Endocrine Pathology

Case Slide Seminar

George Kontogeorgos MD, PhD

Department of Pathology
and Pituitary Tumor Reference Center
G. Gennimatas Athens General Hospital
Athens, Hellas

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Present Complaining History

A 32-year-old housewife woman presented with:

- A 10-day history of fever, headaches, weakness, nausea and vomiting

Past Medical History

- Diabetes mellitus and 6-months amenorrhea without galactorrhea
- 2-months before her admission she underwent a surgical drilling of the right mastoidea due to right mastoiditis
- Histological examination:

  Non-specific inflammatory granulation tissue
- She was placed on i.v. antibiotics and she was discharged afebrile

Clinical Examination

- Pyrexia (38º C) with sinus tachycardia (100/min)
- Unremarkable respiratory, abdominal and neurological examinations
- Normal visual fields and visual acuity
- Non-smoker
- She has not been traveled abroad the last 5 years

Endocrine Investigation

- T3: 1.95 nmol/L (1.07-3.18)
- T4: 76.11 nmol/L (58-174)
- F at 9:00 am <50 nmol/L
- E2 <20 pmol/L
- TSH: 0.4 mU/L
- ACTH <4 pg/ml
- FSH: 3.9 mU/L
- LH: 3.0 mU/L
- **PRL: 1880 mU/L (NR <360)**

Biochemical Investigation

- All blood, sputum and urine cultures were negative for common bacteria, mycobacteria and fungi
- The ZN-stain of CSF was negative for acid-fast bacilli
- Tuberculin skin test was negative
- PCR analysis of CSF, gastric juice and urine was also negative for M. tuberculosis DNA
- HIV test was negative

Imaging Investigation

- Chest and abdomen CT scan: normal
- Whole body scan with Gallium (67Ga): *not diagnostic for sarcoidosis*
- **Cranial MRI scan:** contrast-enhancing 2 cm intrasellar mass
- Heterogeneous appearance
- Suprasellar extension
- Pituitary stalk thickening

*Strongly suggestive of **inflammatory lesion** rather than pituitary adenoma*

Preoperative Differential Diagnosis

Pituitary granulomas, rare specific lesions

- Sarcoidosis
- Tuberculosis
- Langerhans histiocytosis *(Histiocytosis-X)*
- Giant cell granulomatous hypophysitis
- Xanthomatous hypophysitis
- Wegener's granulomatosis
- *Lymphocytic hypophysitis (included in d.d.)*

