An autopsy case of ectopic ACTH-secreting lung carcinoid with Cushing's syndrome.

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Case Report

【Chief Complaint】reduction in appetite and weakness of lower limbs

【Onset and course】

A 81-year-old woman came to our hospital with complaints of reduction in appetite and weakness of lower limbs. She had developed Cushing's features. Initial laboratory evaluation revealed severe hypokalemia, so she were admitted to our hospital for further examination.

【Past History】Uterus myoma

【Familv Historv】Unremarkable

【Physical examination】

Height 137cm, Weight 47kg, BMI 25.0 kg/m^2
Blood Pressure 112/80mmHg,
Pulse Rate 102/min, regular

She had moon face, buffalo hump and skin pigmentation.
Conjunctive was not anemic and not icteric.
Pulmonary, cardiac and neurological examinations were unremarkable.
She had pitting edema in her legs.

Laboratory Findings

<CBC>

WBC	9500 /μL
Neutro	94.3 %
Lymph	4.3 %
Mono	1.4 %
Eosino	0.0 %
RBC	2.86×10^6 /μL
Hb	8.7 g/dL
Ht	26.4 %
MCV	92.3 fL
MCHC	30.4 %
Plt	7.2×10^4 /μL
Retic%	1.3 %
PT	97 %
APTT	26.7 sec
Fbg	152

<Biochemistory>

AST	29 U/L
ALT	46 U/L
LDH	446 U/L
T-Bil	1.3 mg/dL
ALP	218 U/L
γGT	82 U/L
TP	4.2 g/dL
Alb	2.1 g/dL
UN	32 mg/dL
Cr	0.66 mg/dL
UA	2.1 mg/dL
Na	144 mmol/L
K	2.3 mmol/L
Cl	105 mmol/L
CRP	0.09 mg/dL
TG	129 mg/dL
HDL-C	38 mg/dL
LDL-C	86 mg/dL

PG	206 mg/dL
HbA1c	7.1 %
Anti-GAD Antibody	<0.3 U/mL
CEA	12.1 ng/mL
CYFRA	8.0 ng/mL
ProGRP	281.0 pg/mL
NSE	17.1 ng/mL

<Urine>

Pro	(+1)
Glu	(+3)
Ket	(-)
Bil	(-)
Uro	(+1)
OB	(+2)
RBC	10-19 /HPF
WBC	30-49 /HPF

<Endocrinological examinations>

GH	0.15 ng/mL	ACTH	389 pg/mL
IGF-1	32 ng/mL	F	147 μg/dL
LH	0.10 mlu/mL	DHEA-S	689 μg/dL
FSH	0.17 mlu/mL	PRA	0.5 ng/ml/hr
PRL	11.44 pg/mL	PAC	170 pg/mL
TSH	0.06 μIU/mL	U-F	≧3630 μg/day
FT3	0.84 pg/mL		
FT4	0.9 ng/dL		

Daily variation	8:00	16:00	23:00
ACTH(pg/mL)	389	573	438
F(μg/dL)	147	158	127

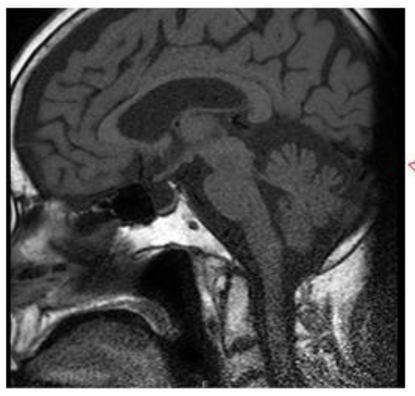
There was loss of Daily variation.

CRH test	ACTH(pg/mL)	F(μg/dL)
Pre	628	140
15min	946	160
30min	889	151
60min	736	141
90min	569	166
120min	559	149

ACTH response was normal.

