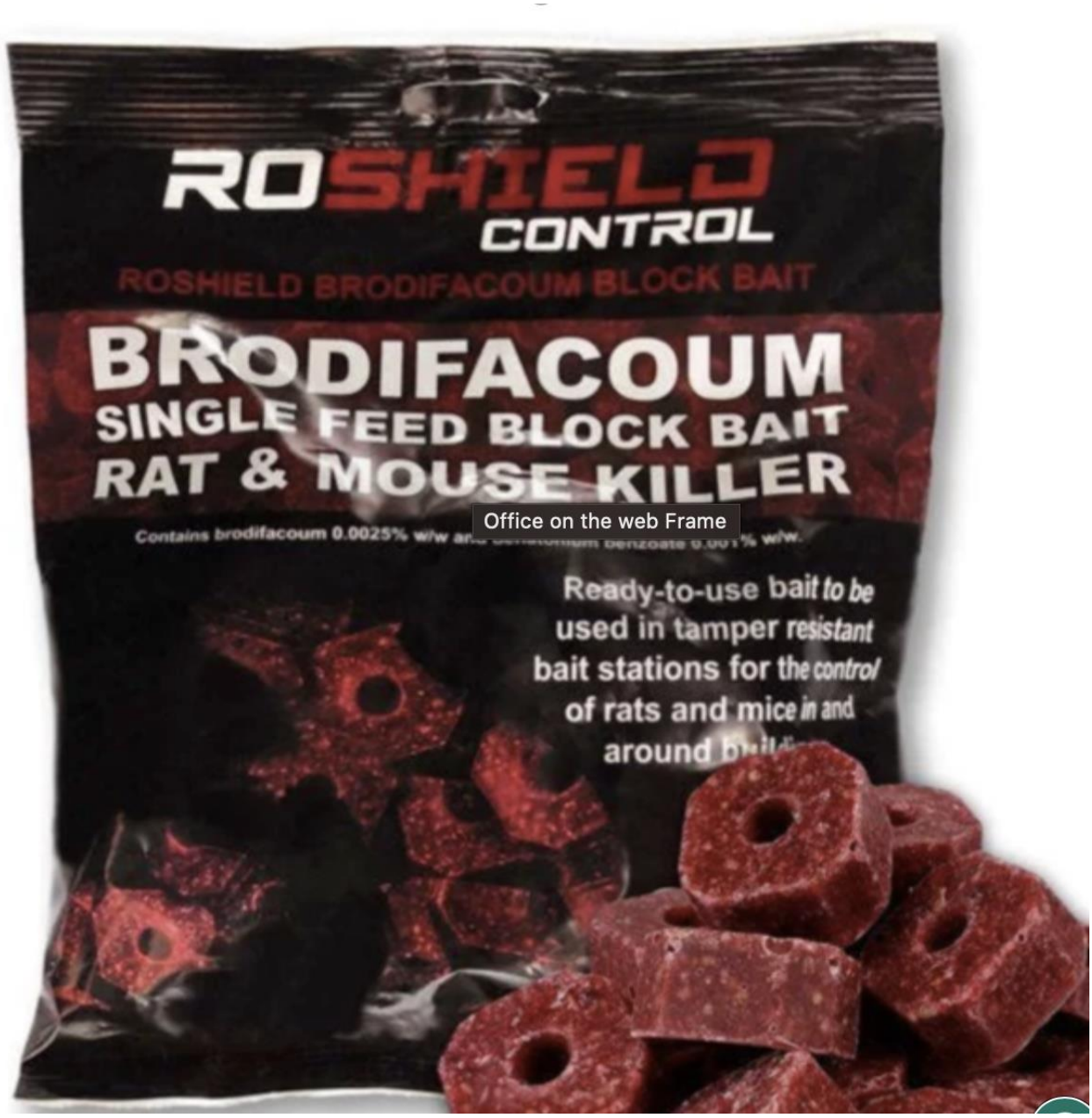
Co-ingestions	
ETOH	<0.05
Salicylate	Undetected
Acetaminophen	Undetected

Stimulus #8
12-lead:



Stimulus #9 Abdominal XR

Stimulus #10 - Brodifacoum



Debriefing Notes: Brodifacoum toxicity

Educational Objectives:

- To create a broad differential for ingestants and causes of bruising/coagulopathies and understand the importance of tailoring appropriate treatment.
- To understand the importance of repeat evaluations in identifying any need for further intervention or testing.
- To recognize limitations in GI decontamination including activated charcoal or whole bowel irrigation which would not be warranted in this case.

