Centre de Référence des Maladies Endocriniennes Rares de la Croissance

Institut E3M Endocrinologie Maladies Métaboliques et Médecine interne

ENDOCRINE MANIFESTATIONS IN ERDHEIM CHESTER DISEASE

Monocentric study of 64 patients

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Annual International ECD Medical Symposium

September 15th 2016

Objectives and patients

- Endocrine manifestations in ECD described only in **case reports**
- Evaluation of the **prevalence and evolution of endocrine manifestations** in a large cohort of ECD patients
- **Observational monocentric study**
- **Patients**
  - With **confirmed ECD**
  - Followed in the **Internal Medicine Department** (Pr Amoura) and addressed in the **Endocrinological Department** (Pr Touraine) in Pitié-Salpêtrière Hospital
  - **Consecutive** patients between October 2007 and May 2013

Endocrine evaluation

- During hospitalization
- Evaluation criteria:
  - ECD (diagnosis, evolution, localizations, treatments)
  - Endocrinology:
    - **Clinics:** BMI, BP, PUPD syndrome, sexual dysfunction, genitals, breasts, thyroid
    - **Biology:** FG, HbA1c, lipid profile, 25(OH)D
    - **Hormones:** anterior and posterior pituitary functions, peripheral glands functions (gonads, adrenals, thyroid, parathyroid)
    - **Imagery:** pituitary MRI, pelvic or testicular sonography, adrenal CT, bone densitometry, thyroid sonography
    - **Other:** sperm count

Endocrine Manifestations in a Monocentric Cohort of 64 Patients With Erdheim-Chester Disease

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J Clin Endocrinol Metab, January 2016, 101(1):305–313

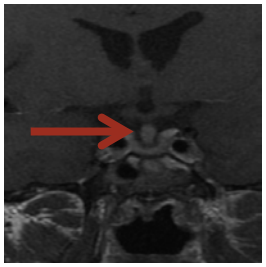
Characteristics of the patients

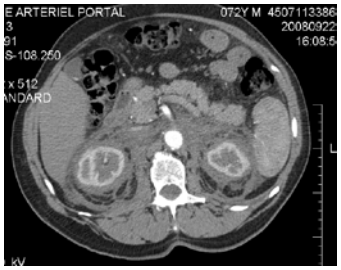
64 patients (50 ♂ / 14 ♀)	Mean +/- SD
Age at diagnosis (years)	54.2 +/- 14.8
Age at 1st clinical signs of ECD (years)	49.6 +/- 15.8
Time before diagnosis (years)	4.9 +/- 6.5
Age at 1st endocrinological symptoms (years)	44.8 +/- 16.1
	N (%)
Inaugural endocrinological manifestations	14/61 (23)
Diabetes insipidus	12/14 (86.7)
Gonadotropic insufficiency	3/14 (21.4)
Age at 1st endocrinological evaluation (years)	57.6 +/- 13.4
Known endocrinological involvement before evaluation	23/64 (35.9)
Diabetes insipidus	21/23 (91.3)
At least one anterior pituitary deficit	9/23 (39.1)

Endocrine manifestations

Hormonal dysfunction	% of patients (N)
Growth hormone deficiency	78.6% (22/28)
Testicular deficiency	53.1% (26/49)
Hyperprolactinemia	44.1% (26/59)
Diabetes insipidus	33.3% (19/57)
Gonadotropic deficiency	22.2% (14/63)
Thyreotropic deficiency	9.5% (6/63)
Thyroid deficiency	9.5% (6/63)
Corticotropic deficiency	3.1% (2/64)
Adrenal deficiency	1.6% (1/64)
NONE	1.6% (1/64)

- **Pituitary (stalk) infiltration** = 24% (10/41)
- Absence of **posterior pituitary bright spot** = 60% (24/40)
- **Adrenal infiltration** = 39% (9/23), bilateral in 2/3 cases

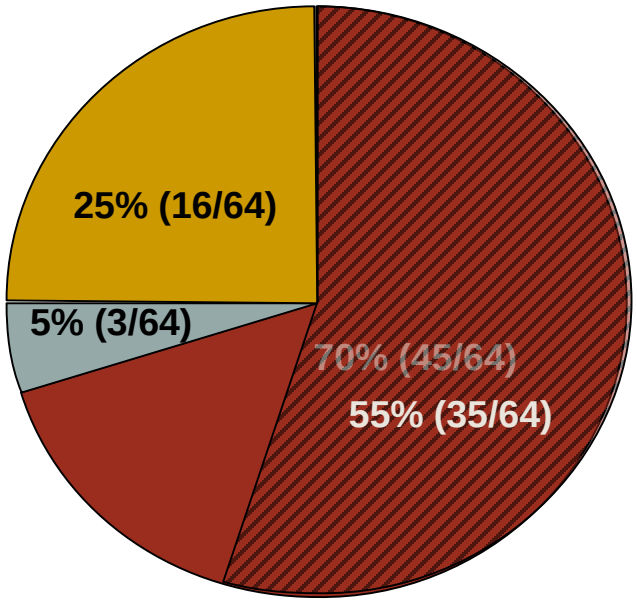




- **No correlation** between anterior and posterior pituitary deficits
- **No gender difference** apart from gonadal insufficiency
- Anterior pituitary deficits in the **same order of frequency** than in LCH or post radiotherapy
- **DI** often inaugural (65%) and permanent

