Plasminogen Deficiency, Type 1: For Gastroenterology



Overview of Plasminogen Deficiency (PLGD)

- PLGD Type 1: a quantitative protein deficiency, with decreased plasminogen activity and decreased antigen
 - Due to a genetic mutation in the gene for plasminogen; > 50 different mutations have been identified; Autosomal Recessive inheritance
 - Most common presenting symptom is ligneous conjunctivitis, but multi-organ, systemic disease that can be life-threatening
- PLGD Type 2: reduced functional activity of plasminogen, but normal antigen levels; patients are asymptomatic

	Normal	PLGD Type 1	PLGD Type 2
Plasminogen Activity	70-130%	Decreased	Decreased
Plasminogen Antigen	6-25 mg/dL	Decreased	Normal
For Patients: My Plasminogen Activity			

Diagnosis

- Complicated by heterogeneous symptoms; symptoms can wax and wane
- Mucosal surfaces of the eyes, ears, nose, gums, airways, lungs, GI tract, kidneys, GU tract, CNS, and skin can all be affected
- Initial point of medical contact therefore includes many disciplines

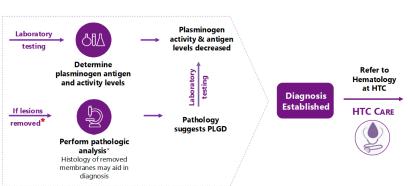
Treatment

- Ryplazim (plasminogen, human-tvmh) given by IV infusion leads to resolution of lesions
- Surgical removal of lesions, though initially helpful, leads to accelerated regrowth
- Referral to a Hemophilia Treatment Center (HTC) to serve as medical home, and:
 - Educate on product use
 - Ongoing symptom monitoring, outcomes, safety
 - Administer doses, determine dosing schedule
 - Teach home infusion

Patient presents with possible ligneous lesions



Establish Diagnosis



Participate in Research to advance knowledge & care



Obtain Genetic Testing

Homozygous or double heterozygous
 Multiple genetic variants of the *plasminogen* gene lead to type 1 deficiency

Additional Care
Through HTC

- Review patient & family history
- Evaluate all siblings: Asymptomatic siblings require preemptive care
- Perform complete review of systems
- Utilize multidisciplinary team to support patient/family including genetic counseling



- Perform complete physical examination
- Document visually-identified lesions; evaluate systems/sequelae where lesions are suspected
- · Determine need for therapy
- Consent for ATHN data systems
- Collect and add data to address unanswered questions
- Follow affected individuals or scheduled ongoing basis
- · Monitor response to therapy

^{*}Lesion removal prior to diagnosis not recommended

Gastroenterology Specific Diagnostic Findings

INITIAL PRESENTATION

- Localized & segmental GI inflammation
- Ligneous lesions
- ♦ Abdominal pain
- ♦ Hematemesis
- ◆ Tenesmus
- ♦ Anemia and iron deficiency

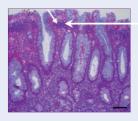


Ligneous lesions

Intreated

ADVANCED DISEASE

- ◆ Ligneous lesions
- Chronic GI ulcers
- Potential inflammatory bowel disease
- ♦ Hematemesis
- Hematochezia
- Melena
- Anemia and iron deficiency
- Abdominal pain



Dense subepithelial fibrin deposition

Balram et al. 2021. Ref 5. Used with permission

Veres et al. 2011. Ref 6. Used with permission

Gastreoenterology Specific Treatment Considerations

- New or suspected diagnosis:
 - o Obtain diagnostic blood test (plasminogen activity level) or refer to hematologist to order
 - If confirmed, refer to HTC to establish care and perform thorough review of systems
 - Patients may have more than one system affected at presentation or occurring over time
- Confirmed diagnosis:
 - Coordinate clinical care and collaborate closely with existing care team at HTC
 - Send clinical notes and photos
- Be suspicious of common diagnoses:
 - Consider plasminogen deficiency in differential diagnoses of patients with ligneous conjunctivitis or gingivitis with any GI symptoms, especially when symptoms suggest IBD or gastrointestinal ulcers
 - New occurrence of gastrointestinal symptoms in patient with known plasminogen deficiency should prompt timely referral and coordination with HTC
- Patients may experience GI involvement related to plasminogen deficiency
- Inflammatory bowel disease has been reported in a few patients with PLGD
- Causal relationship between PLGD and IBD has not been established but warrants further investigation
- PLGD may make healing of inflammatory lesions more difficult
- It is reasonable to provide therapy for both IBD and PLGD to obtain the best outcome
 - o Timely referral to HTC for IV plasminogen management perioperatively is ideal

Learn More:







