ENDOCRINE AND METABOLIC ASSESSMENT IN 18 ADULT PATIENTS WITH LANGERHANS CELL HISTIOCYTOSIS.

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BACKGROUND

Langerhans cell histiocytosis (LCH) is a rare "orphan" disease.

Clinical pictures:

- Single-system LCH (SS-LCH) unifocal or multifocal on bone, skin, lymph nodes, lungs, or central nervous system.
- Multi-system LCH (MS-LCH) 2 or more organs/systems, with or without *risk-organs* involvement (bone marrow, liver, and/or spleen), worse prognosis.
- Pulmonary LCH (PLCH) interstitial lung disease, single organ or multisystemic.

Pathogenesis

- reactive: increased levels of inflammatory cytokines (IL-17, IL-2) or growth factors, regulatory T cell expression,
- neoplastic (also if not malignant): oncogenic mutations, more frequently BRAFV600E, rarely KRAS and TP53

↳ neoplastic process with inflammatory manifestations

BACKGROUND

LCH

DI
15-50%
40% in MS-LCH
More common permanent complication

METABOLIC PROFILE
Probably worse metabolic profile in MS-LCH (scarce evidences) and higher CV risk (pro-inflammatory cytokines?)

ANTERIOR PITUITARY DEFICIT
20-67% in patients with DI.
53-67% GHD
53-58% GnD
1-2% (up to 42%) ACTH deficit
rare TSH deficit

THYROID LOCALIZATIONS
Rare.
Single or in MS-LCH
Association of pulmonary LCH, hypopituitarism and papillary thyroid carcinoma described (case report). Screening not recommended.

Actual recommendations (2013):

- all patients: TSH, FT4 and urine osmolarity.
- only if clinical suspect: cortisol plasma levels, IGF-I, sex steroids, plasma osmolarity etc.

AIM

To evaluate
endocrine and **metabolic** involvement
in a cohort of patients affected by
Langerhans cell histiocytosis (LCH) followed
in our centre.

PATIENTS AND METHODS

CROSS OBSERVATIONAL STUDY

18 adult patients (7 M/11 F, aged 41.8±12.0 years).

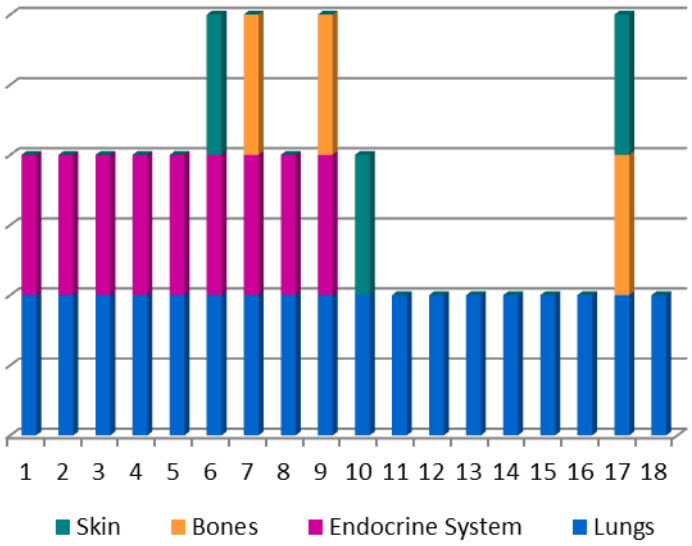
studied for:

-Endocrine involvement: basal (early morning plasma and urine osmolarity, serum cortisol, fT4, fT3, TSH, PRL, GH, IGF-I, LH, FSH and in men total testosterone, albumin and SHBG) and dynamic endocrine lab tests (1 mcg ACTH test, Arg+GHRH test),

-Glucose metabolism: (basal and post-OGTT glucose levels, HbA1c, fasting and post load insulin levels, HOMA-I, BMI, hypertension and lipid metabolism).

-Thyroid involvement: US thyroid scan, AB Tg, AB TPO.

RESULTS



50% (9 patients) with **ENDOCRINE INVOLVEMENT**

- 9 DI
- 5 GHD
- 5 GnD
- 4 hypothyroidism
- 1 hypoadrenalism

Moreover

- 2 Hyperprolactinemia
- 2 Hypothalamic syndrome

5 of the 10 MRI performed had abnormalities (hyper-intense focal lesion, empty sella or thicker hyperintense pituitary gland).

RESULTS: METABOLIC EVALUATIONS

	LCH population	General population (35-45 years , ISTAT DATA 2009)
Obesity	39%	7,7%
IFG or IGT	28%	11,7%
Diabetes	5%	0,9%
Metabolic Syndrome	39%	22%

		ED vs NED				MS-LCH vs P-LCH			
	n	ED (N=9)	n	NED (N=9)	*P*	n	MS-LCH (N=11)	n	P-LCH (N=7)	*p*
BMI (kg/m²)	**9**	**31.2±6.7**	**9**	**25.9±5.4**	**0.058**	**11**	**31.4±6.0**	**7**	**24.0±4.5**	**0.013**
Insulin (mUI/mL)	6	21.9±14.0	9	16.8±27.0	0.126	8	28.8±27.0	7	7.4±4.1	0.021
HOMA-I	6	4.4±2.4	9	4.2±7.3	0.126	8	6.6±7.2	7	1.7±1.3	0.021
QUICKI	6	0.3±0.04	9	0.3±0.05	0.126	8	0.3±0.04	7	0.4±0.03	0.021
Insulin-resistence (%)	**7**	**71**	**9**	**33**	**0.315**	**9**	**78**	**7**	**14**	**0.041**
DM or IFG or IGT (%)	9	44	9	22	0.310	11	45	7	14	0.316

RESULTS: THYROID ASSESSMENT

12 patients thyroid US scan:
5 structure inhomogeneity without focal lesions
2 multinodular goiter.

One total thyroidectomy

papillary multifocal thyroid micro-carcinoma positive for BRAF-V600E mutation

This mutation was also searched on peripheral white blood cell, but it was not found.

CONCLUSIONS

- Hypotalamic-Pituitary localizations are frequent in LCH, but anterior pituitary dysfunctions appear mostly in presence of DI.

- LCH particularly MS-LCH could be associated with higher prevalence of **overweight, obesity, insulin resistance and glucose alterations**, independently from endocrine involvement. More studies needed.

- Possible association between papillary thyroid carcinoma BRAFV600E positive and LCH. (Common eziophatologic factor?) Evaluate **US thyroid scan** screening in LCH patients.

CLINICAL PRACTICAL PROPOSAL

All patients

- Amount daily urine excretion, Urine and plasma osmolarity, serum sodium, glucose
- Gonadal status
  women: ask for menstrual regularity if childbearing age, FSH if post-menopausal
  men: Total Testosterone (TT), Androtest
- BMI, Waist Circumference, Blood Pressure
- Thyroid sonography

2nd level

If MS-LCH or DI/GnD

- IGF-I
- Men: TT, SHBG, Albumine for calculated free testo.
  Women: if menstrual irregularity FSH, LH, 17BE2
- Ft4 , TSH
- Cortisol (h 8.00 a.m.)
- PRL
- Fasting glucose, HbA1c, lipid

- OGTT
- Endocrine consulting and dynamic testing when needed

THANK YOU FOR YOUR ATTENTION!!!!