Case Presentation
Erwinase Panel

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بسم الله الرحمن الرحيم

Case Presentation (1) :

- Patient :

❖ A 12-year-old male diagnosed with ALL

- Treatment history :

❖Currently receiving induction chemotherapy according to a standard pediatric ALL protocol.

❖Received (PEG-asparaginase) as part of his induction regimen (administered 7 days prior to symptom onset).

❖No history of pancreatic disease or gallstones.

❖ No family history of pancreatitis.

Case Presentation (1)

- Presenting complaint:

❖Presents to the emergency department with acute onset of upper abdominal pain, nausea, and non-bilious vomiting.

❖Pain is epigastric, radiates to the back, and worsens with oral intake.

❖No fever, no diarrhea.

❖Normal bowel movements.

Case Presentation (1)

Clinical Findings

- Vital signs: Mild tachycardia, afebrile, normotensive.
- Physical exam: Tenderness in the epigastric region, no guarding or rebound tenderness, decreased appetite.

Laboratory results:

- Serum amylase: 460 U/L (↑)
- Serum lipase: 980 U/L (↑↑)
- Liver function tests: Normal
- Serum calcium and triglycerides: Within normal limits
- Imaging (abdominal ultrasound): Enlarged pancreas with no gallstones or biliary dilation

Case Presentation (1)

Diagnosis:

- ✅ Acute pancreatitis secondary to asparaginase therapy

- Asparaginase-induced pancreatitis is a well-recognized and potentially serious adverse event.
- It is usually drug-induced and not dose-dependent, and can occur even after a single dose.

Case Presentation (1)

Management Plan :

1. Immediate Supportive Care

- Discontinue asparaginase immediately and notify the oncology team.
- NPO initially; start IV fluids (isotonic saline) for hydration.
- Administer IV antiemetics and analgesics (e.g., acetaminophen or morphine as needed).

Case Presentation (1)

2. Monitor Clinical and Laboratory Parameters

- Monitor vital signs, urine output, and signs of worsening (e.g., hypoxia, hypotension).
- Repeat serum lipase/amylase, electrolytes, and glucose daily.
- Watch for complications: pseudocyst, pancreatic necrosis, or systemic inflammatory response syndrome (SIRS).

Case Presentation (1)

3. Nutritional Support

- Begin enteral feeding (oral or nasogastric) once pain subsides and patient tolerates fluids.
- Avoid parenteral nutrition unless absolutely necessary.

4. Long-Term Oncology Considerations

- Permanent discontinuation of asparaginase is generally recommended after moderate to severe pancreatitis.
- If mild and fully resolved, rechallenge is controversial and generally avoided in children due to risk of recurrence.

Case Presentation (1)

Teaching Point:

- Asparaginase-induced pancreatitis is a potentially serious but non-dose-dependent complication, occurring in approximately 2–10% of pediatric ALL patients.
- Management is primarily supportive.
- Re-exposure is not recommended in most cases due to the risk of recurrence, which can be more severe.

Case Presentation (2)

Patient:

✓A 10-year-old female with newly diagnosed acute lymphoblastic leukemia (ALL).

Treatment history:

- Currently undergoing induction chemotherapy per standard pediatric ALL protocol.
- Received a single dose of pegaspargase (Oncaspar) 5 days ago.
- No prior history of pancreatic or gastrointestinal disease.

Case Presentation (2)

Current status:

- The patient remains clinically well and asymptomatic.

- No abdominal pain, nausea, vomiting, or changes in appetite or bowel habits.

Case Presentation (2)

Laboratory Findings (routine monitoring):

- Serum amylase: 185 U/L (↑ mildly elevated)
- Serum lipase: 410 U/L (↑ significantly elevated)
- No electrolyte abnormalities.
- Normal liver function tests.
- Abdominal exam: Soft, non-tender, no organomegaly.
- Vital signs: Stable.