Results

Anterior pituitary deficits

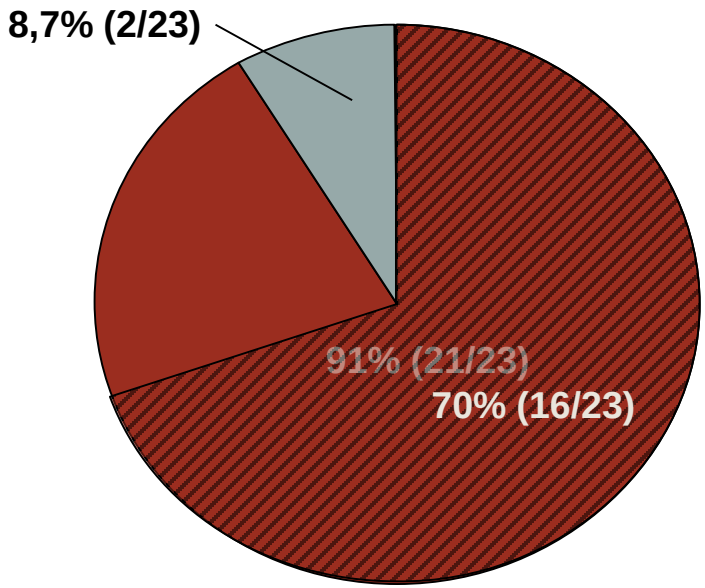


≥ 1 deficit

No anterior pituitary dysfunction

No anterior pituitary dysfunction, but incomplete explorations

≥ 2 deficits



≥ 1 deficit

No anterior pituitary dysfunction

≥ 2 deficits

Complete explorations

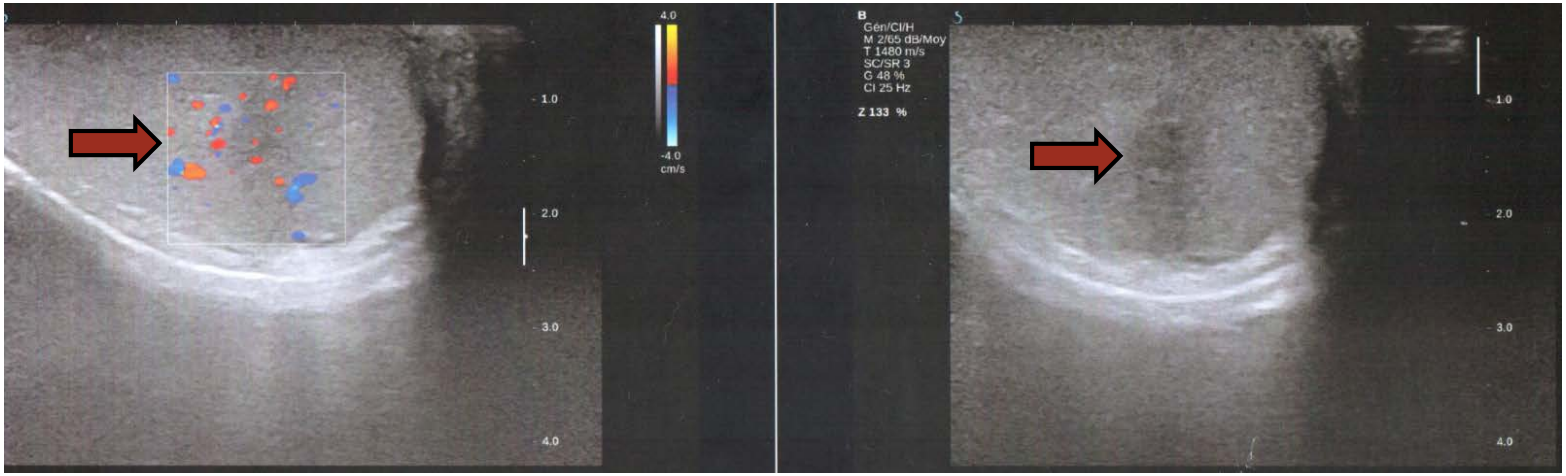
Gonadal function in men

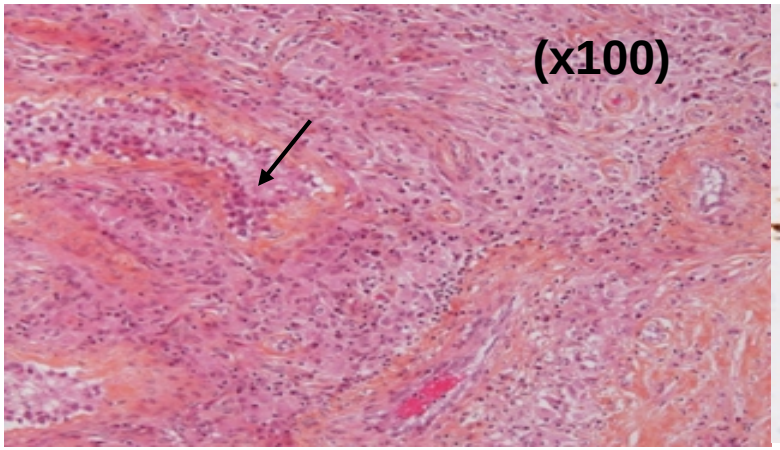
♂ 57.4 ± 12.8 yrs	Results	N (%)
Hormonal evaluation	Normal pituitary – testicular axis	**13/49 (26.5%)**
	Gonadotropic deficiency	**10/49 (20.4%)**
	Testicular deficiency	**26/49 (53.1%)**
Ultrasonography	Testicular volume < 15 ml	**22/27 (81.5%)**
	Normal testicular structure	**22/31 (71%)**
	Unilateral infiltration	**3/31 (9.7%)**
	Bilateral infiltration	**6/31 (19.4%)**

- **Alteration of sperm counts** (5/6)
- **No correlation** between gonadotropic / gonadal function, sperm count and testicular US findings
- **Strong correlation** between testicular volume and gonadic function

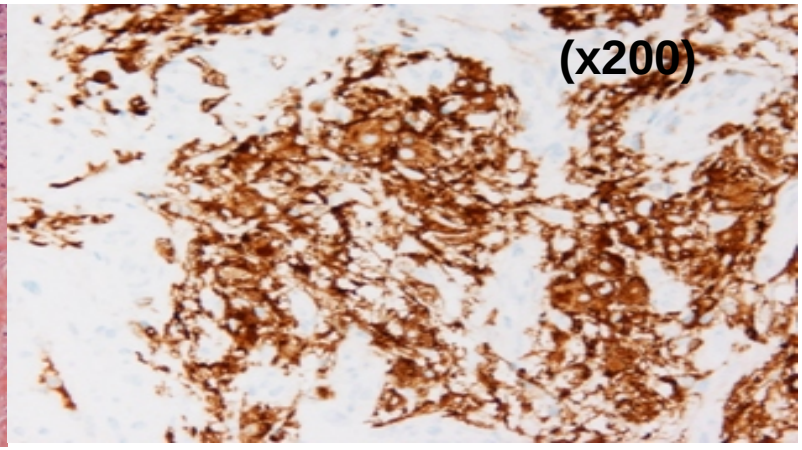
Results

Testicular infiltration





HES staining showing histiocyte infiltrate surrounding a seminiferous tubule (→)



Positive anti-CD163 immunostaining on the histiocyte infiltrate

Results

Recommendations

	CLINICAL EVALUATION	MORPHOLOGICAL EVALUATION	BIOLOGICAL EVALUATION