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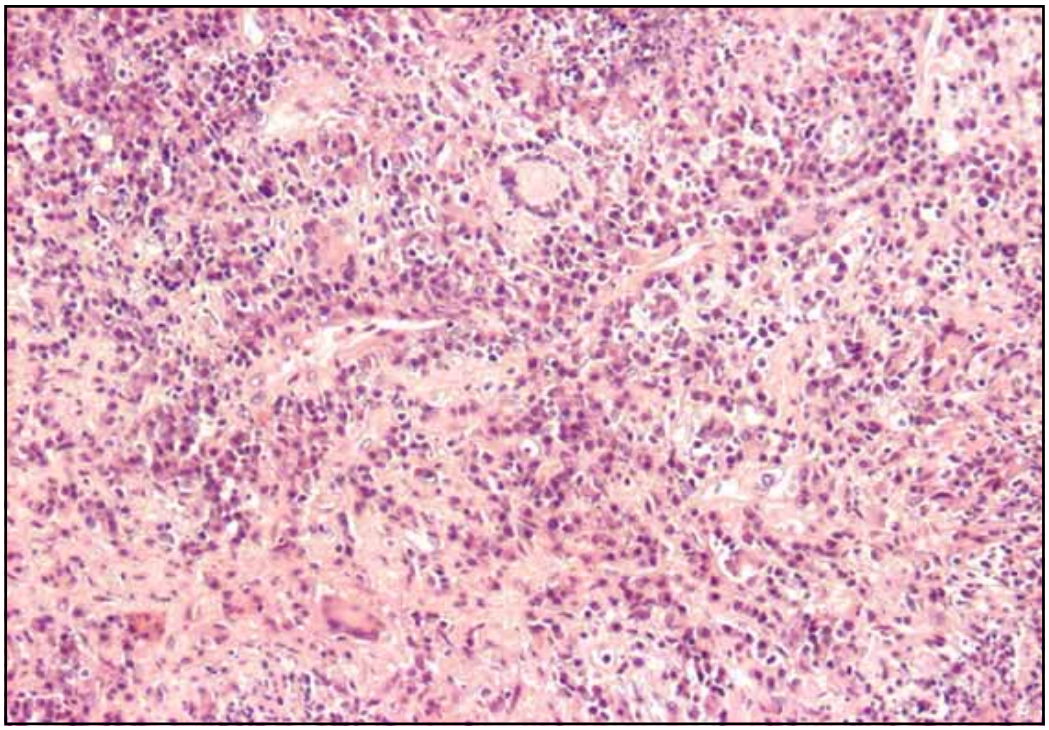
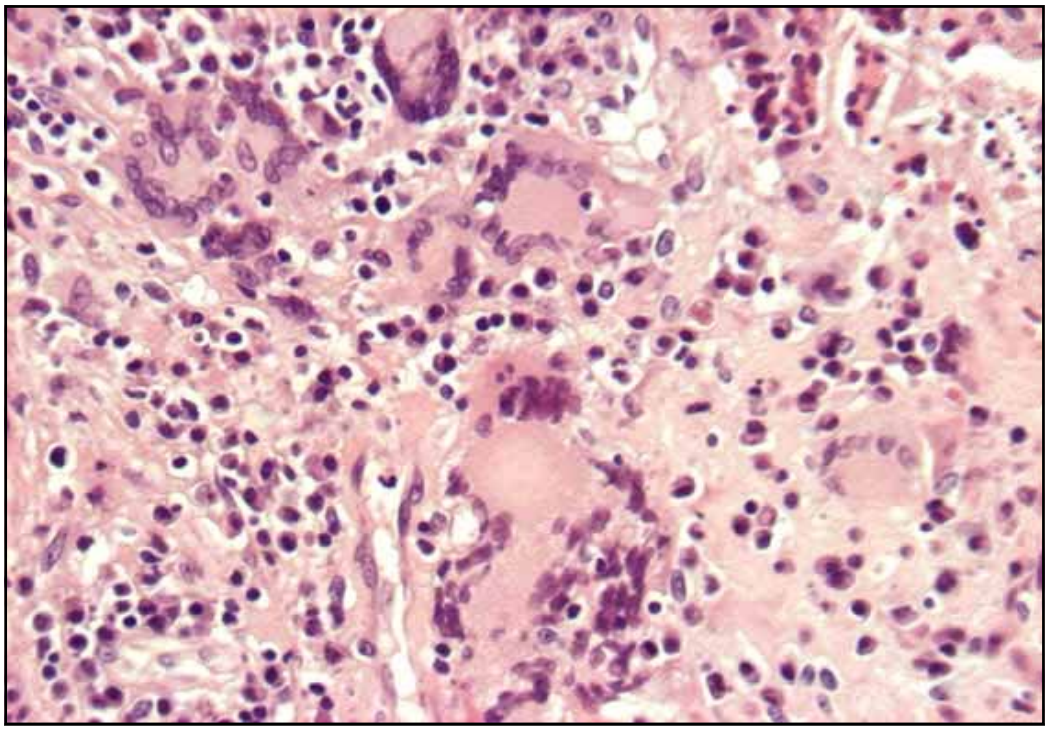
Surgery

