Government of Western Australia
Department of Health

FIONA STANLEY hospital

Pituitary Case 2

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Western Australia

History

- 65yo Chinese Singaporean male referred with androgen deficiency and abnormal CT brain
- Two month history of lethargy and low mood.
- Low libido and erectile dysfunction for 10years
- No visual disturbance

History

- PMHx
  - HTN
  - Social anxiety and depression
- Medications
  - Candesartan 16mg
- SHx
  - Lives with wife, two children.
  - Ex smoker with 5 pack year smoking hx
  - Approximately 2 standard drinks per week
- FHx
  - Brother treated for TB

Examination

- Reduced muscle bulk over deltoids.
- Absent body hair. Pubic hair present.
- No gynaecomastia
- Testes volume reduced
- Formal ophthalmological assessment showed no significant visual field defect

Investigations

- **Testosterone <0.3nmol/L (9-35nmol/L)**
- **SHBG 72 (15-50nmol/L)**
- LH 2.0 (1-9IU/L)
- **Prolactin 599 (<320mIU/L)**
- CT brain and pituitary
  - Suprasellar avidly enhancing soft tissue nodule measuring 7x9x9mm

Investigations

- **Testosterone LCMS 0.3nmol/L** (8.0-35nmol/L)
- **LH <0.1U/L** (1.0-8.0U/L)
- **Prolactin 440mU/L** (<340mU/L)
- IGF-1 64ug/L (69-200ug/L)
- TSH 0.8mU/L (0.40-4.0mU/L), T4 12pmol/L (9-19pmol/L)
- 9am Cortisol 270nmol/L (150-700nmol/L), ACTH 7.1pmol/L (2.0-10.0)
- Short synacthen test (abbot assay)
  - Cortisol basal 280, 30min 460, 60min 530. (>430nmol/L at 30minutes)

