

Optic neuropathy following radiotherapy for Cushing's disease followed by the diagnosis of pituitary carcinoma

Krystallenia Alexandraki, Georgios Boutzios, Georgios Nikolopoulos, Panagoula Roussaki, Maria Chrysochoou, Eleftherios Chatzellis, Marina Tsoi, Maria Kaltsatou, Panayiotis Moschouris, Gregory Kaltsas

Endocrine Unit, Department of Pathophysiology, University of Athens, Medical School, Laiko Hospital, Athens, Greece

BACKGROUND

Adrenocorticotrophin secreting pituitary carcinomas are rare neoplasms but there are not factors to predict their aggressive evolution nor a standard practice to their management.

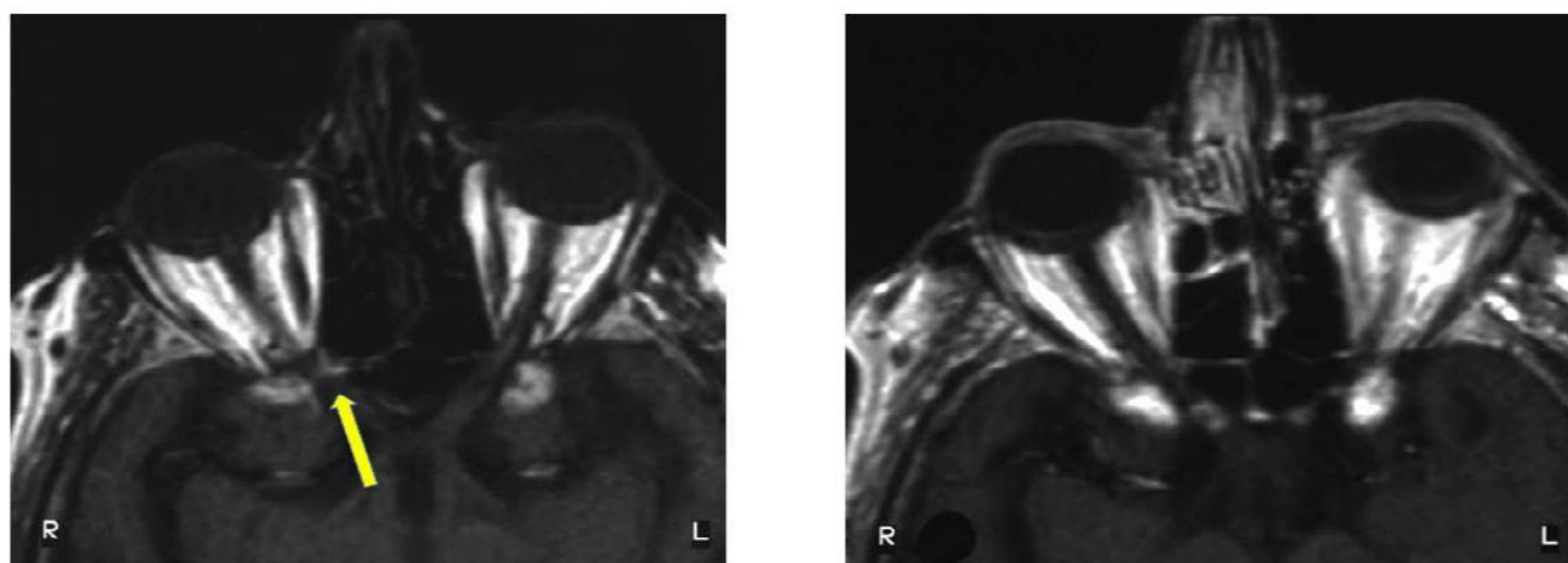
CASE REPORT

43 year old female patient presented in 1990 with Cushing's syndrome due to adrenocorticotrophin secreting pituitary microadenoma

THERAPEUTIC MANAGEMENT

1990: Trans-sphenoidal surgery with cure (post-operative cortisol serum levels <50nmol/L).
 2000: clinical, biochemical and imaging recurrence (10 years after her first remission)
 2001: repeat surgery with cure (post-operative cortisol serum levels <50nmol/L)
 2002: recurrence
 2002-2004: Ketoconazole (increased doses up to 1200 mg) + cabergoline + somatostatin analogues therapy
 2005: no tumour was documented in imaging studies; she received external beam irradiation (in total a dose as high as 54 Gy)
 2005: increased doses of metyrapone up to 4000mg and ketoconazole up to 1200mg
 2005: UNCONTROLLED hypercortisolaemia → bilateral adrenalectomy