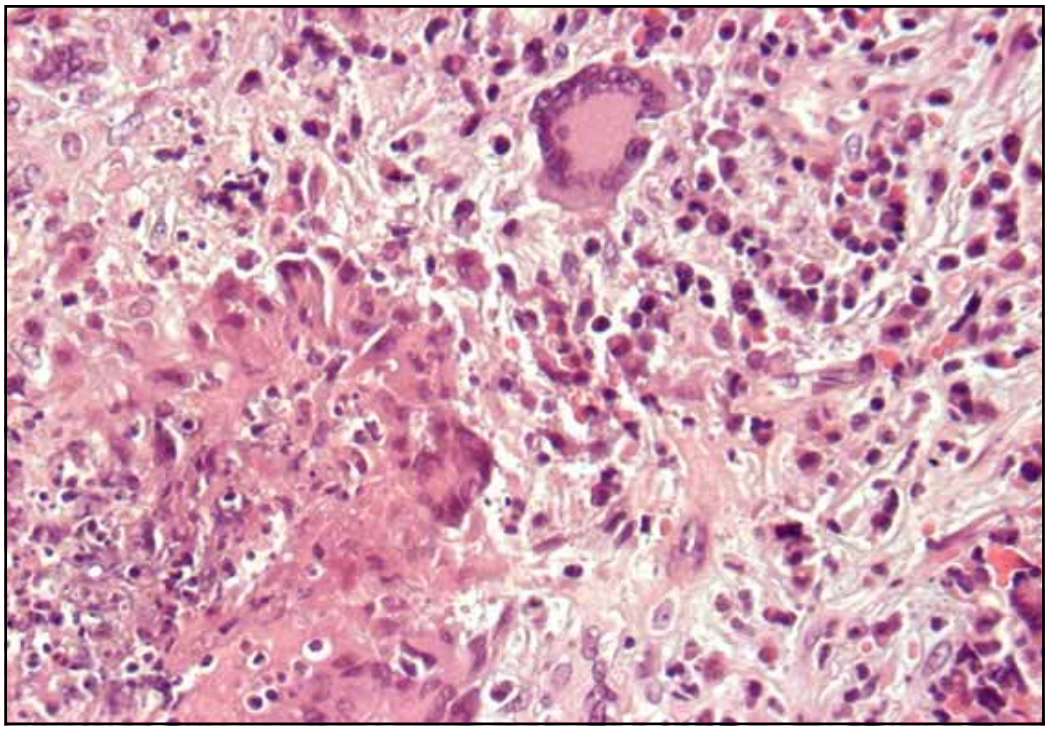
- Excision of the pituitary mass by a transsphenoidal approach

