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

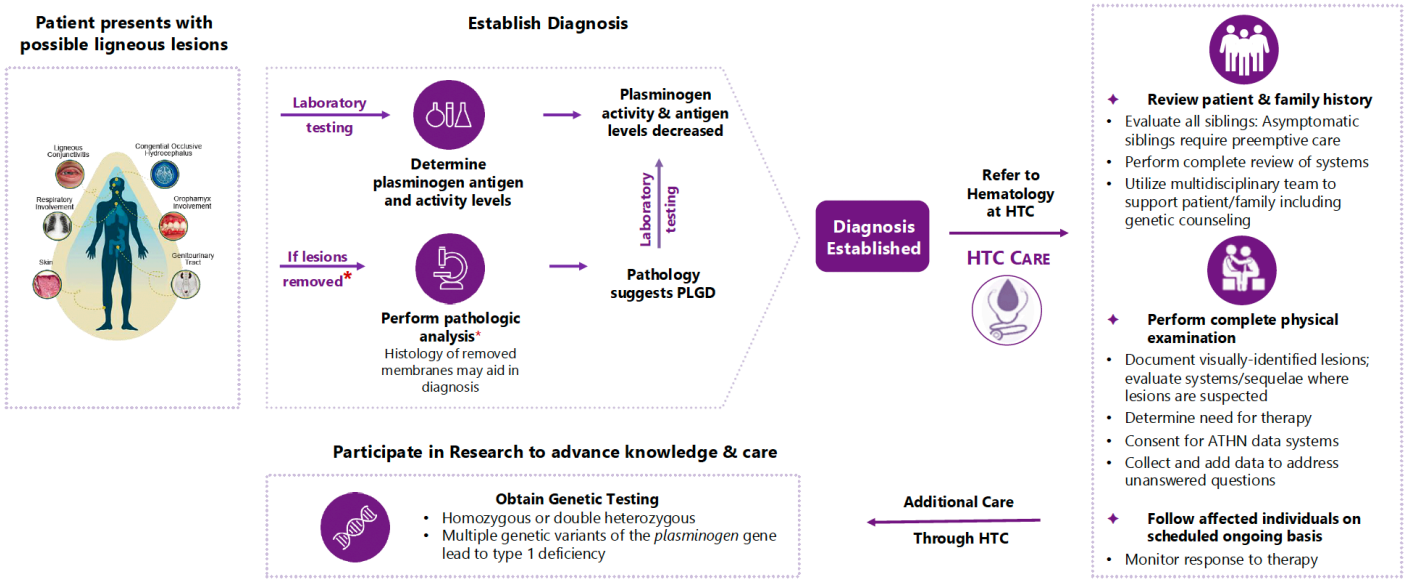
	Normal	PLGD Type 1	PLGD Type 2
Plasminogen Activity	70-130%	Decreased	Decreased
Plasminogen Antigen	6-25 mg/dL	Decreased	Normal
For Patients: My Plasminogen Activity			

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



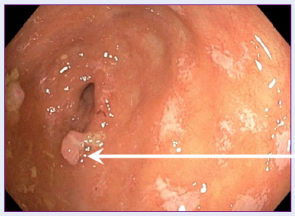
*Lesion removal prior to diagnosis not recommended

Nakar, et al. Plasminogen deficiency laboratory evaluation found on http://www.rarecoagulationdisorders.org/diseases/plasminogen-deficiency/%20laboratory-evaluation. Accessed 27 January 2023; Image on left from https://www.plgdeficiency.com/ Accessed 27 January 2023

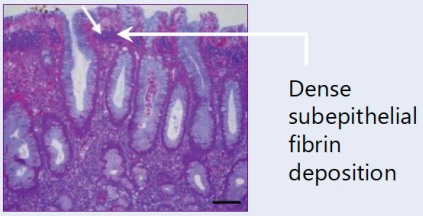
Gastroenterology Specific Diagnostic Findings

INITIAL PRESENTATION	ADVANCED DISEASE
✦ Localized & segmental GI inflammation ✦ Ligneous lesions ✦ Abdominal pain ✦ Hematemesis ✦ Tenesmus ✦ Anemia and iron deficiency	✦ Ligneous lesions ✦ Chronic GI ulcers ✦ Potential inflammatory bowel disease ✦ Hematemesis ✦ Hematochezia ✦ Melena ✦ Anemia and iron deficiency ✦ Abdominal pain

Untreated



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:
  - 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
  - Timely referral to HTC for IV plasminogen management perioperatively is ideal

Learn More:

Partners in Bleeding Disorders Education

PLASMINOGEN DEFICIENCY FOUNDATION

The Plasminogen Deficiency Foundation gratefully acknowledges Partners in Bleeding Disorders Education for their assistance and for granting permission to use several graphics in creating this document.