Learning points

- Historically, arsenic and heavy metals were more common in rodenticides, now highly potent and long-acting vitamin K antagonists are the most common. (Bromethalin, a potent electron chain uncoupler is very prevalent as well).
- Commonly available baits have brodifacoum concentrations around 0.0025% which equates to 50 mg/kg in the bait itself.
- Some of the older agents, such as barium carbonate can be visualized on abdominal x-ray.
- Heavy metal testing with a combination of blood and urine tests can be complicated and should be left to inpatient care as the main goal is to correct the toxidrome.
- Utilization of poison control is essential, particularly for the management of uncommon ingestions. The phone number is 1-800-222-1222.

Clinical Presentation

- Prolonged PT and INR
- Bleeding that is disproportionate to the level of injury
- Gingival bleeding, epistaxis, hematemesis, hematuria, petechiae, ecchymosis

Toxic Dose

- 1.5 mg for a 10 kg child is enough to cause symptoms
- 30 g of bait is a toxic dose. This is approximately equivalent to a teaspoon

Pharmacokinetics

- Superwarfarins (brodifacoum, difenacoum, bromadiolone, chlorophacinone)
- Competitive inhibitor of Vitamin K epoxide reductase complex 2
- Inhibits clotting cascade factors 2, 7, 9, 10
- Half-life is very long: 16 - 62 days
- Symptoms usually present within 24 - 72 hours of ingestion

Diagnosis

- Subacute to chronic superwarfarin ingestion with bleeding
- Epistaxis
- Hematuria
- Petechiae and ecchymosis

Emergency and Supportive Care

- In an acute bleeding event, consider the need for blood product replacement and emergent reversal with PCC.
- Supportive care for symptoms
- Vitamin K q3-6h, 2.5 - 5 mg max of 7mg/kg/24 hours

Decontamination

- GI Decontamination with activated charcoal or lavage could be considered in some instances as it may limit some absorption if ingestion had occurred within 1 to 2 hours of presentation. For this case we do not know when the last known ingestion is, but the patient is already symptomatic at presentation to the ED so an argument against it could be made.

Specific Drugs and Antidotes

- Give vitamin K q3-6 h
- Typical dosing of IV vitamin K for warfarin reversal is 2.5 - 5 mg
- Consider higher doses of vitamin K than typical and consult pharmacy
- Resources suggest giving up to 7 mg/kg over 24 hours divided into 4 doses

Prognosis

- The prognosis is good unless there is a critical bleeding event
- The PT/INR will likely not normalize for months, and the patient will need continued vitamin K dosing

Resources

1. Ingels et. al. A Prospective Study of Acute, Unintentional, Pediatric Superwarfarin Ingestions Managed without Decontamination. Ann Emerg Med. 2002;40:73-8.
2. Rodenticide toxicity - statpearls - NCBI bookshelf. Accessed November 7, 2023. https://www.ncbi.nlm.nih.gov/books/NBK554428/.
3. Queensland; c=AU; o=The S of. Rat poison contamination. Queensland Government. November 15, 2017. Accessed November 7, 2023. https://www.qld.gov.au/health/condition/accidents-injuries-and-poisonings/poisonings-and-chemical-exposures/rat-poison-contamination#:~:text=Commonly%20available%20baits%20contain%20up,number%20of%20teaspoon%20size%20doses.
4. Murphy A. Pediatric abdomen (AP supine view): Radiology reference article. Radiopaedia. March 23, 2023. Accessed November 7, 2023. https://radiopaedia.org/articles/paediatric-abdomen-ap-supine-view?lang=us.
5. Muzio BD. Normal chest - child: Radiology case. Radiopaedia. November 25, 2022. Accessed November 7, 2023. https://radiopaedia.org/cases/normal-chest-child?lang=us.
6. Burns E, Buttner R, Buttner EB and R. Sinus tachycardia. Life in the Fast Lane • LITFL. March 11, 2021. Accessed November 7, 2023. https://litfl.com/sinus-tachycardia-ecg-library/.
7. Case courtesy of Jeremy Jones, Radiopaedia.org. From the case rID: 10236
8. Bruno GR, Howland MA, McMeeking A, Hoffman RS. Long-acting anticoagulant overdose: brodifacoum kinetics and optimal vitamin K dosing. Ann Emerg Med. 2000 Sep;36(3):262-7. doi: 10.1067/mem.2000.108317. PMID: 10969235.
9. Centers for Disease Control and Prevention. (2018, April 4). *CDC*. Centers for Disease Control and Prevention. https://emergency.cdc.gov/agent/superwarfarin/casedefinition.asp#:~:text=Clinical%20description,occur%20within%2024%2D72%20hours.
10. Yip, L., Stanton, N. V., & Middleberg, R. A. (2020). Vitamin K1 treatment duration in patients with Brodifacoum poisoning. *New England Journal of Medicine*, *382*(18), 1764–1765. https://doi.org/10.1056/nejmc1916199