Pediatric Erdheim-Chester disease: clinical characterization and long-term outcome of 24 cases

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Disclosures

None

Introduction and Background

	Pediatric ECD *published cases, n*=18
Female, n (%)	8 (44)
Age at onset, *years* - median (IQR)	10 (6-13)
Bone, n (%)	15 (83)
CNS, n (%)	9 (50)
Hypothalamic/pituitary, n (%)	6 (33)
Facial/orbit, n (%)	2 (13)
Heart, n (%)	1 (6)
Large vessels, n (%)	-
Lung, n (%)	3 (17)
Perirenal, n (%)	4 (22)
Skin, n (%)	3 (17)
BRAF^{V600E}, n (%)	5/6 (83)
Associated LCH, n (%)	8 (44)

blood® Letter to *Blood*

TO THE EDITOR:

Childhood-onset Erdheim-Chester disease in the molecular era: clinical phenotypes and long-term outcomes of 21 patients

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Methods

Retrospective study

International collaboration:

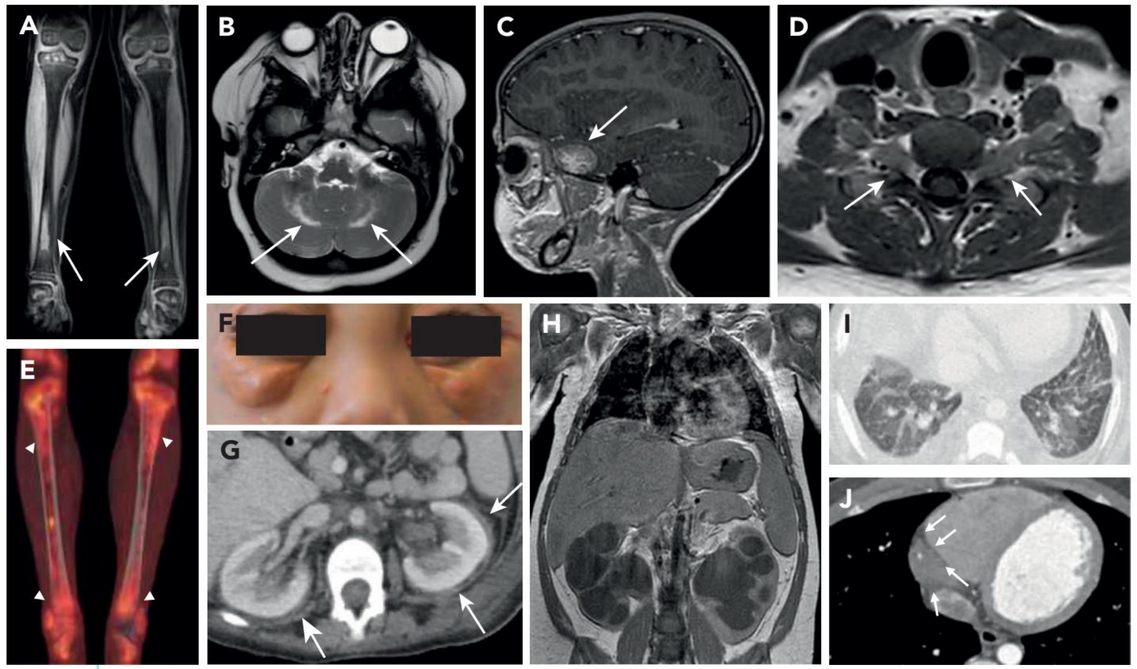
- First screening at the Italian and French Histiocytosis networks
- Study proposal circulated
  - Histiocyte Society
  - ECD Global Alliance
- Case reports on pediatric ECD (2014-2022)

SCREENING

- Age at onset <18y
- Histological diagnosis of ECD

Screened patients n=32

Results



sex	M	F	F	M	F	M	F	F	M	F	F	F	F	M	M	F	M	M	F	M	F	M	F	M	
age at ECD onset (y)	8	6	1	4	16	16	2	5	1	6	2	5	9	9	3	6	1	4	3	16	1	17	7	15	
bone																									
peri-renal																									
peri-aortic																									
heart																									
xanthelasma																									
other skin lesions																									
CNS lesions																									
neurodegeneration																									
lung																									
facial/orbit																									
hypothalamic/pituitary																									
mixed ECD/LCH																									
mixed ECD/RDD																									
BRAF^{V600E}																									

Results

Baseline characteristics

Female	14 (58%)
Long bone	20 (83%)
CNS	15 (63%)
Neurodegeneration	7 (29%)
Facial/orbit	15 (63%)
Heart	4 (17%)
Large vessel	5 (21%)
Lung	3 (13%)
Retroperitoneal	6 (26%)
Hypothalamic/Pituitary	13 (54%)
Skin	9 (38%)
Xanthelasma-like	4 (17%)
Papules/patches/nodules	5 (21%)
≥4 involved sites	15 (63%)
Mixed forms	12 (50%)
ECD-LCH	10 (42%)
ECD-RDD	2 (8%)
Somatic mutations	15 (63%)
BRAF^{V600E}	12 (50%)
MAP2K1	3 (13%)

Mixed ECD-LCH

Lytic bone lesions (n=10)
Lymph nodes (n=3)
Bone marrow infiltration (n=1)

