



High diversity of Cushing's disease in patients with corticotroph macroadenoma



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Introduction. Cushing's disease is usually caused by corticotroph microadenoma, but in 7%-20% of cases it is due to ACTH-producing macroadenoma. There are a lot differences in clinical and biochemical characteristic of Cushing's disease depending on size of pituitary adenoma. There is an evidence that macroadenomas causing Cushing's disease are more refractory to surgical treatment and show variable response to adjunctive radiotherapy or farmacological therapy.

Material and methods. Retrospective analysis of medical records of 9 patients [5F; 4M] hospitalized in 2002-2015.

Results. Four of the patients [2 F and 2 M] were diagnosed before they were 40 years old [mean age 28.5] and 5 [3 F and 2 M] over 40 years old [mean age 50].

In 3 women tumour was initially discovered as microadenoma. A woman [23 years old] first underwent bilateral adrenalectomy because of inability to neurosurgery and 5 years later Nelson's syndrome developed. In two consecutive cases [49y and 52y] at the moment of diagnosis MRI revealed microadenomas 9x7mm and 5x4 mm respectively. In the first female 2 years after initial neurosurgery consecutive 4 transsphenoidal reoperations, stereotactic radiotherapy and bilateral adrenalectomy were conducted. Then she developed Nelson's syndrome. Propter a rapid tumour's invasion, themozolomide and bevacuzimab were introduced. She died 7 years after the diagnosis. In the second patient tumour regrowth was observed 6 years after the first neurosurgery and because of failure of second adenomectomy and mild hypercortisolism she was qualified to pasireotydy therapy.

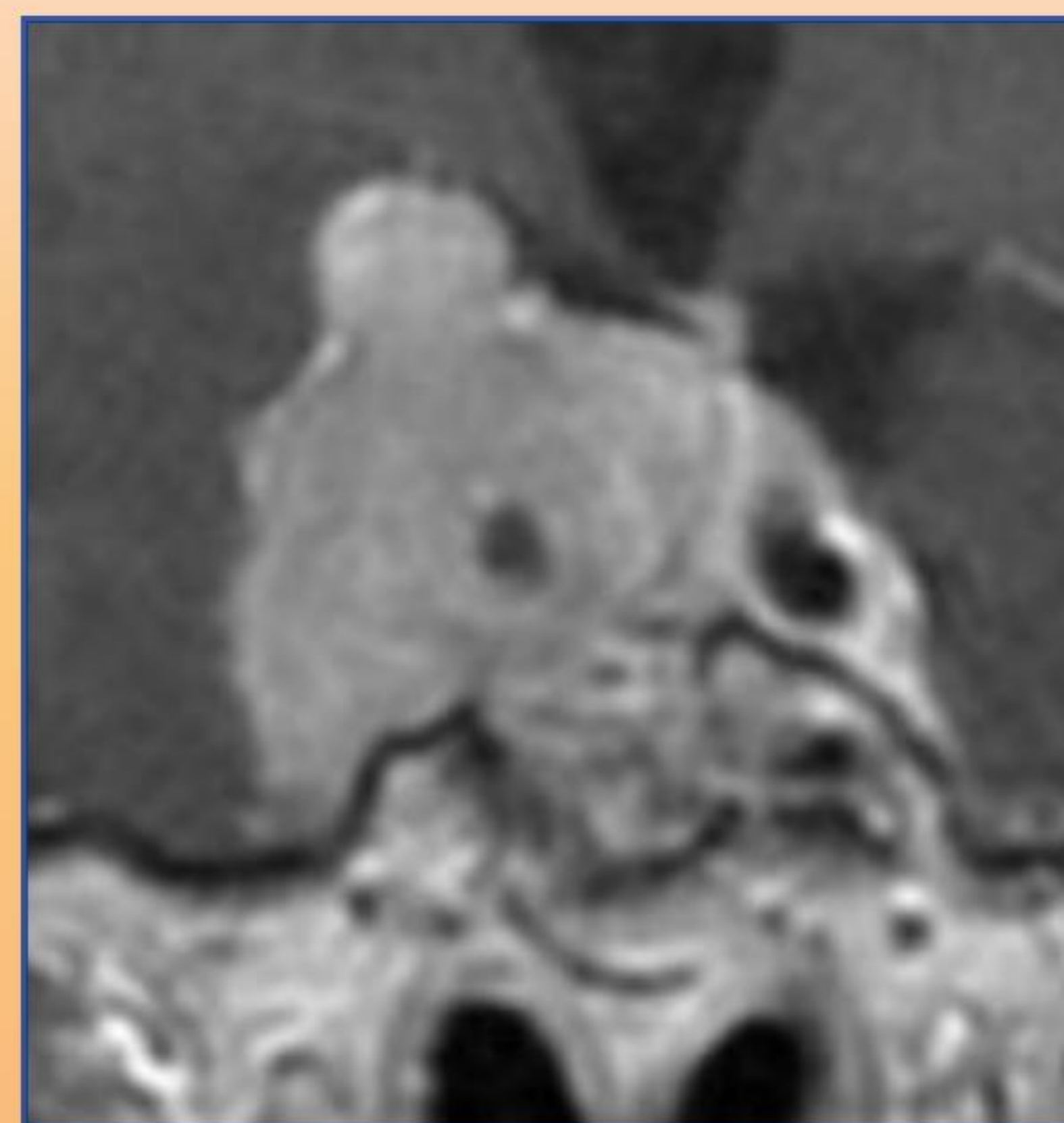
In 6 patients [2 F and 4 M] the pituitary tumours were initially diagnosed as macroadenomas. One patient with 5 cm tumour size and overt hypercortisolism died after first craniotomy. Another patient presented cyclic Cushing's syndrome with pituitary macroadenoma discovered after 7 years' observation.