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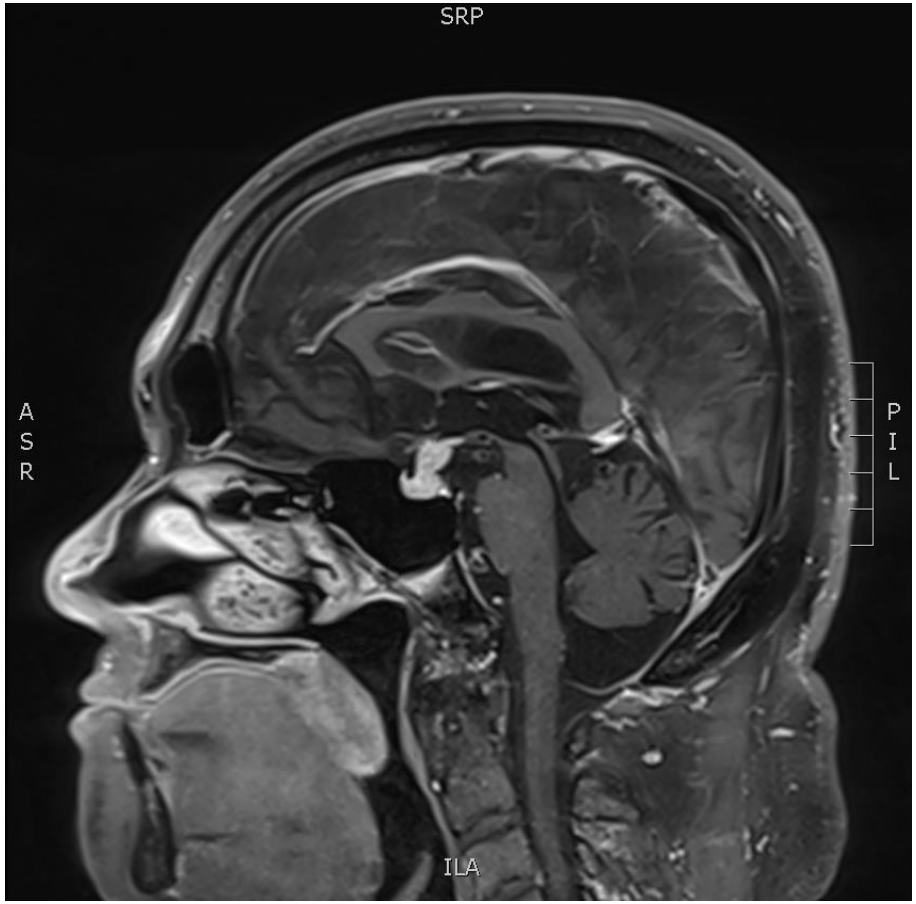
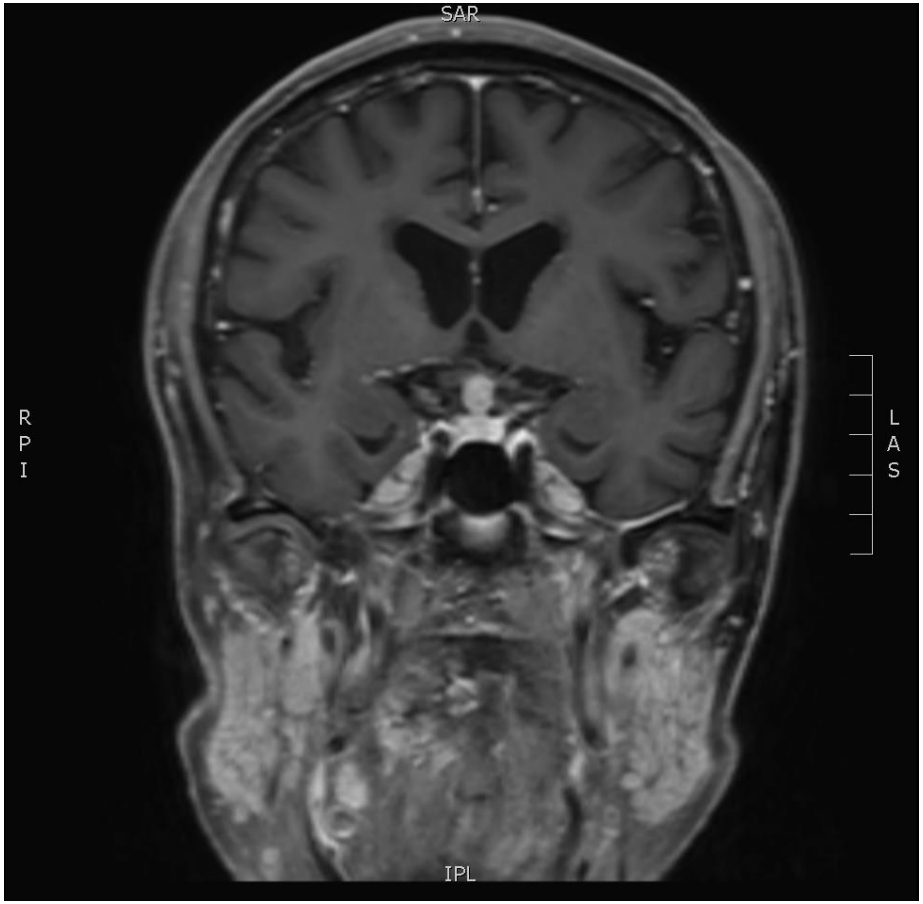
MRI brain





MRI brain

- Thickening and enhancement of pituitary infundibulum, 3rd ventricular floor and infundibular recess
- Nodular leptomeningeal thickening and enhancement
- Nodular enhancing lesions in the cauda equina.
- Appearances suggestive of a leptomeningeal process with CSF seeding.

Differential Diagnosis?

- Lymphoma
- Metastatic disease
- Granulomatous disease such as neurosarcoidosis, tuberculosis
- IgG4-related disease

Further investigations

- Serum ACE 38 (20-70U/L)
- βHCG <1 (<2IU/L)
- AFP 2 (<11kIU/L)
- PSA <0.01 (<4.50ug/L)
- ESR 11 (1-30mm/hr)
- **ANA 25 (<7IU/mL)**
- ANCA <2 (<4 units)
- C3 1.17 (0.88-1.98g/L),C4 0.25 (0.16-0.52g/L)
- dsDNA 1 (<7IU/L)
- ENA negative
- Rheumatoid factor negative

Cerebrospinal fluid

- Glucose 2.6 (2.7-4.4mmol/L)
- **Protein 1.37 (0.15-0.45g/L)**
- LDH 23U/L
- Angiotensin converting enzyme <2.0 (<2.0U/L)
- Acid fast bacilli not seen
- Immunophenotyping no evidence of monoclonal B cell or aberrant T cell population
- **Cytology: Increased atypical inflammatory cells**
- IgG1 0.81g/L, IgG2 0.28g/L, IgG3 <0.09g/L, IgG4 0.09g/L, IgG 0.1g/L