Case Presentation (2)

Diagnosis:

- ✅ Asymptomatic hyperamylasemia and hyperlipasemia following Oncaspar (pegaspargase)
- Pegaspargase is known to cause asymptomatic pancreatic enzyme elevations in a subset of patients.
- Not all elevations represent clinical pancreatitis

Case Presentation (2)

Management Plan

1. Clinical Monitoring

- Since the patient is asymptomatic, no signs of abdominal pain or systemic illness, no immediate intervention is needed beyond observation.

- Perform a thorough physical exam daily to monitor for early signs of pancreatitis (pain, vomiting, feeding intolerance).

Case Presentation (2)

2. Repeat Pancreatic Enzymes

- Recheck serum amylase and lipase in 48–72 hours to monitor trend.
- If enzymes normalize or decrease without symptoms → continue routine therapy.
- If levels rise further or patient develops symptoms → evaluate for clinical pancreatitis.

3. Maintain Hydration

- Ensure adequate hydration, either orally or IV, especially during chemotherapy.
- Avoid medications that can further stress the pancreas.

Case Presentation (2)

4. Do Not Re-Challenge Prematurely

- If the patient develops signs of clinical pancreatitis later on, discontinue asparaginase.

- If no symptoms and enzyme levels normalize, continuation of asparaginase may be considered,
depending on institutional protocols.

Case Presentation (2)

Teaching Point:

- Transient, asymptomatic elevations in serum amylase and lipase are relatively common following pegaspargase administration and

  do not necessarily indicate acute pancreatitis.

- In the absence of clinical symptoms, these enzyme elevations typically resolve spontaneously and do not warrant discontinuation of therapy.

- Close monitoring and repeat labs are essential to distinguish between benign enzyme elevations and evolving pancreatitis.

Expect panel recommendations
For pancreatitis management

Chemical pancreatitis

- Elevation of serum amylase and/or lipase

Treatment continuation with Elevated amylase and lipase Value <**3ULN**
(ULN :Upper Limit of Normal)

Clinical pancreatitis

- Elevation of serum amylase and/or lipase
- Mild to severe symptomatic manifestations , e.g. nausea vormiting , abdominal pain , tachycardia , hypotension , fever
- Mortality rate of 30% in patients with severe pancreatitis

Permanent discontinuation with elevated amylase and lipase Values > **3ULN** for > 3 days and/or pancreatic pseudocyst

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Case Presentation (3)

Patient:

A 9-year-old male with (ALL) undergoing induction chemotherapy according to a standard pediatric protocol.

Treatment history:

- Received a dose of pegaspargase (Oncaspar) intravenously as part of induction therapy.
- Tolerated previous doses of chemotherapy well.
- No known drug allergies prior to this event.

Case Presentation (3)

Presenting event:

- Approximately 10 minutes into the Oncaspar infusion, the patient developed:
- Sudden onset of generalized urticaria
- Facial swelling
- Shortness of breath and wheezing
- Hypotension (BP 75/40 mmHg)
- Tachycardia and mild cyanosis

Infusion was stopped immediately, and the emergency response team was called.

Case Presentation (3)

Diagnosis:

- ✅ Acute anaphylaxis secondary to (Oncaspar)
- Anaphylaxis is a known and potentially life-threatening adverse reaction to asparaginase products, particularly with IV pegaspargase.
- It can occur even in patients with no prior allergic history and may present during or shortly after infusion.

Case Presentation (3)

Management Plan :

◦ Immediate Emergency Management (Per Anaphylaxis Protocol):

1. Stop the infusion immediately.
2. Administer intramuscular epinephrine (0.01 mg/kg, max 0.5 mg per dose) in the lateral thigh.