In the next patient unique cause of Cushing's disease was Crooke's macroadenoma, refractory to two neurosurgeries with good response to themozolomide.

In 2 cases [female and male] macrocorticotropinomas were discovered as incidentalomas and operated as clinically inactive (silent) tumours. In these patients the tumour recurred 5 years after the first neurosurgery and visible hypercortisolism developed.

The aim of the study was to present our observations concerning etiologic, clinical and therapeutic diversity of Cushing's disease in patients with macrocorticotropinomas.

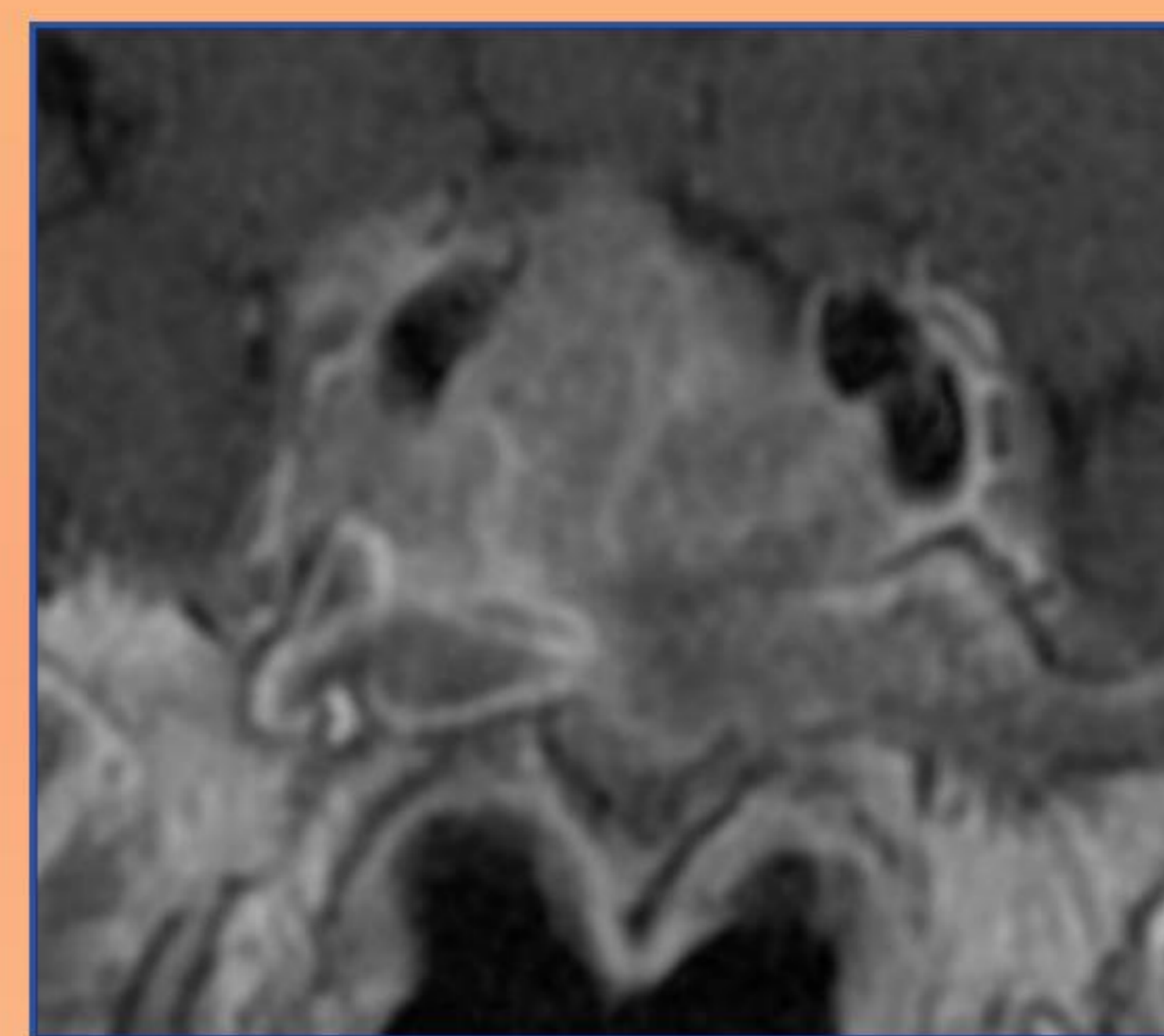
Conclusion. Macrocorticotropinomas are very heterogenic group of pituitary tumours with high etiologic, clinical and therapeutic diversity.



