TABLE 1: Summary of clinical and histopathologic features of complex lymphatic anomalies

COMPLEX LYMPHATIC ANOMALY	CLINICAL MANIFESTATIONS	HISTOPATHOLOGY/ MOLECULAR GENETICS
Gorham-Stout Disease (GSD)	• "Vanishing" bone disease→ pathologic fractures, functional issues, CSF leaks, meningitis, spinal instability, deformity • Effusions • Chronic pain	PROX-1, D2-40 positive abnormal lymphatics with increased osteoclast activity and destruction of bone cortex Mutation: unknown
Generalized Lymphatic Anomaly (GLA)	• Multisite lymphatic malformation of soft tissue, viscera (spleen, and liver common) and bones- bone lesions are multiple and non-contiguous • Effusions • Chronic Pain	Increased number of dilated anastomosing lymphatic channels, lined by endothelial cells, stains PROX-1 and D2-40 positive Mutation: *PIK3CA*
Central Conducting Lymphatic Anomaly (CCLA)	• Enlarged lymphatic channels/cysts in abdomen and/or thorax • Reflux of lymphatic fluid → pleural and pericardial effusions, ascites, massive edema • Protein loss • Recurrent infections • Organ dysfunction	Dilated lymphatic channels-vessels aren't malformed but are dysfunctional or distally obstructed Mutation: *EPHB4*
Kaposiform Lymphangiomatosis (KLA)	• Multifocal lymphatic anomaly that often involves thorax, bones, viscera • Progressive involvement, severe morbidity, high mortality rate • Coagulopathy: severe hypofibrinogenemia, thrombocytopenia and high rate of bleeding complications • Effusions • Hemorrhage • Respiratory and multiorgan failure	Focal areas of spindled lymphatic endothelial cells with abnormal lymphatics; similar to KHE but the spindle cell component is more dispersed and arranged in poorly defined clusters or anastomosing strands/sheets Mutation: *NRAS*