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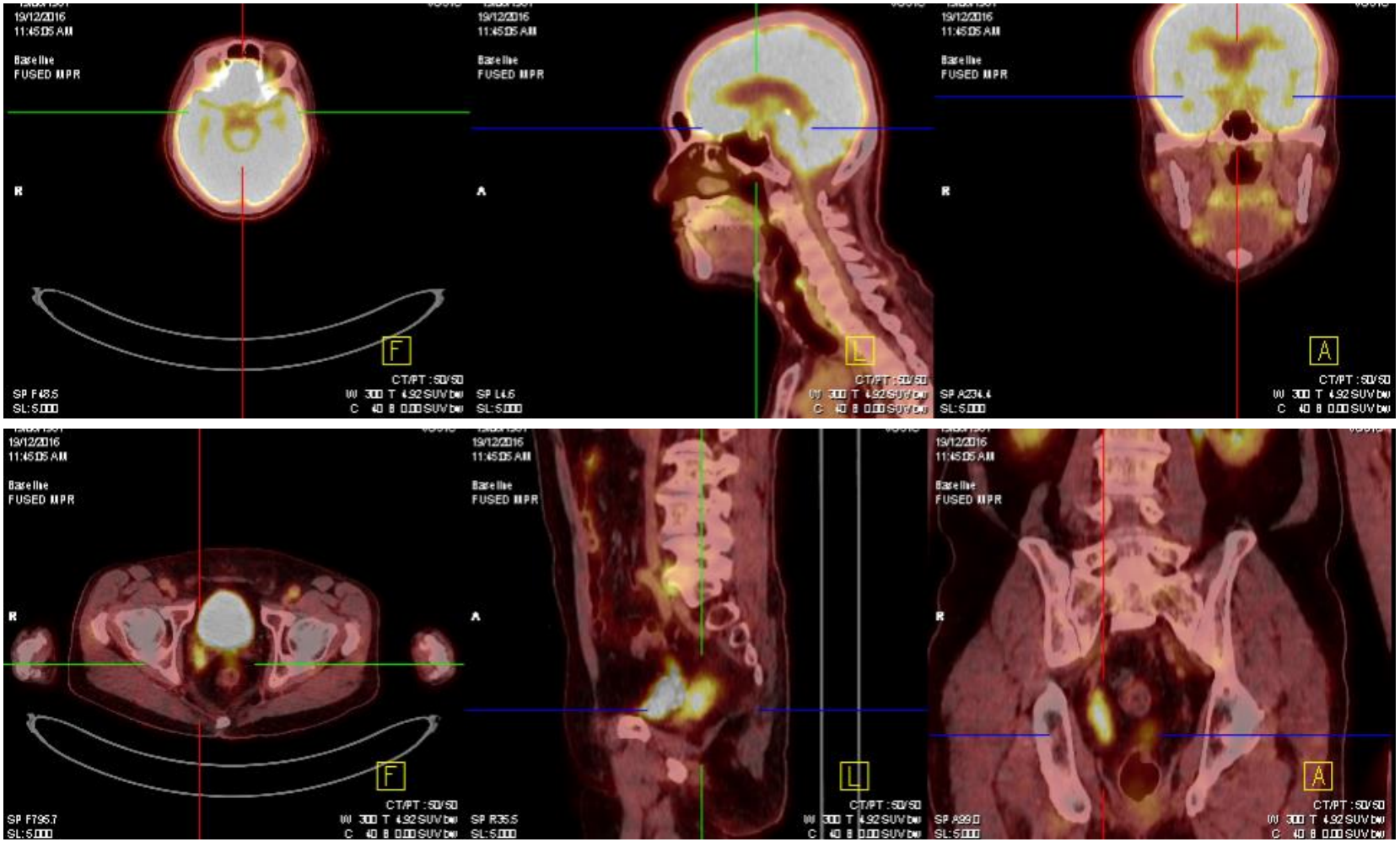
Whole body PET/CT



Whole body PET/CT

- Overall metabolic appearances are suggestive of lymphoma, but the differentials of metastases and granulomatous inflammatory process (such as Sarcoidosis) are not excluded.