2006: Orbital MRI T1 revealing optic neuropathy



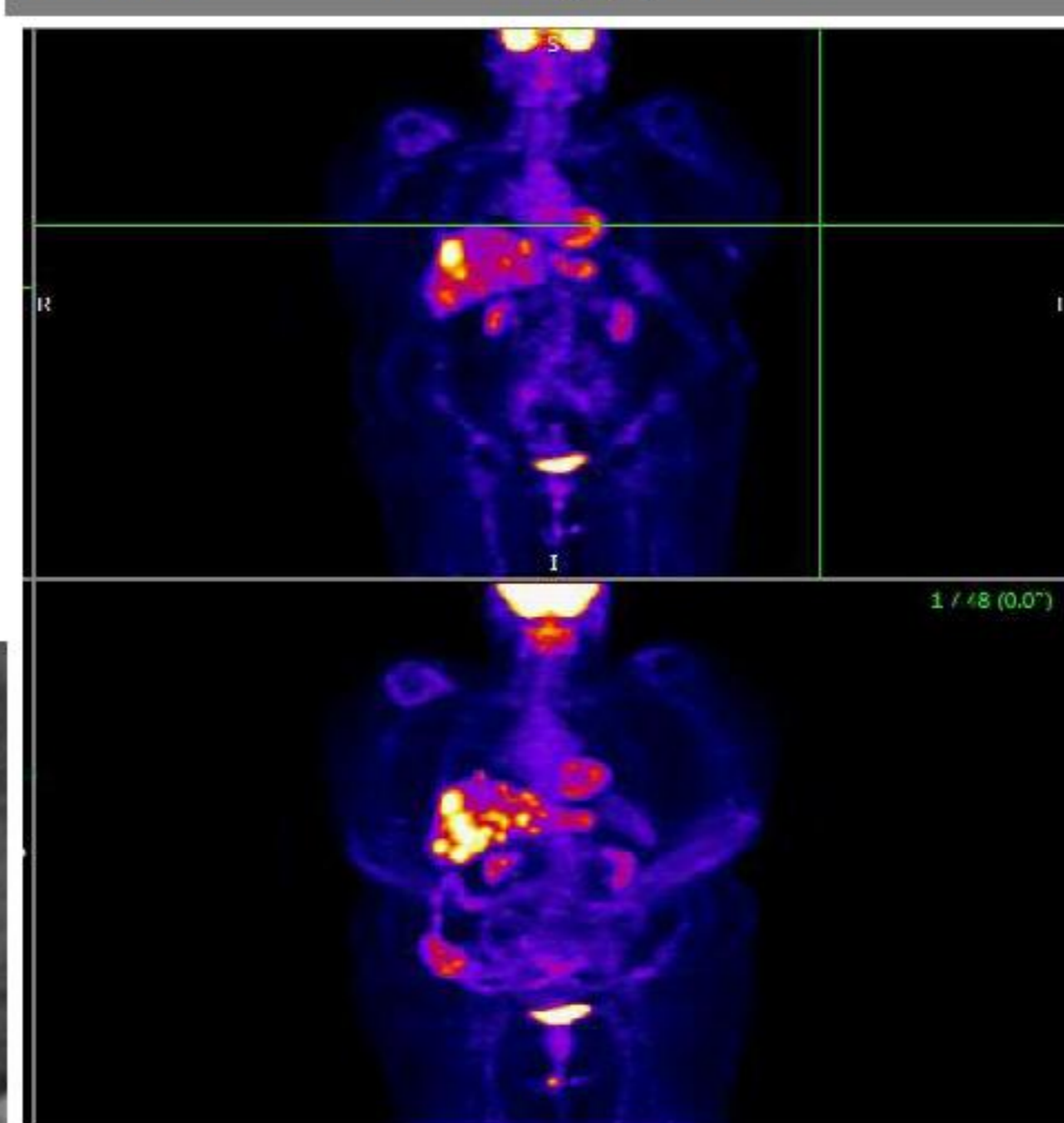
5 days IV administration of corticosteroids → aggravation