   Repeat every 5–15 minutes if needed based on response.
3. Ensure airway, breathing, and circulation:

- Administer 100% oxygen
- Provide IV fluid bolus (normal saline, 10–20 mL/kg rapidly) for hypotension

Case Presentation (3)

4. Administer adjunctive medications:

- Antihistamines: Diphenhydramine IV
- Corticosteroids: Methylprednisolone IV to reduce late-phase reactions
- Inhaled beta-agonists (e.g., salbutamol) for bronchospasm

Case Presentation (3)

Post-Stabilization Monitoring:

- Observe in a monitored setting for at least 4–6 hours (or longer if severe reaction).
- Monitor for biphasic anaphylaxis, which may occur hours later.

Case Presentation (3)

Long-Term Oncology Management:

1. **Discontinue all forms of pegaspargase permanently.**

- Re-exposure is contraindicated due to high risk of recurrent anaphylaxis.

2. **Substitute with Erwinia asparaginase**

(e.g., Erwinase or Rylaze):

Case Presentation (3)

Erwinia-derived asparaginase has a different protein structure and is often tolerated in patients with hypersensitivity to E. coli–derived formulations.

- Dosing schedule is more frequent (e.g., 3×/week) due to shorter half-life.

Case Presentation (3)

Teaching Point:

- Anaphylaxis is a serious, IgE-mediated hypersensitivity reaction to pegaspargase, occurring in up to10% of patients.

- Prompt recognition and treatment with IM epinephrine is lifesaving.

- Re-challenging with the same preparation is contraindicated;
- Erwinia-derived asparaginase is the standard alternative in such cases.

Management of asparaginase – associated toxicities in AYA and adult patients

Hepatotoxicity	Pancreatitis	Thrombosis/bleeding	Hypersensitivity	Hyperglycaemia	Neurological complications	Hyperammonaemia
• Hold asparaginase • treatment if hyperbilirubinaemia or transaminitis • Vitamin B complex 1 tablet orally 2x per day and L-carnitine 50 mg/kg/day IV in 6 divided doses if direct bilirubin> 3 mg/dL and/or AST/ALT >3 x ULN • Reintroduce ONCASPAR if bilirubin/AST/ ALT return to normal range and positive benefit/risk ratio	• Discontinue asparaginase if symptomatic • Permanent discontinuation if clinical pancreatitis with amylase/ lipase elevation > 3x ULN for > 3 days and / or pancreatic pseudocyst • Treat as for any –cause pancreatitis : bowel rest , IV fluids , nutrition support , pain management	• No standard or reliable parameters for predicting or preventing complications related to coagulatory alterations • On-demand fibrinogen or antithrombin replacement • Enoxaparin for at • Least four weeks after each ONCASPAR dose[1] • Unfractionated heparin for thrombosis treatment if clinical status tenuous , low molecular weight heparin in stable patients	• Monitor patients for 1 hour following administration[6,7] • Administer antihistamines, corticosteroids and vasopressors depending on symptoms • Switch from ONCASPAR to Erwinaze if ≥Grade 3 hypersensitivity and asparaginase activity level <0.1 IU/mL • Discontinue asparaginase for serious hypersensitivity reactions	• Hold asparaginase • Regulate blood glucose with insulin • Monitor blood and urine glucose levels • Resume asparaginase treatment at prior dose level once blood glucose regulated	• Discontinue asparaginase • Lactulose therapy indicated for hyperamonaemia • Standard supportive care	• Increase the infusion time to ≥2hours • For patients with metabolic disorders , treat with L-arginine , metformin or sodium phenylacetate/ sodium benzorate

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Management of asparaginase – associated toxicities in AYA and adult patients

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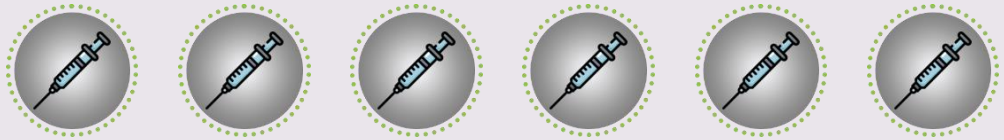
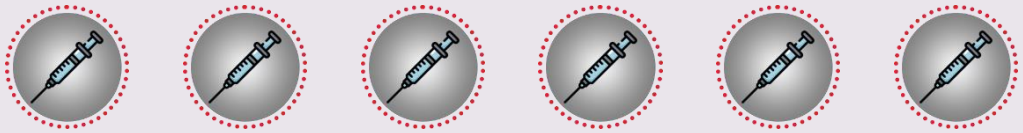
Less frequent dosing versus other asparagiases

