Table SI. Summary of the main clinical-pathological features characterizing non-Langerhans-cell histiocytosis

	Erdheim-Chester disease	Xanthoma disseminatum	Adult xanthogranuloma	Progressive nodular histiocytosis	Benign cephalic histiocytosis
M:F	3:1	2.5:1	3:1	2/3:1	2:1
Age (years)	55–60	25–40	20–40	10–30	0–3
Diagnosis	Clinical-pathological, radiological and molecular (?)	Clinical-pathological	Clinical-pathological	Clinical-pathological	Clinical-pathological
Bone	95% (bilateral symmetric lesions of long bones).	Uncommon	Uncommon	None	None
CNS/Diabetes insipidus (DI)	30% DI. Neurodegenerative CNS involvement described.	40% DI. CNS lesions, uncommon.	Uncommon	None	None
Skin	Xanthelasma (33%), papules, plaques.	Xanthelasma, papules (confluent) plaques, nodules. Mucosal involvement	Single papules or nodules. Less often multiple papules	Hundreds of large nodules or tumor-like lesions all over the skin surface. Mucosal involvement	Several small papules distributed on head and neck region only
Histology	Polymorphic histiocytic infiltrate with foamy cells (prevalent especially in late phase of disease), Touton giant cells and sometimes (PNH) spindled histiocytes. Background with mixed inflammatory infiltrate.			Monomorphic non-foamy, non-epitheliomorphic histiocytic infiltrate admixed with few lymphocytes.	
Electron microscopy	Lipid vacuoles, myeloid bodies, highly developed endomembrane system, lysosomes, phagosomes.			Coated vesicles, comma-shaped bodies (20%)	
Immunohistochemistry	CD163+, CD68/PGM1+, CD68/KP1+, CD14+, CD4+, fXIIIa+, Vimentin+, S100+/–, CD1a–, CD207–. Low Ki67 (5–10%)				
BRAF	50% [13]	n.d	7% [13]	n.d.	n.d.
Other mutations	45% [13]	n.d	50–60% [13]	n.d.	n.d.

The table highlights the great overlap among these entities, which makes a correct diagnosis difficult to make.