6/2006 : Hyperbaric oxygen therapy (20 cycles, 2 Atm for 30 min)- no result

Visual acuity: 0/10 in both eyes



2009-2010: ACTH: 5.858 → 22.240 pg/ml



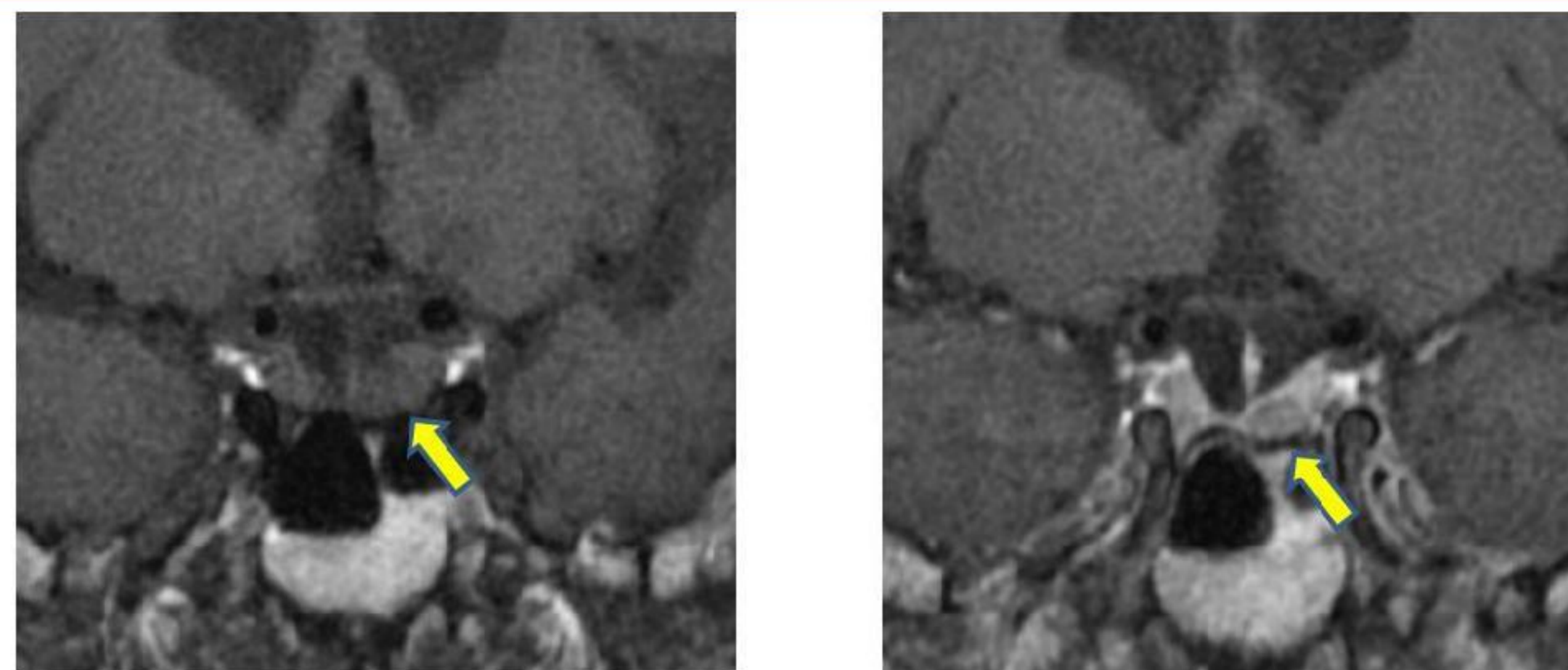
2010: FDG-PET Scan: multiple metastatic deposits in liver (SUVmax 21,2 -12), pituitary: (SUVmax 9,1); no lymph nodes/ bones/ brain

2008: ACTH: 200 pg/ml (9-52)
 Pituitary MRI: post-op changes

References

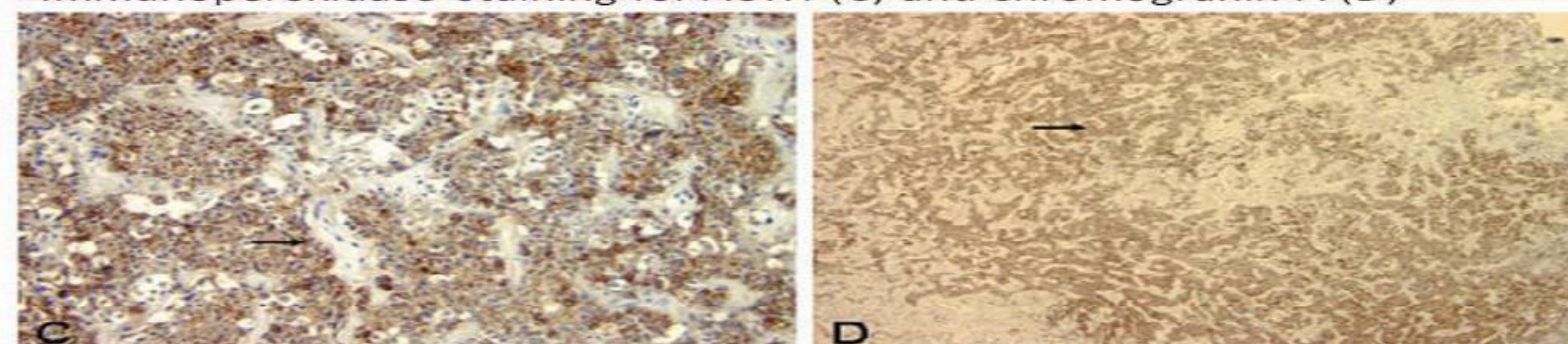
Koumariou et al. *Endocrine-Related Cancer*, 2012; Heaney. *JCEM* 96:3649-3660, 2011; Dudziak et al. *September 2011*, 96:2665-9; Ann I. McCormack. *Eur J Clin Invest* 2011; 41: 1133-48