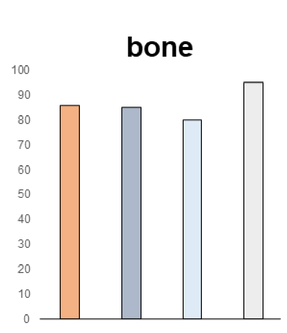
→ Higher frequencies of:
Systemic symptoms (100% vs. 39%, p=0.007)
Diabetes insipidus (75% vs. 23%, p=0.032)
Pituitary insufficiency (75% vs. 15%, p=0.023)

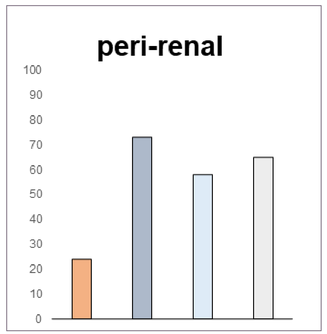
***BRAF*^{V600E} mutation**

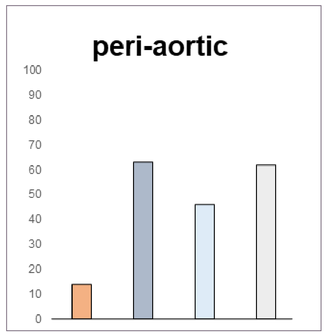
→ Higher frequencies of exophthalmos (58% vs. 0%, p=0.007)

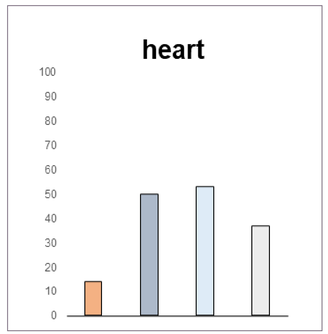
Results

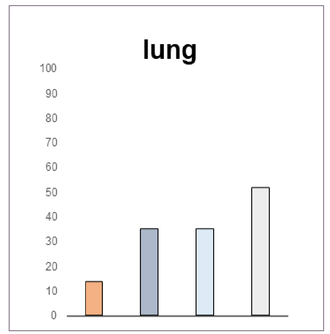
Differences from adult-onset ECD

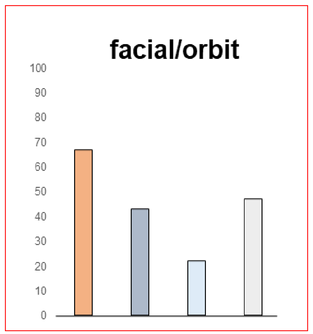


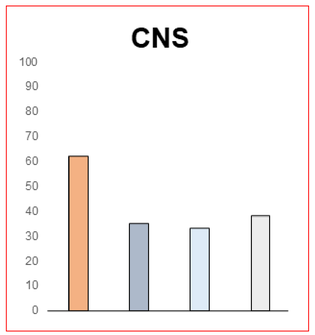


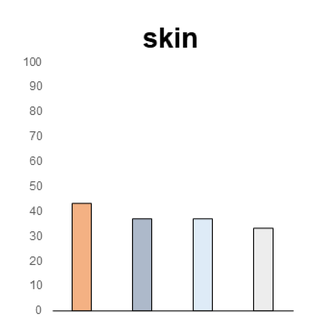


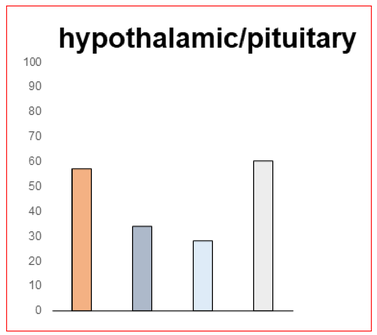


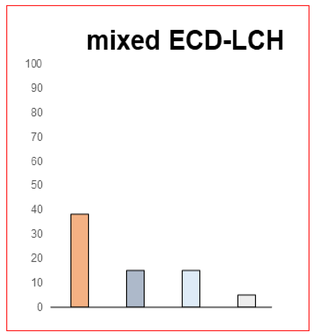


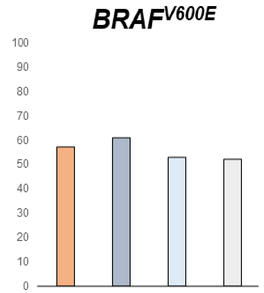












Current pediatric series

Adult series

- Chazal 2022
- Cohen-Aubart 2019
- Estrada-Veras 2017

Results

Treatment and outcome

First-line treatments

- CT, n=8 (33%)
- IFNa, n=7 (29%)
- Targeted, n=7 (29%)

Sustained objective responses

- BRAFi/MEKi (9/9, 100%)
- IFNa (5/9, 56%)
- CT (2/9, 22%)

Twelve patients (50%) → ≥1 line of treatment (toxicity or disease progression)

Median follow-up 55 months (IQR 34–92)

→2 patients died (chemotherapy-related toxicity; unknown causes)

→stable disease (n=7) or response (n=15) in the remainig 22

Conclusions

- Pediatric ECD is an exceptionally rare entity that shares many features with its adult counterpart
- Facial/orbit, CNS, and hypothalamic/pituitary involvement are more common in children
- High frequency of mixed ECD/LCH
  → LCH patients with atypical findings consistent with ECD should be screened for mixed forms (better responses to ECD-centered treatments)
- Targeted treatments are safe and effective

For Additional Information

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