Dosing per 14 days from prescribing information :
1 dose versus up to 6 doses

* The recommended dposology in adults aged > 21 years in 2000 U/m^2 every 14 days

Pegaspargase (IM/IV)2500 U/m^2	 1 dose every 2 weeks
Native E.coli[2] asparaginase (IM/IV)6000 IU/m^2	
Erwinia asparaginase [3]‡ (IM) 25,000 IU/m^2	

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Indications for Switching from Oncaspar to Erwinia Asparaginase

- Switching from pegaspargase (Oncaspar) to Erwinia-derived asparaginase is indicated in the following clinical scenarios:

Indications for Switching from Oncaspar to Erwinia Asparaginase

1. (Anaphylaxis or Allergic Reaction)

- Immediate hypersensitivity (e.g., anaphylaxis, urticaria, bronchospasm, hypotension) occurring during or shortly after Oncaspar infusion.
- Any IgE-mediated or non-IgE mediated allergic reaction that requires treatment and discontinuation of Oncaspar.

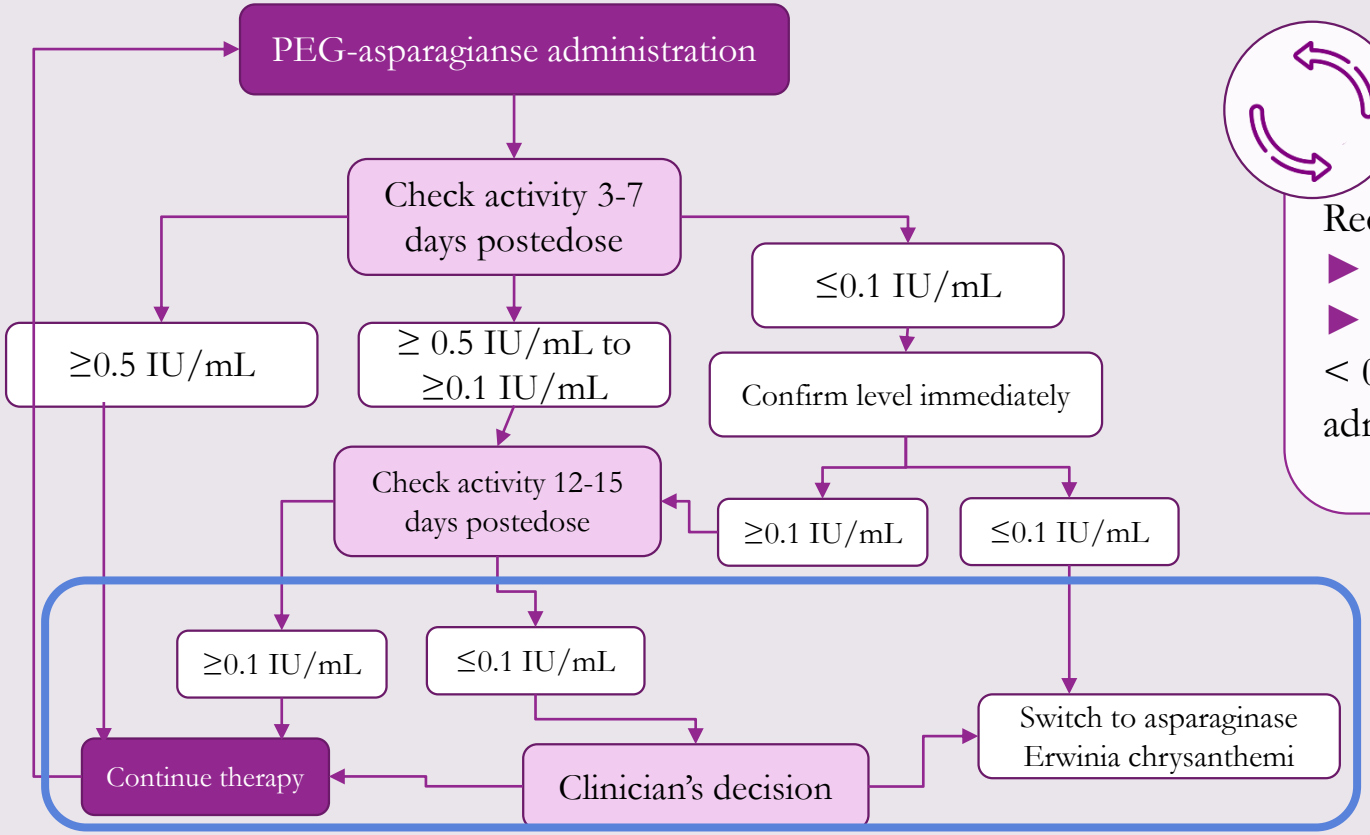
Indications for Switching from Oncaspar to Erwinia Asparaginase

