Plasminogen Deficiency, Type 1: For ENT/Otolaryngology

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

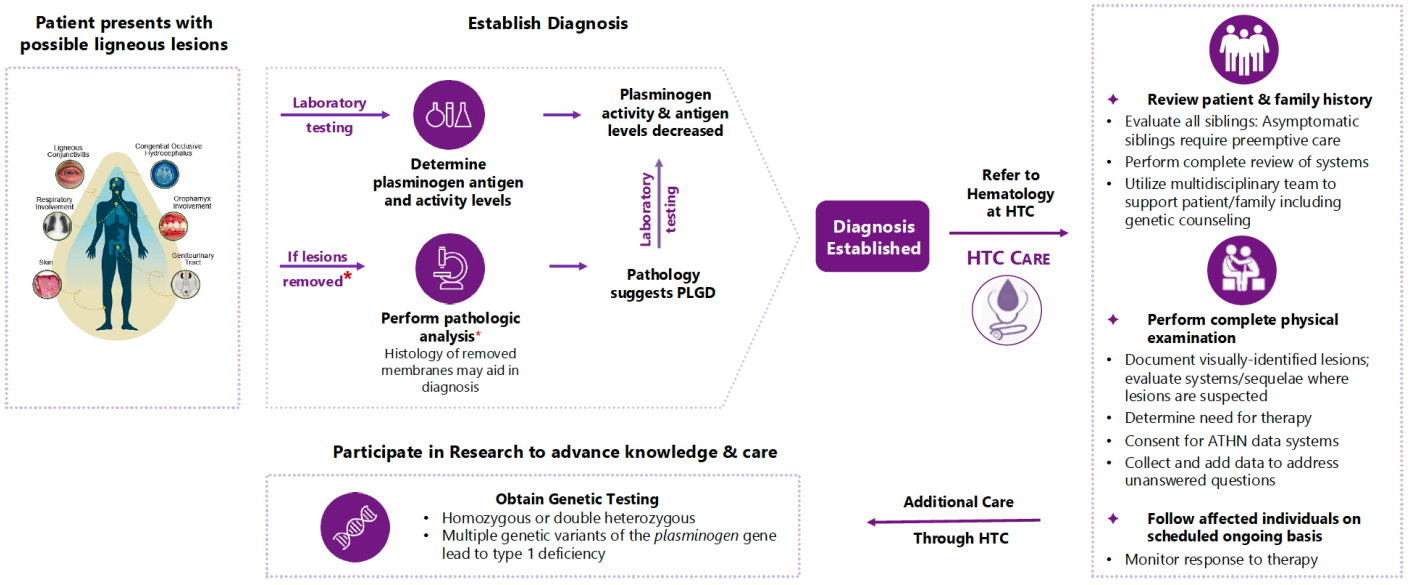
	Normal	PLGD Type 1	PLGD Type 2
Plasminogen Activity	70-130%	Decreased	Decreased
Plasminogen Antigen	6-25 mg/dL	Decreased	Normal
For Patients: My Plasminogen Activity			

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



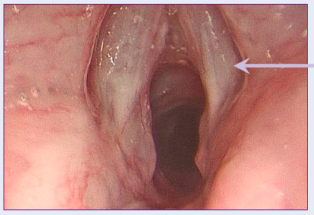
*Lesion removal prior to diagnosis not recommended

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

ENT / Otolaryngology Specific Diagnostic Findings

INITIAL PRESENTATION

- Sinusitis & congestion
- Nasal plaques
- Chronic nasal congestion
- Rhinorrhea
- Epistaxis
- Ligneous tonsillitis
- Acute and chronic hoarse voice
- Vocal cord edema, nodules
- Otitis media
- Middle ear effusion
- Otorrhea
- Reversible hearing impairment



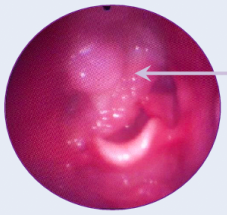
Glottis laryngeal edema

Courtesy of Christopher T. Wootten MD; Children's Hospital Vanderbilt

Untreated

ADVANCED DISEASE

- Chronic sinusitis
- Nasal polyps
- Chronic nasal and/or sinus obstruction
- Persistent ligneous tonsillitis
- Aphonia
- Permanent vocal cord dysfunction
- Cholesteatoma
- Ossicular erosion
- Permanent hearing impairment
- Deafness



Airway obstruction

Cohen et al, 2012. Ref 3. Used with permission

ENT/Otolaryngology 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 for thorough review of systems
    - Patients may have more than one system affected at presentation or occurring over time
    - Early referral to HTC is critical to reduce risk of permanent sequelae
- Confirmed diagnosis:
  - Coordinate clinical care with existing care team at HTC; send clinical notes and photos and work closely in collaboration with HTC
- Be suspicious of common diagnoses in PLGD patients, as they may be the result of the condition
  - Chronic hoarseness due to edema or lesions of the vocal cords
  - Chronic sinusitis
  - Nasopharyngeal involvement
    - Nasal cavity lesions leading to irritation, epistaxis, and obstruction
    - Recurrent tonsillitis, with or without tonsilloliths
    - Recurrent ear infections with frequent malfunction of myringotomy tubes (e.g., otorrhea, tube obstruction/extrusion), or otitis media with effusion (OME)
  - Laryngotracheobronchial tree involvement
  - Cholesteatoma-like complications of the middle ear with involvement of the mastoid system
  - Ligneous conjunctivitis (often the first noticeable symptom of PLGD)
- Coordination with HTC assures optimal outcomes from interventions (e.g., bronchoscopy, laryngoscopy, PE tube placement)

Learn More:

Partners in Bleeding Disorders Education

PLASMINOGEN DEFICIENCY FOUNDATION

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