CT guided FNA right pelvic lymph node

- CT guided FNA right pelvic lymph node
  - Acid fast bacilli not detected
  - Immunophenotyping – no evidence of a monoclonal B cell or aberrant T cell population
  - Cytology negative for malignancy
  - Sample insufficient to evaluate for IgG4-related disease

Subsequent investigations

- Quantiferon positive
  - Indicative of latent or active TB
- Immunoglobulin G subclasses
  - IgG1 6.14 (4.90-11.40g/L)
  - **IgG2 7.14 (1.50-6.40g/L)**
  - IgG3 0.25 (0.20-1.10g/L)
  - **IgG4 11.80 (0.08-1.40g/L)**
  - **IgG 16.8 (6.1-13.0g/L)**

- Haematology; lymphoma unlikely
- Infectious diseases; TB not excluded

Further investigations

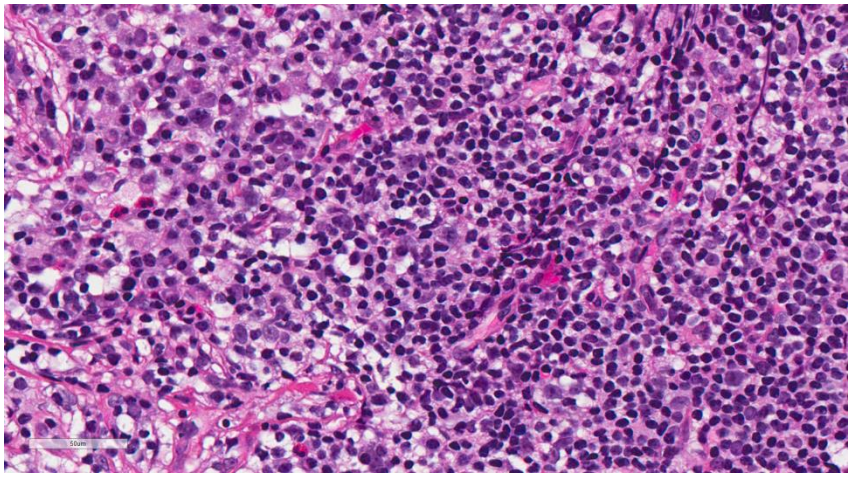
- **Cortisol 100 (150-700nmol/L)**
- **Short synacthen test (abbot assay)**
  - **Cortisol basal 46, 30min 240, 60min 280** (Normal at 30mins >430nmol/L)
- ACTH 2.6 (2.0-10.0pmol/L)
- TSH 0.54 (0.40-4.00mU/L), **T4 8 (9-19pmol/L)**
- Commenced glucocorticoid and thyroxine replacement.

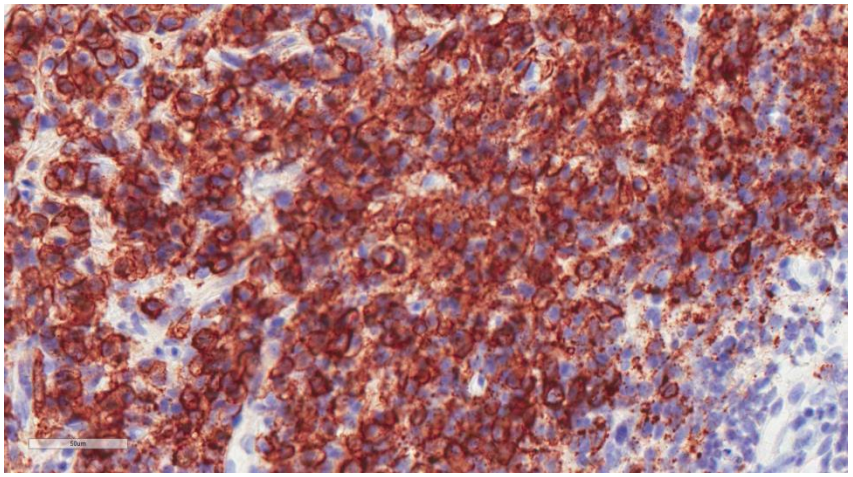
Where to from here?