2. Silent Inactivation

- Development of neutralizing anti-asparaginase antibodies without clinical signs of allergy, leading to:
- Undetectable serum asparaginase activity despite Oncaspar administration.
- Subtherapeutic drug levels confirmed by therapeutic drug monitoring (TDM).

TDM recommandations

- Standard use of TDM recommended in NCCN guidelines
- More and more implemented in ALL protocols for children , AYA and adults paitents (e.g. ALLTogether , DFCI , GMALL protocols)
  Example of algorithm foe pegaspargase activity monitoring:



Recommandations for switching to erwinase :

- if severe hypersensitivity reactions
- if confirmed asparagianse activity < 0.1IU/mL (at day 3-7 and 12-15 after administration)

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Indications for Switching from Oncaspar to Erwinia Asparaginase

3. Pancreatitis

- Development of asparaginase-induced pancreatitis, especially moderate to severe cases.
- If Oncaspar is permanently discontinued due to pancreatitis and continuation of asparaginase is deemed necessary, Erwinia-derived products may be used under strict monitoring.

Indications for Switching from Oncaspar to Erwinia Asparaginase

4. Hepatotoxicity or Thrombosis

- In rare cases of severe hepatotoxicity or asparaginase-associated thrombosis where Oncaspar is discontinued but continuation of asparaginase is essential, switching to Erwinia may be considered cautiously (based on risk-benefit assessment).

5. Scheduling Needs or Drug Shortage

- In some settings, supply limitations or scheduling constraints may lead to substitution, particularly if Oncaspar is unavailable or delayed.

Expect panel recommendations for coagulopathy management

- Monitoring
- Management
- Prophylaxis

Thrombosis

- Monitoring of antithrombin III level at baseline and twice weekly for at least 4 weeks after each pegaspargase dose
- Therapy continuation after thromnolism with co-administration of low molecular weight heparin (LMWH)
- Prophylactic use of LMWH in children and controversial in adults(not routinely used)

Hemorrhage &bleeding

- Monitoring of fibrinogen level at baseline and 3 times per week for at least 4 weeks after each pegaspargase dose
- Use of cryoprecipitate for fibrinogen replacement , and therapy continuation (no bleeding recurrence)
- Use of cryoprecipitate with caution (including thrombogenic factor VIII)

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Indications for Switching from Oncaspar to Erwinia Asparaginase

- **Teaching Point:**
- Erwinia asparaginase is derived from a different bacterial source (Erwinia chrysanthemi) and has minimal cross-reactivity with E. coli–derived asparaginase (like Oncaspar).

- It is used as a standard alternative when Oncaspar is discontinued due to allergy or inactivation, ensuring that patients still receive the full therapeutic benefit of asparaginase during ALL treatment.

Thanks
For
Your attention