PITUITARY CARCINOMA DIAGNOSIS



Presence of lesion 7.5mm in the left lateral part of pituitary, not clear margin . Optic chiasm atrophy.

Immunoperoxidase staining for ACTH (C) and chromogranin A (D)

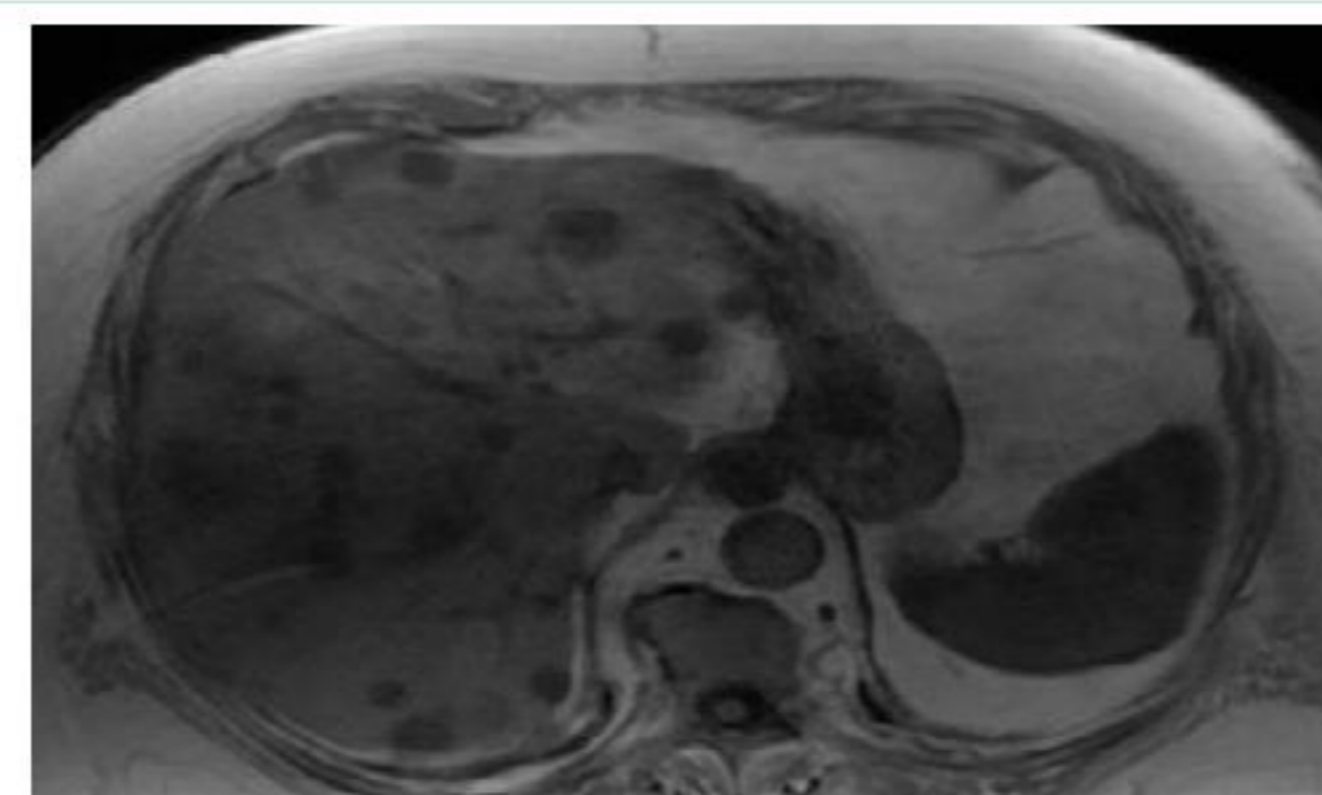


29/12/2012. Liver biopsy. Well differentiated endocrine carcinoma. Immunohistochemistry: Ker 18 (+), Syn (+), CgA (+), CD 56 (+), Ki-67=3%, ACTH (+). OCTREOSCAN: (-)ve

