

Plasminogen Deficiency, Type 1: For Pulmonology



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

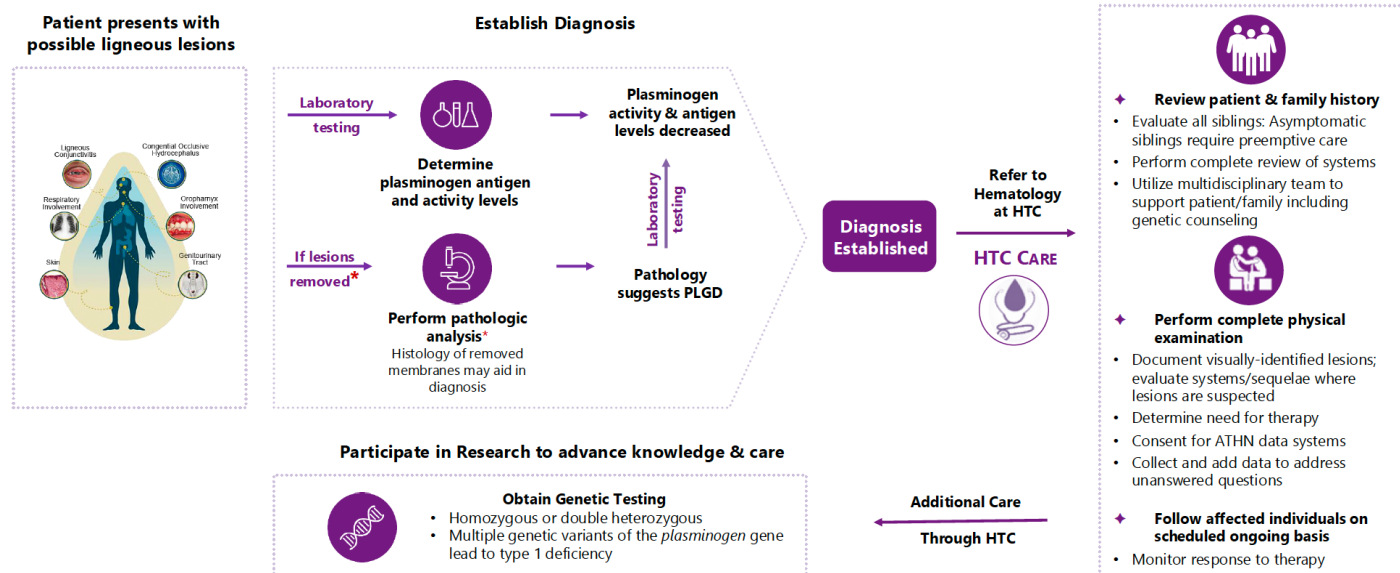
	Normal	PLGD Type 1	PLGD Type 2
Plasminogen Activity	70-130%	Decreased	Decreased
Plasminogen Antigen	6-25 mg/dL	Decreased	Normal
For Patients: My Plasminogen Activity			

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

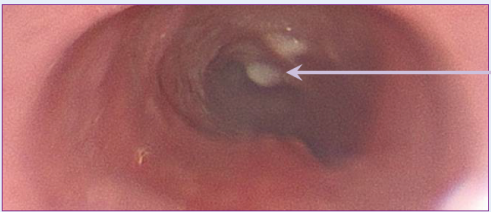
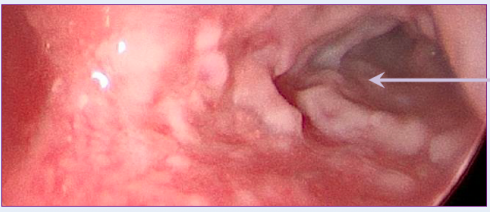
Treatment

- 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

Pulmonology Specific Diagnostic Findings

INITIAL PRESENTATION		ADVANCED DISEASE
◆ Ligneous lesions ◆ Upper tract ◆ Lower tract ◆ Airway obstruction ◆ Chronic cough or presumed asthma ◆ Atelectasis ◆ Recurrent pneumonia	Untreated 	◆ Bronchiectasis ◆ Permanent atelectasis & scarring ◆ Decreased lung capacity ◆ Obstructed airways with cough, hemoptysis, or hypoxia ◆ Respiratory distress ◆ Mortality
 Sparse ligneous lesions adherent to the tracheal wall		 Ligneous lesions narrowing right mainstem bronchus

Images courtesy of Christopher T. Wooten MD, Children's Hospital Vanderbilt

Pulmonology 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 to perform a thorough review of systems
- Confirmed diagnosis:
 - Coordinate clinical care with existing care team at HTC
 - Coordinated procedures with HTC hematologist to ensure adequate plasminogen coverage
- Be suspicious of common diagnoses as they may be PLGD-related; ligneous airway lesions can resemble:
 - Reactive airway disease
 - Atelectasis
 - Recurrent pneumonia
 - Chronic cough
- Patients starting plasminogen therapy may slough lesions, develop hemoptysis, hypoxia and life-threatening obstruction of airways when large lesions detach
- ICU/PICU admission is recommended for patients with significant lung involvement for therapy initiation especially in young children
- Direct bronchoscopy should be considered early in patient management
- Patients with any respiratory symptoms must be closely monitored, particularly young patients with small airways, due to possibility of obstruction

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