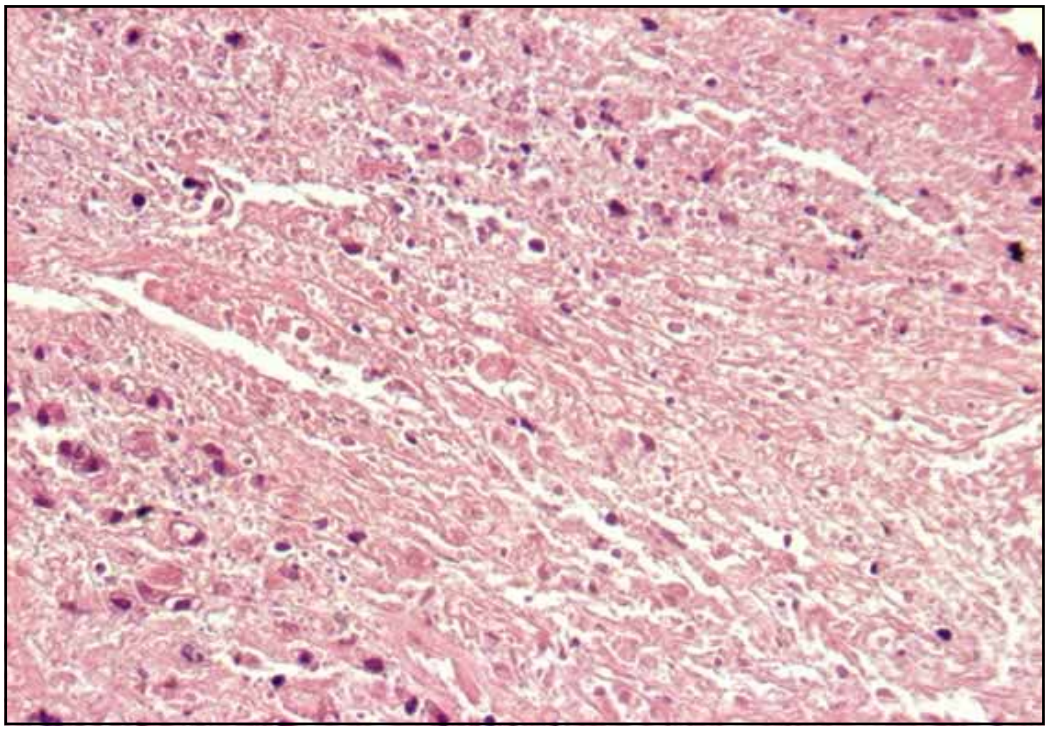
Histology

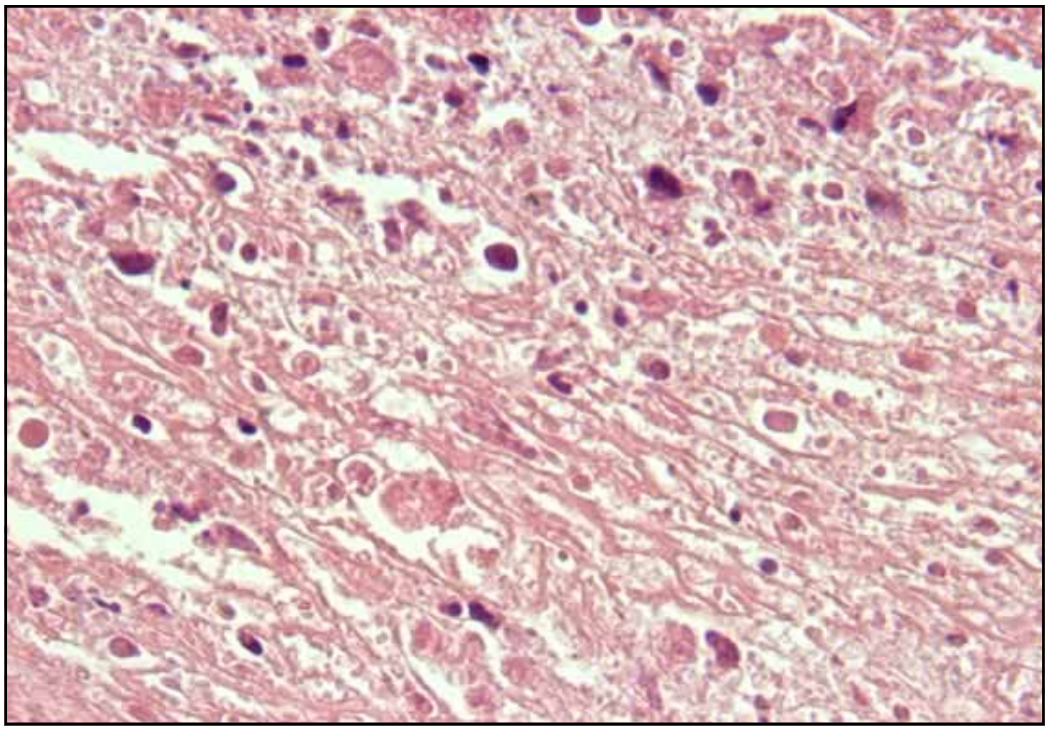
- No evidence of pituitary adenoma
- Destruction of adenohypophysis by epitheloid granulomas with partial caseous necrosis and microabscess formation
- Repeated Z-N stain failed to reveal acid-fast bacilli

