Table S1. Listing of baseline characteristics

			Clinical manifestations of disease			Plasminogen	
Patient	Sex	Age (yr)	Age at Diagnosis	Lesion (symptom) history	Lesion Duration	Prior treatments of disease	Activity* (%)	Antigen† (mg/dL)
1	F	39	1 yr	Conjunctiva	6 mo‡	Surgery: ear	29	3.8
				Ear (pain, itching)	38 yr			
				Cervix (pain)	22 yr‡			
2	M	35	10 mo	Conjunctiva (discharge, pain)	15 yr‡	Eye drop: heparin, cyclosporine, plasminogen	43	5.4
						Surgery: conjunctival (9)		
3	F	16	3 yr	Conjunctiva (discharge, tearing, redness)	4 yr	Eye drop: heparin, cyclosporine	28	5.6
				Ear (pain)	12 yr	Infusion: FFP		

Table S1. Listing of baseline characteristics

				Clinical manifestations of disease			Plasminogen	
Patient	Sex	Age (yr)	Age at Diagnosis	Lesion (symptom) history	Lesion Duration	Prior treatments of disease	Activity* (%)	Antigen† (mg/dL)
4	F	24	2 yr	Conjunctiva (discharge, tearing, redness)	8 yr	Eye drop: heparin, chloramphenicol	28	13.4
				Nasopharynx	10 yr	Surgery: cervical (1)		
				Gingiva	19 yr‡	Infusion: FFP		
				Tonsils (pain, swelling)	17 yr			
				Vocal cords	11 yr			
				Lungs (pain in chest)	1 mo‡			
				Cervix	6 yr			
				Ovaries	6 yr			
				Urethra	6 yr			
5	M	20	10 yr	Conjunctiva (discharge)	1 yr	Eye drop: heparin	22	2.1

Table S1. Listing of baseline characteristics

				Clinical manifestations of disease			Plasminogen	
Patient	Sex	Age (yr)	Age at Diagnosis	Lesion (symptom) history	Lesion Duration	Prior treatments of disease	Activity* (%)	Antigen† (mg/dL)
6	F	37	14 yr	Conjunctiva (discharge) Gingiva Nasopharynx Lungs (chronic cough, wheezing, respiratory distress, airway obstruction) Kidneys Cervix Uterus	35 yr‡ 8 yr‡ 1 mo‡ 29 yr‡ 8 yr‡ 1 yr§ 1 yr§	Eye drops: heparin, cyclosporine, corticosteroid, naphazoline, plasminogen Surgery: conjunctival (at least 18), nasal, tracheal, cervical, uterine Other: laryngoscopy/bronchoscopy (at least 43)	<5	<0.5
7	F	24	10.5 yr	None (cervical bleeding and pain)	NA	None	31	5.2
8	F	5	5 yr	Conjunctiva (discharge, tearing) Vagina (bleeding)	1 yr‡ 1 mo‡	Eye drop: moxifloxacin, heparin, cyclosporine, fluorometholone Surgery: conjunctival (3)	22	3.4

Table S1. Listing of baseline characteristics

				Clinical manifestations of disease			Plasminogen	
Patient	Sex	Age (yr)	Age at Diagnosis	Lesion (symptom) history	Lesion Duration	Prior treatments of disease	Activity* (%)	Antigen† (mg/dL)
9	F	16	8 yr	Conjunctiva (ligneous conjunctivitis, tear duct infection) Vagina (ligneous vaginitis) Colon (constipation, blood stools, rectal mucous discharge, tenesmus)	3 yr 2.5 yr‡ 6 mo‡	Surgery: pseudomembrane (4) Eye drop: moxifloxacin, prednisolone, loteprednol, cyclosporine, olopatadine, FFP Infusion: FFP	20	4.8
10	F	11	5 yr	Conjunctiva (discharge, tearing, redness)	11 yr‡	Surgery: pseudomembrane (4) Eye drop: heparin, prednisolone, cyclosporine, FFP Infusion: FFP	17	3.5
11	M	6	5 yr	Conjunctiva (discharge) Vocal cords (hoarse voice)	1 mo 1 yr§	Surgery: pseudomembrane (2) Eye drop: heparin, cyclosporine	29	5.5
12	M	33	Birth	Conjunctiva (ligneous conjunctivitis) Nose (nasal congestion) Delayed wound healing‖ Palmar/plantar warts‖ Lungs (airway obstruction)	UNK‡ 3 yr§ UNK‡ UNK‡ UNK§	Surgery: conjunctival (1) Infusion: FFP	<5	<0.5