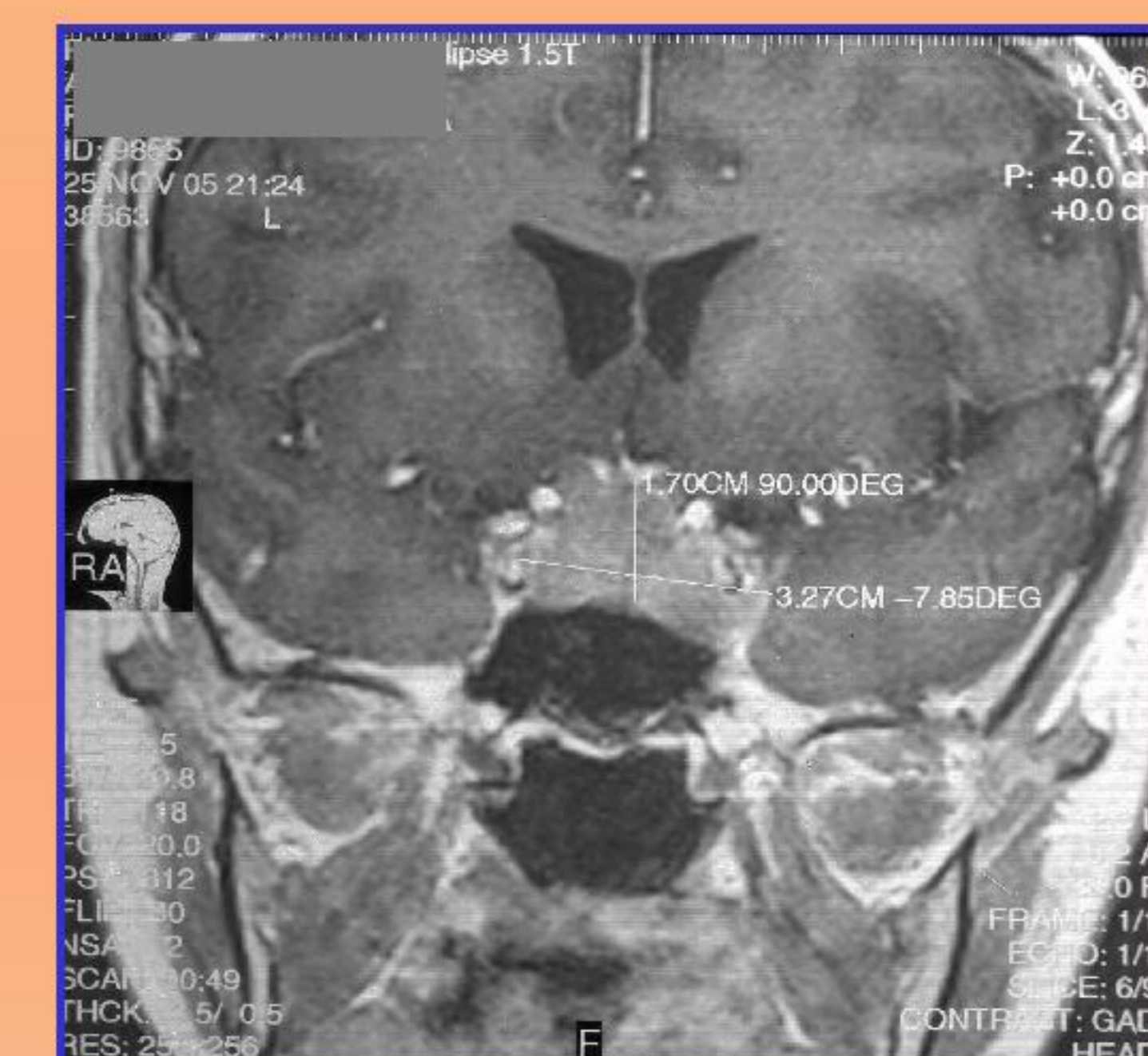
Ryc. 1 Frontal MR picture of invasive corticotroph macroadenoma in patient with primarily diagnosed microadenoma.



Ryc. 2 Patient with macroadenoma in Nelson's syndrome



Ryc.3 Frontal MR picture in patient with Crooke's cell macroadenoma



Ryc. 4 Frontal MR in patient with Nelson syndrome

Tab.1 Patients with Cushing's disease caused primarily by corticotroph microadenoma

Patient	Gender	Age	Micro size mm	Macro Size mm	ACTH in micro stadium	ACTH in macro stadium
FU	F	23	<5	17 x 35	-	10 560 pg/ml [n:10-46]
MB	F	49	9 x 7	34.4 x 39.2	81pg/ml [n:<46]	23 830 pg/ml [n:7.2-63.3]
SM	F	52	5 x 4	15 x 15 x 10	-	93 pg/ml [n:7.2-63.3]

Tab.2 . Patients with Cushing's disease caused primarily by macrocorticotropinoma

Patient	Gender	Age	Macrotumour size mm	ACTH level pg/ml
FE	M	28	60 x 40 x 40	219 [n: 10-46]
LW	M	51	32 x 29 x 24	170 [n:7.2-63.6]
CZ	M	37	50 x 30 x 40	68.2 [n:10-46]
GW	M	56	15 x 13 x 15	217.5 [n:7.2-63.6]
SE	F	31	22 x 18 x 12	68.2 [n:10-46]
OK	F	66	23 x 17 x 15	17.63 [n:7.2-63.6]