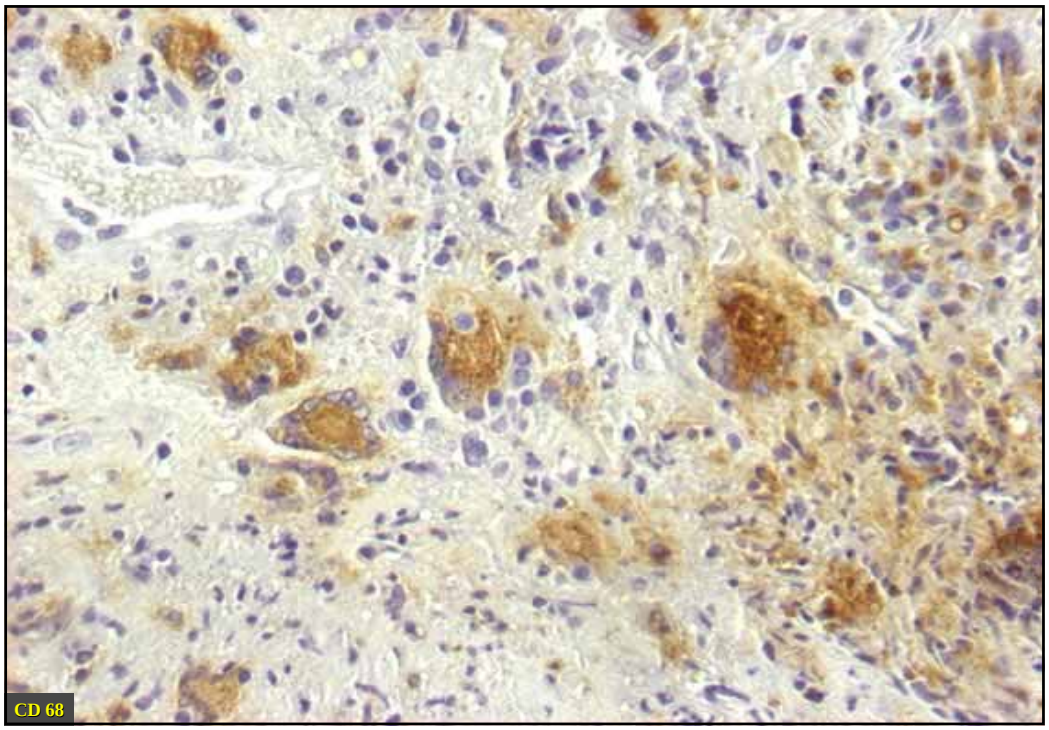








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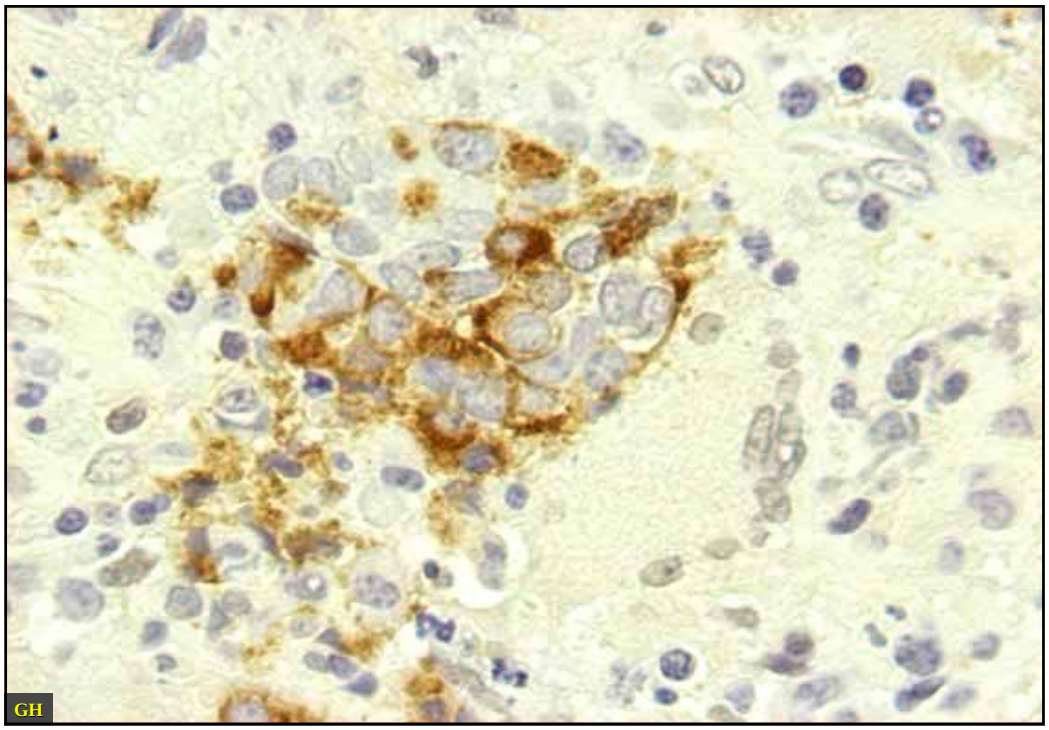
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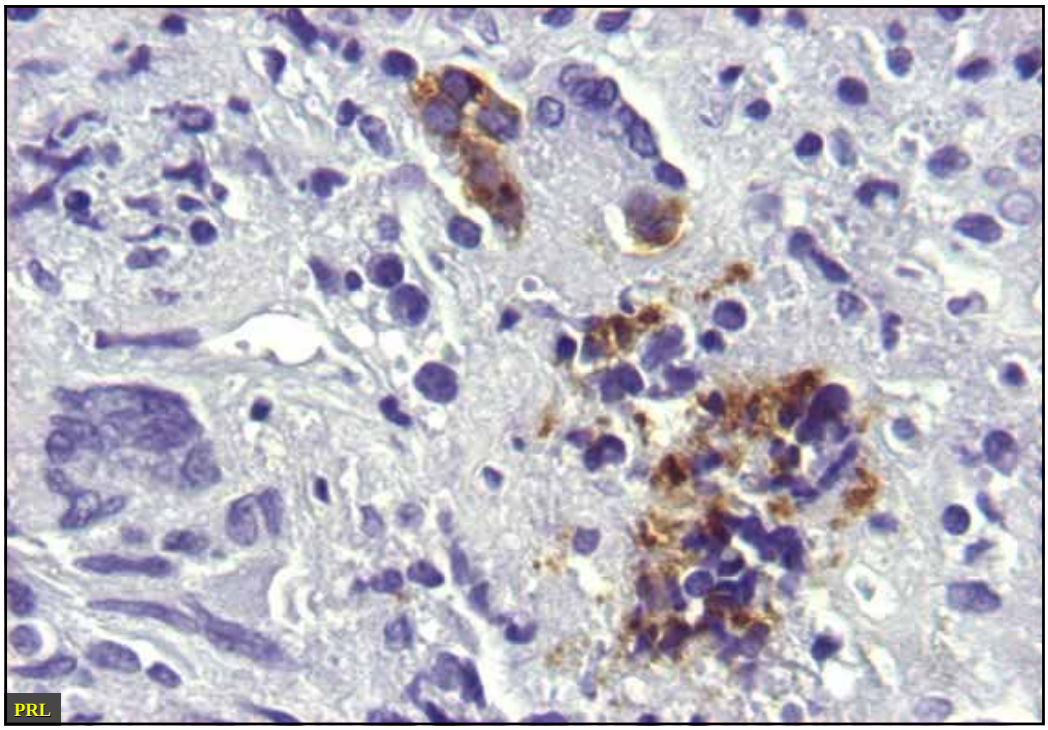