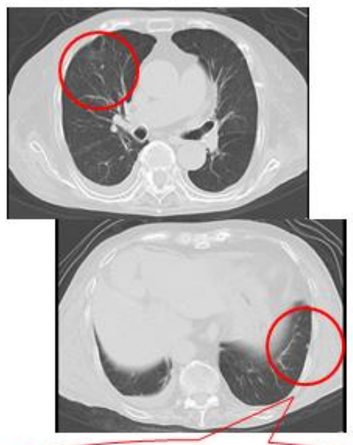
Imaging Test

【Pituitary MRI】



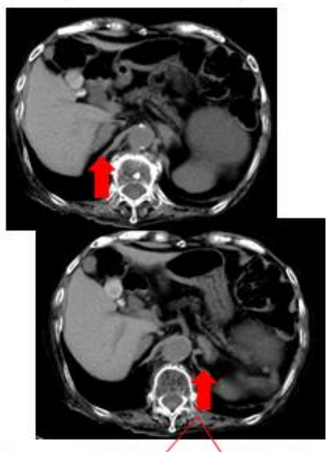
- Empty sella
- No pituitary tumor

【Chest CT(thin slice)】



・Only non-specific inflammatory change

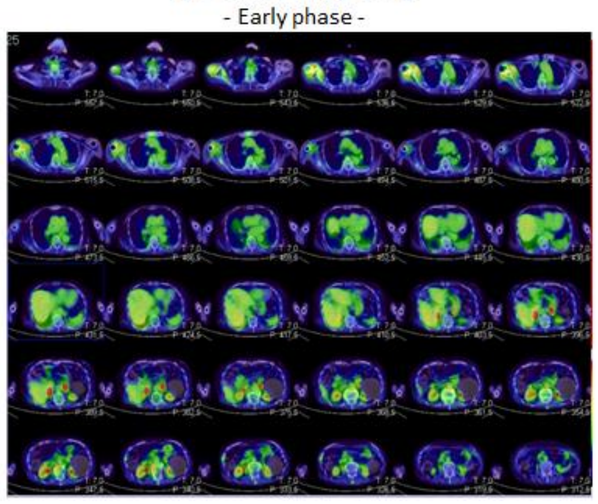
【Abdominal CT】



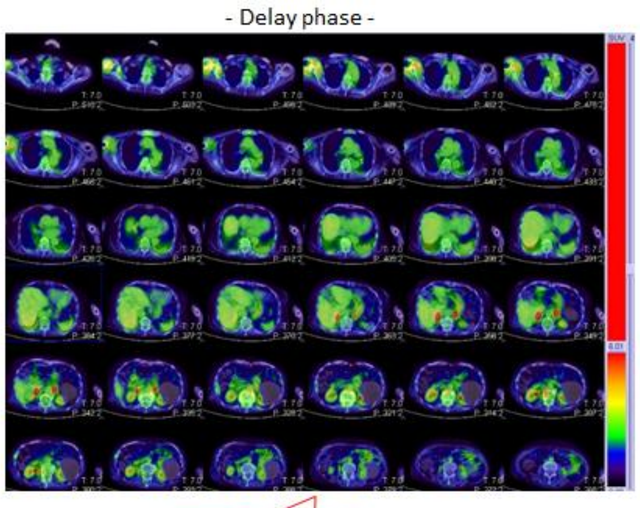
・Bilateral adrenal enlargement

【FDG PET/CT】

- Early phase -

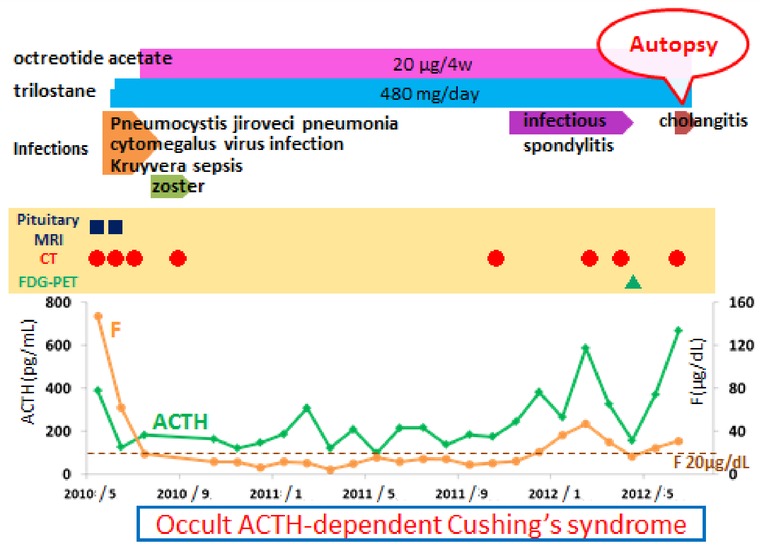


- Delay phase -



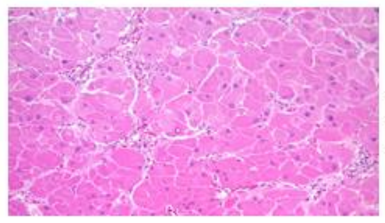
・No obvious tumor

Crinical Course



Occult ACTH-dependent Cushing's syndrome

Pathological Findings

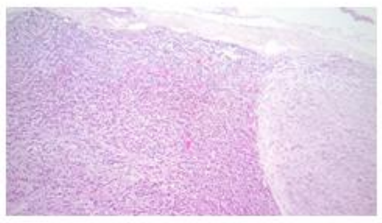


<Adrenal glands> HE ×40

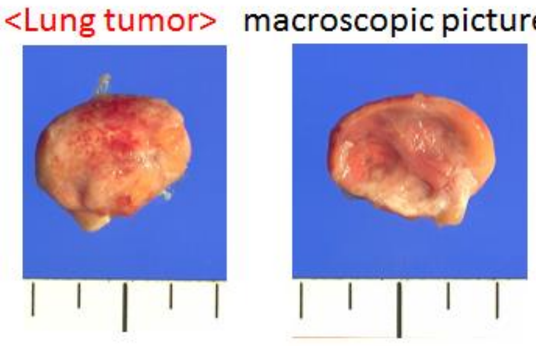
- Right 5×2.5×1.5cm
- Left 4×2.5×1.2cm
- Diffuse enlargement

<Pituitary> HE ×4

- 915g
- Unremarkable

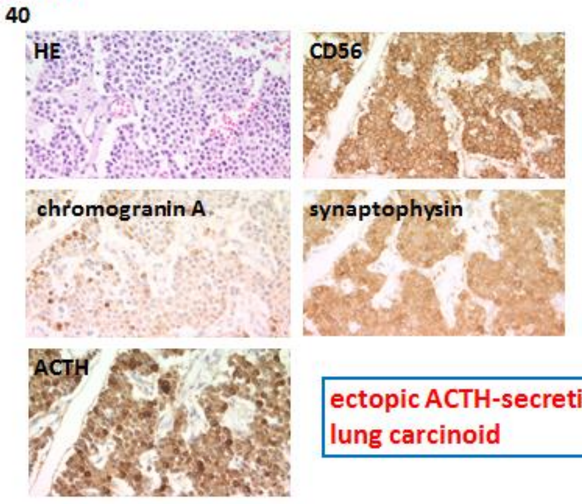


<Lung tumor> macroscopic picture



Left lower lobe, 17mm diameter

<Lung tumor>
×40



ectopic ACTH-secreting lung carcinoid

Discussions

【Examinations for differentiate ectopic ACTH syndrome from Cushing's disease】