Table S1. Listing of baseline characteristics

				Clinical manifestations of disease			Plasminogen	
Patient	Sex	Age (yr)	Age at Diagnosis	Lesion (symptom) history	Lesion Duration	Prior treatments of disease	Activity* (%)	Antigen† (mg/dL)
13	F	33	UNK	Conjunctiva (ligneous conjunctivitis)	33 yr‡	Surgery: conjunctival (1)	15	4.0
				Delayed wound healing (scars)‖	33 yr‡	Eye drop: plasminogen		
				Uterus	23 yr§	Infusion: FFP		
14	F	42	39 yr	Conjunctiva (ligneous conjunctivitis)	42 yr‡	None	<5	<0.5
				Gingiva	42 yr‡			
				Tumors, wrists‖	UNK‡			
				Palmar/plantar warts‖	UNK‡			
				Lung (airway obstruction)	UNK§			
				Abdomen (pain)	15 yr§			

F indicates female; FFP, fresh frozen plasma; M, male; NA, not applicable; and UNK unknown.

*Plasminogen activity normal range is 70-130%.

†Plasminogen antigen normal range is 6-20 mg/dL.

‡Lesion ongoing and assessed in the study.

§Lesion ongoing but not assessed in the study.

‖Skin lesions represent manifestations of abnormal wound healing due to congenital plasminogen deficiency.

Table S2. Listing of genetic profiles

Patient	Sex	Age (yr)	Plasminogen Activity* (%)	Plasminogen Antigen† (mg/dL)	Genetic profile
1‡	F	39	29	3.8	Heterozygous missense variant (c.112A>G, p.Lys38Glu) in exon 2 of *PLG*, with 3 additional common heterozygous variants detected (c.330C>T, p.Asn110Asn; c.1083A>G, p.Gln361Gln; and c.1414G>A, p.Asp472Asn)
2‡	M	35	43	5.4	Heterozygous missense variant (c.112A>G, p.Lys38Glu) in exon 2, with 3 additional common heterozygous variants detected (c.330C>T, p.Asn110Asn; c.1083A>G, p.Gln361Gln; and c.1414G>A, p.Asp472Asn)
3	F	16	28	5.6	Heterozygous missense variant (c.112A>G, p.Lys38Glu) in exon 2 of *PLG*
4	F	24	28	13.4	Heterozygous missense variant (c.112A>G, p.Lys38Glu) in exon 2 of *PLG* and a heterozygous missense mutation (c.2278A>G, p.Ser760Gly) in exon 19 of *PLG*
5	M	20	22	2.1	Homozygous missense variant (c.112A>G, p.Lys38Glu) in exon 2 of *PLG*, with 2 homozygous silent variants (c.330C>T and C.1083A>G) and 1 homozygous missense variant (c.1414G>A, p.Asp472Asn)