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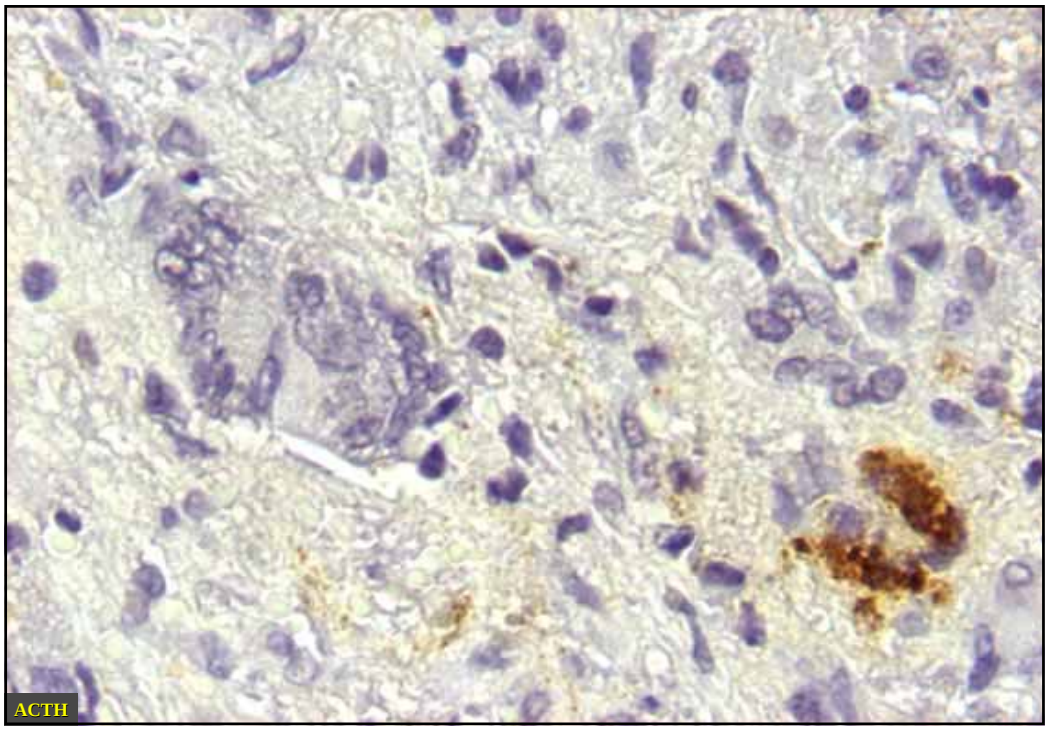
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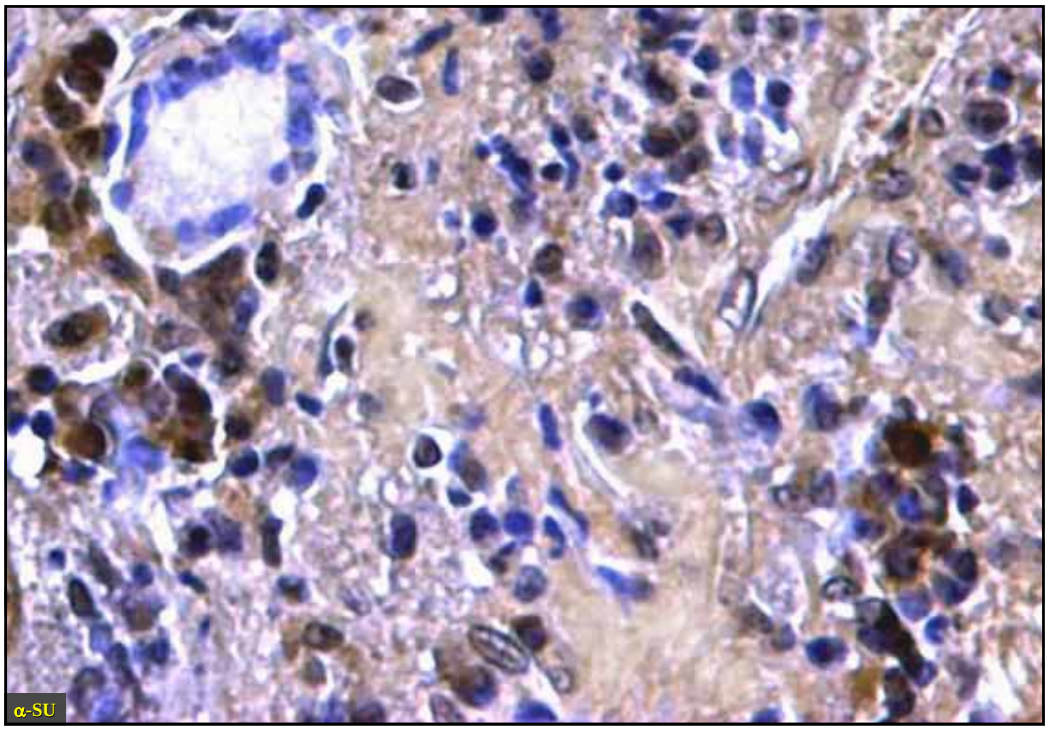
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YEAH, I KNOW - AND HE ISN'T EVEN GOOD, BUT RULES ARE RULES!
DON'T SHOOT THE PIANIST
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Post Histology