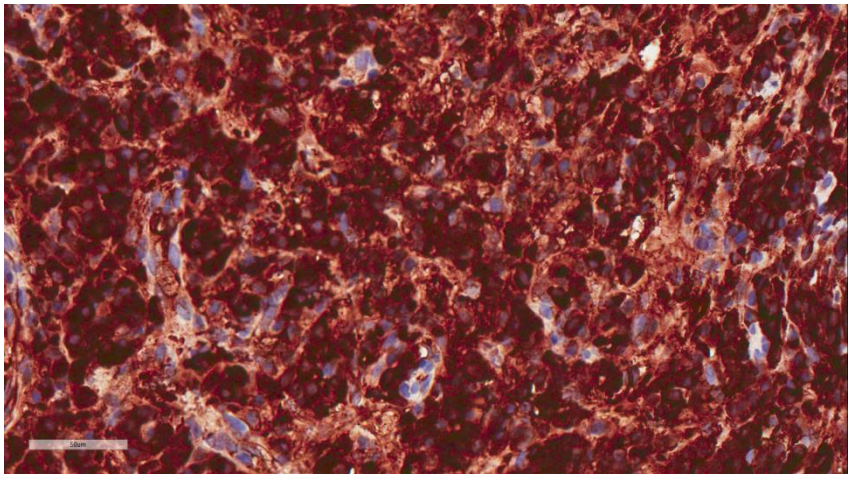
- Further investigations
  - Pituitary or lymph node biopsy?
  - Repeat LP?
- Empirical glucocorticoid therapy?

- Large volume LP negative for acid fast bacilli
- ID team conclude active TB unlikely.
- Requires treatment for latent TB if for immunosuppression

Lymph node biopsy







IgG4-related hypophysitis

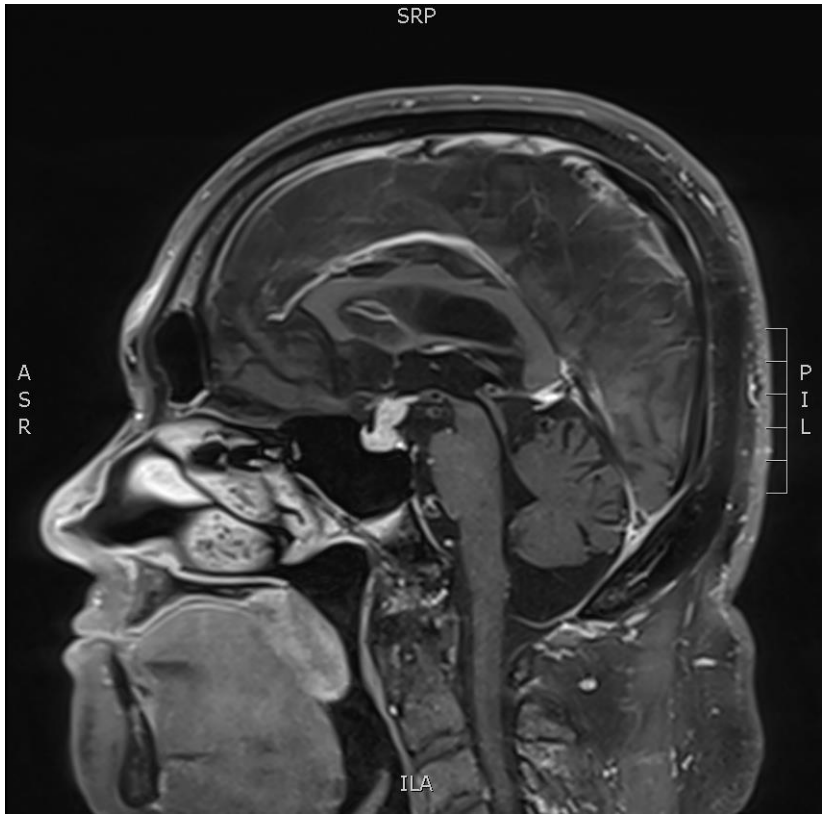
- Diagnosis
  - Characteristic MRI findings
  - Elevated serum IgG4 (DDx pancreatic cancer, Wegener's granulomatosis, Castleman's disease, idiopathic plasmacytic lymphadenopathy)
  - IgG4 positive cell infiltration on biopsy
  - Therapeutic response to corticosteroids.