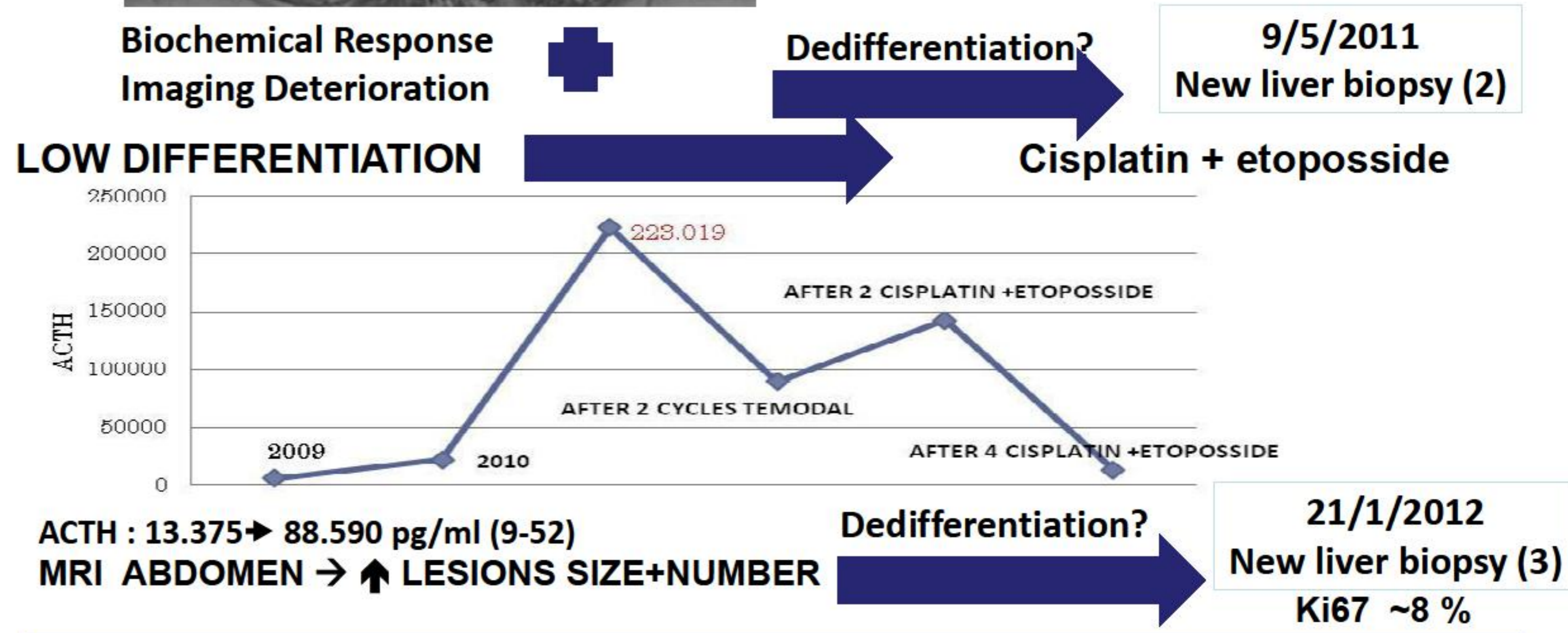


THERAPEUTIC MANAGEMENT

❖ 3 cycles of temozolamide (Temodal) 100 mg 5 days / week PO + bevacizumab IV (Avastin) 200mg /week



ACTH: 223.019 → 89.900 pg/ml
 BUT MRI ABDOMEN → ↑ LESIONS SIZE; MAX 39x39mm → 52x51 mm (33.3%↑)



MGMT (methylguanine DNA methyltransferase) Methylation specific PCR (MS11/9/2012 RADIOFREQUENCY RIGHT LIVER LOBE P): LOW BUT Temozolamide + Bevacizumab

SEPSIS → MYELOTOXICITY → CONSERVATIVE TREATMENT
 DECEASED : 19/9/2014

CONCLUSIONS

The appearance of pituitary carcinoma cannot be excluded by the cure post trans-sphenoidal surgery nor be prevented by a high dose of irradiation even this is so high to cause radiation-induced optic neuropathy