- *As the histopathological findings were highly suggestive of a mycobacterium related infection, we proceeded to molecular analysis of the pituitary samples*

Nested PCR Analysis

- Nested PCR was positive for mycobacterial DNA
- The amplified, purified and sequenced product was identified as Mycobacterium malmoense, an atypical nontuberculous mycobacterium (NTM)
- This PCR technique has been found to be useful in cases when only paraffin-embedded tissue is available

Richter et al., 1995, J Pathol

Nested PCR Analysis

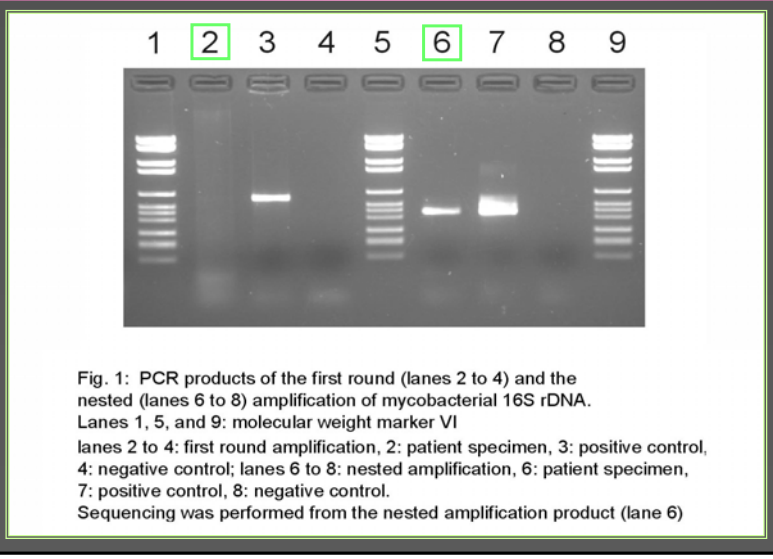

Fig. 1: PCR products of the first round (lanes 2 to 4) and the nested (lanes 6 to 8) amplification of mycobacterial 16S rDNA.
Lanes 1, 5, and 9: molecular weight marker VI
lanes 2 to 4: first round amplification, 2: patient specimen, 3: positive control, 4: negative control; lanes 6 to 8: nested amplification, 6: patient specimen, 7: positive control, 8: negative control.
Sequencing was performed from the nested amplification product (lane 6)

Postoperative Data

- The patient was placed on appropriate antimycobacterial treatment *(isoniazid, rifampicin, ethambutol, ciprofloxacin and clarithromycin)*
- She was also placed on hormonal replacement therapy
- 6-months later a new pituitary MRI scan showed that the pituitary lesion had been completely disappeared
- She is doing well, free of any sings and symptoms of the disease after a 7 year follow-up

Discussion I

- Pituitary granulomas are discovered because of mass effect symptoms
- Hypopituitarism, hyperprolactinaemia, diabetes insipidus, visual field disturbances and aseptic meningitis are the most usual manifestations
- None of these signs and symptoms are specific for these lesions
- Pituitary granulomas are often misdiagnosed as pituitary adenomas

Discussion II

- *Mycobacterium tuberculosis* is responsible for 0.15% - 4% of intracranial tumors and tumor-like lesions in western countries
- Atypical nontuberculous mycobacteria (NTM), represent a novel agent of pituitary granuloma
- Lung is the most important site of localized NTM infection in non-immunocompromised patients (especially of *Mycobacterium avium complex*)
- Surgical resection is advocated for localized NTM infections
- Multiple drug therapy is strongly recommended

Conclusion

This is an unusual case of isolated pituitary granuloma, in a non-immunosuppressed patient, caused by infection with mycobacterium malmoense, which was confirmed by nested PCR

Nested PCR Analysis

- Sections were cut from the paraffin-embedded tissue and deparaffinized
- DNA was isolated using a QIAamp Tissue Kit (Qiagen, Hilden, Germany)
- The gene encoding the ribosomal 16S RNA (16S rDNA) was amplified by PCR and was positive for mycobacterial DNA
- The amplified product was purified and sequenced
- Based to the individual 16S sequence, it was identified as Mycobacterium malmoense, an atypical nontuberculous mycobacterium (NTM)
- This PCR technique has been found to be useful in cases when only paraffin-embedded tissue is available (Richter et al., 1995, J Pathol)