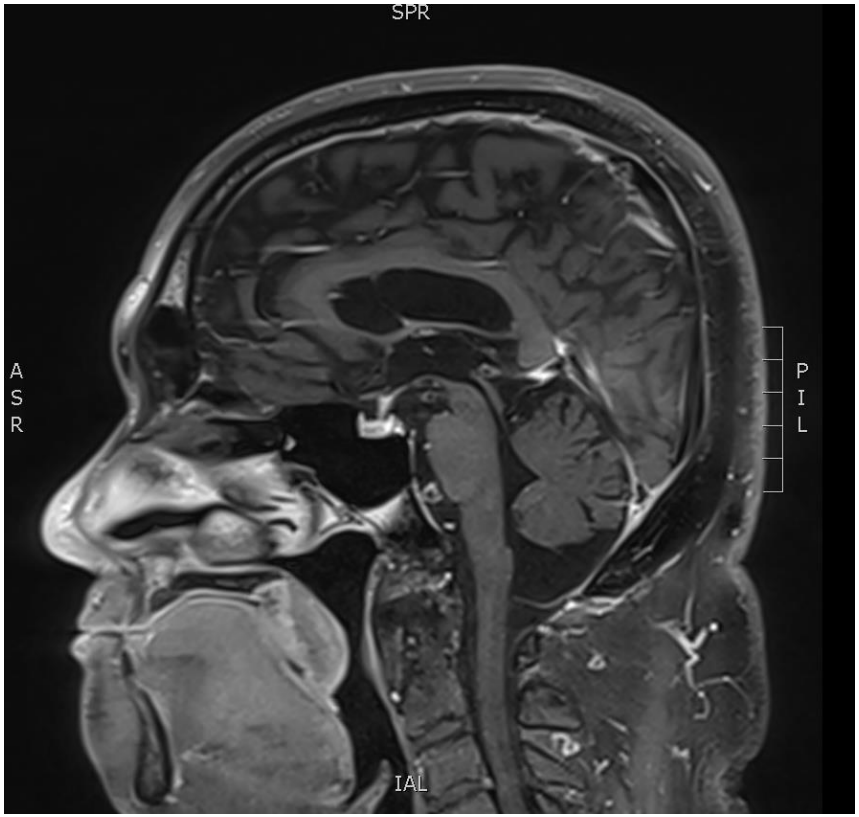
- Leporati P et al (2011) J. Clin. Endocr. Metab. 96:1971–1980
- Shikuma et al (2017) Pituitary 20:282–291

Treatment

- Prednisolone 60mg daily
- Isoniazid 300mg, pyridoxine 25mg daily for 9/12

Follow up





Follow up

	Dec 2016	April 2017	May 2017
IgG1 (4.90-11.40g/L)	6.14	**4.08**	**4.14**
IgG2 (1.50-6.40g/L)	**7.14**	5.70	4.93
IgG3 (0.20-1.10g/L)	0.25	**0.14**	**0.14**
IgG4 (0.08-1.40g/L)	**11.80**	**4.76**	**2.94**
IgG (6.1-13.0g/L)	**16.8**	11.5	8.9

Ongoing management

- Weaning regimen prednisolone +/- consideration of steroid sparing agent
- Repeat MRI spine
- For reassessment of anterior pituitary function

IgG4-related disease

- Multisystem inflammatory disorder
- Neurological involvement is relatively uncommon
  - Hypertrophic pachymeningitis
  - Hypophysitis
- IgG4-related CNS disease can mimic a variety of malignant, granulomatous and infectious diseases including TB

IgG4-related hypophysitis

- Typically affects older males
- May present with panhypopituitarism, anterior pituitary dysfunction or central diabetes insipidus
- Mostly have elevated serum IgG4 levels
- Associated retroperitoneal fibrosis, salivary gland disease and pancreatic disease

- Shikuma et al (2017) Pituitary 20:282–291

IgG4-related hypophysitis

- Treatment with glucocorticoids
  - Most cases demonstrate improvement in size of pituitary mass and stalk thickening
  - Some cases of anterior pituitary insufficiency improve
  - Most cases of DI do not improve
- High rates of recurrence
- Steroid sparing agents such as azathioprine and rituximab have been described

- Iseda et al Endocrine Journal 2014, 61 (2), 195-203
- Khosroshahi et al Arthritis Rheum. 2010;62(6):1755

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