Plasminogen Deficiency, Type 1: For Obstetrics/Gynecology

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

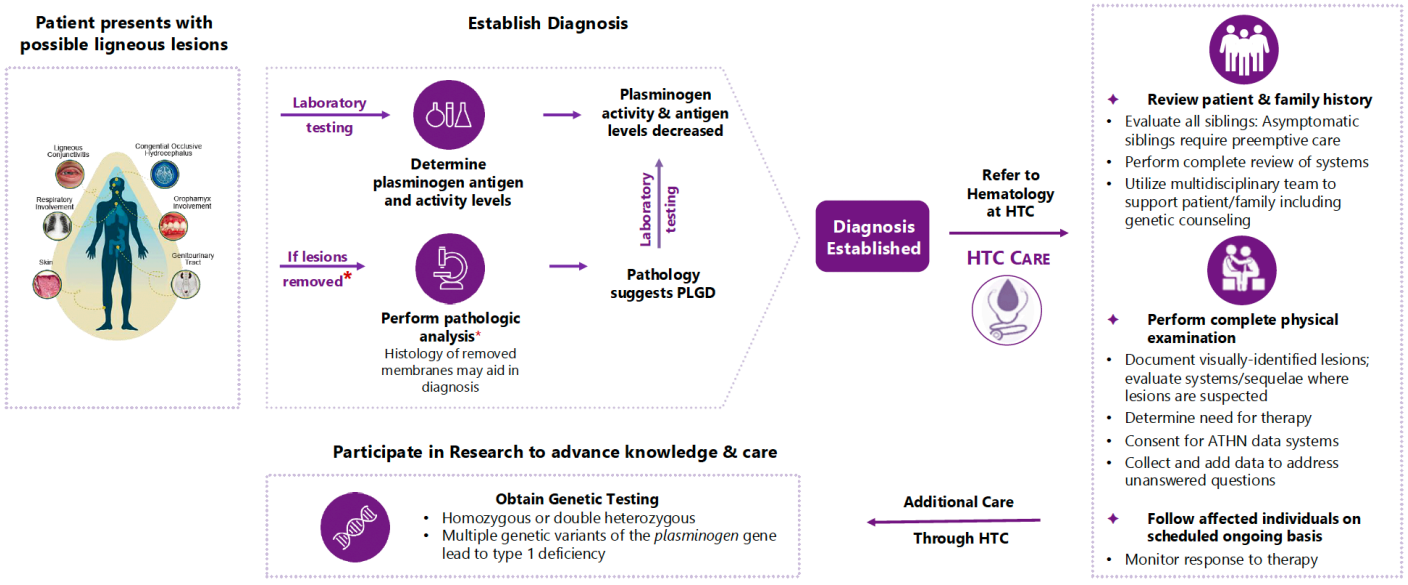
	Normal	PLGD Type 1	PLGD Type 2
Plasminogen Activity	70-130%	Decreased	Decreased
Plasminogen Antigen	6-25 mg/dL	Decreased	Normal
For Patients: My Plasminogen Activity			

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

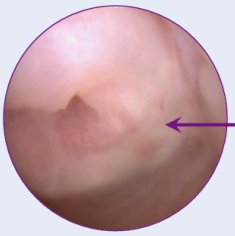


*Lesion removal prior to diagnosis not recommended

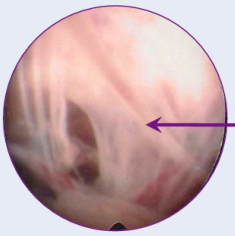
Nakar, et al. Plasminogen deficiency laboratory evaluation found on http://www.rarecoagulationdisorders.org/diseases/plasminogen-deficiency/%20laboratory-evaluation. Accessed 27 January 2023; Image on left from https://www.plgdeficiency.com/ Accessed 27 January 2023

Obstetrics / Gynecology Specific Diagnostic Findings

INITIAL PRESENTATION		ADVANCED DISEASE
✦ Vaginal, cervical, endometrial, fallopian tube, ovarian ligneous lesions ✦ Vaginal passage of fibrous tissue ✦ Premenarchal vaginal bleeding ✦ Dysmenorrhea, menorrhagia ✦ Dyspareunia	Untreated	✦ Vaginal, cervical, endometrial, fallopian tube, ovarian ligneous lesions ✦ Vaginal passage of fibrous tissue ✦ Dysmenorrhea, menorrhagia ✦ Dyspareunia ✦ Obstructed fallopian tubes ✦ Ovarian fibrosis ✦ Infertility



Ligneous lesions at the ectocervical junction



Ligneous membranes in cervical canal

Courtesy of Dr. Lesley L. Breech, Cincinnati Children's Hospital

Baithun et al. 2018. Ref 4. Used with permission

Obstetrics / Gynecology 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
  - Manage procedures, pregnancies, and surgeries in close collaboration with HTC
- Be suspicious of common diagnoses:
- Dysmenorrhea and irregular abnormal menses might be due to ligneous lesions
- Persistent vaginal discharge or passage of vaginal tissue may be a premenarchal symptom of PLGD
- In patients with type 1 plasminogen deficiency, GU complications can occur
  - Vaginal, cervical, uterine, tubal, and ovarian lesions
  - Abnormal fallopian tube morphology
  - Ovarian disease
- Approximately 27% of females of childbearing age with PLGD are diagnosed with infertility
- Pregnancy in PLGD patients should be considered high risk

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.