Examinations	sensitivity	specificity
HDDST	80-94 %	80-94 %
CRH test	90-100 %	85 %
IPSS	90 %	67 %
γ3-MSH	unknown	unknown

(Wajchenberg, BL, et al, Endocr Rev, 15: 752-87, 1994)
(Newell-Price, J, et al, Endocr Rev, 19: 647-72, 1998)
(Swearingen, B, et al, J Clin Endocrinol Metab, 89: 3752-63, 2004)
(Hideki, K, et al, ACTH RELATED PEPTIDES, 1927-30, 2008)

【Localization diagnosis for ectopic ACTH syndrome】

Examinations	positive predictive value
Chest CT/MRI	68 %(25/37 case)
somatostatin receptor scintigraphy	60 %(8/12 case)
FDG-PET	66 %(4/6 case)
(for lung cartinoid) Lung artery sampling	unknown

(Ejaz, S, et al, Cancer, 117(19): 4381-9, 2011)
(Miho, S, et al, Endocline Journal, 57(11): 959-64, 2010)

Conclusion

- We experienced a case of lung carcinoid that we could not detect a localization regardless of repeated radiological imaging, but autopsy confirmed its diagnosis.
- For localizing primary lesion of ACTH-secreting tumor, repeatedly and fully imaging tests is very important.