Table S2. Listing of genetic profiles

Patient	Sex	Age (yr)	Plasminogen Activity* (%)	Plasminogen Antigen† (mg/dL)	Genetic profile
6	F	37	<5	<0.5	Heterozygous, single amino acid deletion (c.687_689delGAA, p.Lys230del) in exon 7 of *PLG*, heterozygous frameshift deletion (c.2125_2125delG, p.Gly709fs) in exon 17 of *PLG*, with 5 heterozygous silent variants (c.330C>T, c.771T>C, c.942C>T, c.1083A>G, and c.2286T>G) and 1 common heterozygous missense variant (c.1414G>A, p.Asp472Asn)
7	F	24	31	5.2	Heterozygous missense variant (c.112A>G, p.Lys38Glu) in exon 2 of *PLG*, with a heterozygous frameshift deletion (c.2335_2336deltC, p.Trp780fs) of unknown significance in exon 19 of PLG and 4 heterozygous silent variants (c.330C>T, c.771T>C, c.942C>T and c.1083A>G) and 1 heterozygous missense variant (c.1414G>A, p.Asp472Asn)
8	F	5	22	3.4	Heterozygous missense variant (c.112A>G, p.Lys38Glu) in exon 2 of *PLG*, with a heterozygous splice site mutation (Chr6:161152265, G>A) 1bp downstream from the end of exon 11 of *PLG* and 5 heterozygous silent variants (c.330C>T, c.771T>C, c.942C>T, C.1083A>G, and c.2286T>G) and 1 heterozygous missense variant (c.1414G>A, p.Asp472Asn)

Table S2. Listing of genetic profiles

Patient	Sex	Age (yr)	Plasminogen Activity* (%)	Plasminogen Antigen† (mg/dL)	Genetic profile
9	F	16	20	4.8	Heterozygous missense variant (c.112A>G, p.Lys38Glu) in exon 2 of *PLG*, with heterozygous missense variant (c.704G>A, p.Arg235His) in exon 7 of *PLG*, with 5 heterozygous silent variants (c.330C>T, c.771T>C, c.942C>T, c.1083A>G, and c.2286T>G) and 1 heterozygous missense variant (c.1414G>A, p.Asp472Asn)
10	F	11	17	3.5	Heterozygous pathogenic variants (c.112A>G, p.lK38E in exon 2 and c.185+1G>T in intron 2) of *PLG* and a heterozygous variant (c.1468G>A, pG490R) in exon 10 of *CACNA1C*
11	M	6	29	5.5	Homozygous missense variant (c.112A>G, p.Lys38Glu) in exon 2 of *PLG*, with 2 homozygous silent variants (c.330C>T and c.1083A>G) and 1 homozygous missense variant (c.1414G>A, p.Asp472Asn)
12§	M	33	<5	<0.5	Homozygous missense variant (c.2T>C, p.Met1Thr) in the start codon of *PLG*, with 2 homozygous silent variants (c.330C>T and c.1083A>G) and 1 homozygous missense variant (c.1414G>A, p.Asp472Asn)
13	F	33	15	4.0	Heterozygous missense variant (c.112A>G, p.Lys38Glu) in exon 2 of *PLG* and a heterozygous deletion (c.493_516del_TATACTACTGATCCAGAAAAGAGA, p.Tyr165_Arg172del) of unknown significance in exon 5 of *PLG*., with 4 heterozygous silent variants (c.330C>T, c.1083A>G, c.2082T>C and c.2286T>G) and 1 heterozygous missense variant (c.1414G>A, p.Asp472Asn)

Table S2. Listing of genetic profiles

Patient	Sex	Age (yr)	Plasminogen Activity* (%)	Plasminogen Antigen† (mg/dL)	Genetic profile
14§	F	42	<5	<0.5	Homozygous missense variant (c.2T>C, p.Met1Thr) in the start codon of *PLG*, with 2 common homozygous silent variants (c.330C>T and c.1083A>G) and 1 homozygous missense variant (c.1414G>A, p.Asp472Asn)

DNA was extracted from whole blood samples prior to targeted multiplex polymerase chain reaction to selectively amplify the exonic regions of the plasminogen gene, including flanking regions with splice sites. Next, generation sequencing was performed on the amplified fragments, and the sequence was compared to the reference Human genome 19 sequence. The minimum read depth was set to 40 reads per base pair for acceptable sequencing. All mutations, disease-associated polymorphisms, benign polymorphisms, and other known variants of undetermined significance were noted and described. Plasminogen genetic testing was performed centrally by Machaon Diagnostics, Oakland, California.

F indicates female and M, male.

* Plasminogen activity normal range is 70-130%.

† Plasminogen antigen normal range is 6-20 mg/dL.

‡ Patient 1 and Patient 2 are siblings.

§ Patient 12 and Patient 14 are siblings.