PITUITARY	Search for signs of anterior pituitary deficits 24hours diuresis and water intake	**Pituitary MRI**	**FSH, LH, E2** ♀ **/ Testosterone** ♂ **PRL** **TSH, FT4** **IGF1, GH** under insulin tolerance test **ACTH, Cortisol** under insulin tolerance test or after synacthen test **Natremia** and **urinary osmolarity**
GONADS	Evaluation of testicular volume and search of palpable testicular nodules	**Gonadal sonography** (and in case of men with testicular infiltration, **sperm cryopreservation**)	**FSH, LH** **E2** ♀ **Testosterone + inhibine B** ♂
THYROID	Search of a goitre and of nodules	**Thyroid sonography** if clinical anomalies	**TSH, FT4** (and TPO + ATG in patients under IFN therapy)
ADRENAL	Search of signs of adrenal deficiency	**Abdominal or adrenal CT scan**	**ACTH, Cortisol** under insulin tolerance test or after synacthen test **Renin** and **aldosterone**
BREAST	Search for lumps ♀ ♂	**Mammography +/- mammary sonography** if presence of clinical lumps	-
METABOLISM	Blood pressure Electrocardiogram	-	**Fasting glycemia** +/- **HbA1c** **TC, TG, HDL-c, LDL-c**

Conclusions

Acknowledgments

- **Stéphanie LAUGIER-ROBIOLLE**
- Philippe TOURAINE

- **Julien HAROCHE**
- Fleur COHEN
- Zahir AMOURA

THANK YOU FOR YOUR ATTENTION

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