A CASE OF IgG4-RELATED XANTHOMATOUS HYPOPHYSITIS

A CASE REPORT

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ABSTRACT

Introduction: Hypophysitis is an inflammatory disease of the pituitary that may mimic tumors. Primary hypophysitis has been classified as lymphocytic (LH), granulomatous (GH), and *xanthomatous (XH).* It has been recently proposed to be an IgG4-related autoimmune disease (serum IgG4 concentration:135mg/dl), proven by tissue IgG4 immunostaining.

Case description: A 23-year-old man suffered from typical cluster type headache. Two years after the first symptoms, diabetes insipidus occurred. His testosterone level was low with low serum FSH and LH suggesting central hypogonadism, but all the other anterior pituitary hormone levels were normal. Sella MRI scan depicted a 17 mm inhomogenous mass. After the transsphenoidal surgery the pituitary tissue showed accumulation of foamy cells and *xanthomatous epithelioid cells*. After stopping the preoperative hydrocortisone therapy the headache returned. The endrocrine work-up revealed hypadrenia (morning cortisol: 96 nm/l, ACTH:3.38 pm/l), hypothyroidism (ft4:10.5 pm/l), hypogonadism (testosterone: 3.44 nm/l) with FSH:3,3 mIU/l and LH:2,8 mIU/l. Hydrocortisone, levothyroxine and testosterone were stepwise reintroduced. During the follow-up we could stop hydrocortisone, levothyroxine, whereas he has permanently required desmopressin and testosterone substitution. Occasionally headache attacks occur and dissappear with glucocorticoid administration. Two years after the initial diagnosis the **hypophysitis was proven to be IgG4- related** by his tissue *IgG4 immunostaining* as well as by his elevated serum *IgG4 concentration (815 mg/l).*

Conclusion: We describe a case of *IgG4 related xanthomatous hypophysitis* causing cluster type headache permanenty requiring ddAVP (desmopressine) and testosterone supplementation without need for maintenance medication with hydrocortisone and levothyroxin. In periods of headaches the patient requires glucocorticoids supporting the possible autoimmune origin of the disease.

We report a **23-year-old** man with XH who presented with cluster type headache, diabetes insipidus and pituitary MRI-proven intrasellar mass.
Since 2009 our patient suffered from reccurent **headache**. CT scan, ophthalmological, neurological investigations revealed no obvious cause of the symptoms
In April 2011 polyuria-polydipsia occured, the endrocrine investigations revealed **diabetes insipidus**. The anterior pituitary hormone levels:TSH:1.3 mIU/l, FSH:2.4 IU/l, LH:3.7 IU/l, PRL:197 mIU/l, ACTH:7.78 pm/l, cortisol 08 h:444 nm/l despite low testosterone level (7.36nm/l). After initialization of ddAVP treatment, diuresis returned to normal.
The pituitary MRI scan revealed a 14x10x17 mm inhomogenous lesion with the disappearance of the hyperintense signal of the neurohypophysis.
In July 2011 **transsphenoidal surgery** was performed. The histology proved **xanthomatous hypophysitis**.
Without having any perioperative complication we could stop the glucocorticoid (GC) treatment.The headache resolved but the diabetes insipidus persisted.
After the surgery the anterior pituitary function was normal: serum cortisol 08 h: 404-445 nm/l, ACTH:6.49 pm/l, FSH:3.1 mIU/l, LH:4.2 mIU/l, TSH:1.61 mIU/l.
2 months later severe cluster type headache occured. The endocrine investigations revealed **hypadrenia**, **hypothyroidism** and peripheral **hypogonadism**:
serum cortisol 08 h.: 96 nm/l, TSH:1,32 mIU/l, ft4:10.5 pm/l ,testosterone:3.44 nm/l, FSH:3.3 mIU/l, LH:2.8 mIU/l, ACTH:3.38pm/l.
LHRH test results: FSH: 0.min.:2,8, 30 min.:4,7, 60 min.:5,1 mIU/l, LH: 0.min:2,9, 30 min.:13,5, 60 min.:13,8 mIU/l.
The postoperative pituitary MRI scan proved the persistent presence of the inhomogenous mass.
After initialization of glucocorticoid replacement the headache disappeared. With levothyroxin, testosterone supplementation and gradually lowered dosage of GC and all symptomps disappeared but the diabetes insipidus. Despite of low IGF 1 (92 ng/ml,age matched reference rate:117-329 ng/ml) and hGH (0,08 ng/ml) levels GH therapy was not introduced. **Autoimmune screen -** ANA, antiCL,antib2GP, anti transglutaminase, anti TPO, anti parietal cell antibody-was negative.
Regularly performed sella MRI scans showed no change in tumor size and appearance after the the surgery and after the introduction of hormone replacement therapy.
The patient requires GC supplementation only in case of recurrent cluster type headache, but no persistent replacement is needed.
In January 2013 we had the possibility to measure the patients's serum IgG4 level, which was markedly increased (***serum IgG4 concentration: 815 mg/l)*** suggesting **the xanthomatous hypophysitis to be IgG4- related**

Conclusion:

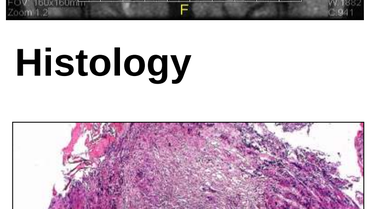
In our case typical cluster type headache, diabetes insipidus and severe, persistent hypogonadism were the main symptoms of the xanthomatous hypophysitis (XH)

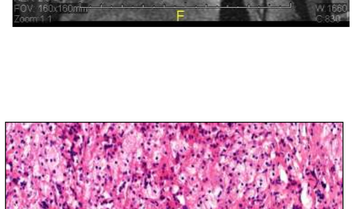
The patient requires GC supplementation only in case of cluster type headache, but permanent testosterone replacement

The patient's elevated serum IgG4 concentration is suggesting the XH to be IgG4 related disease

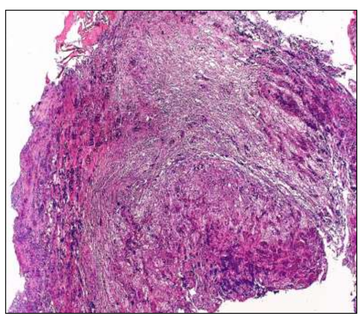
The cause of the XH is still unknown, but as our data suggests it could be IgG4 related disease

Sella MRI

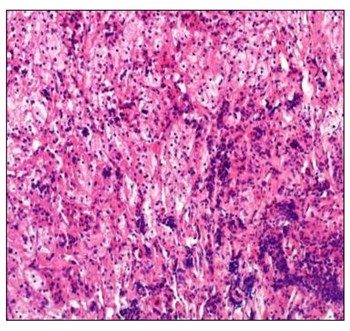




Histology

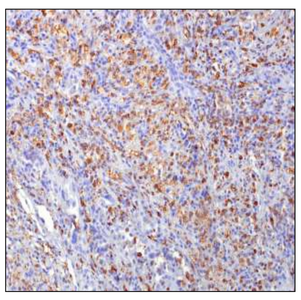


HE,5x

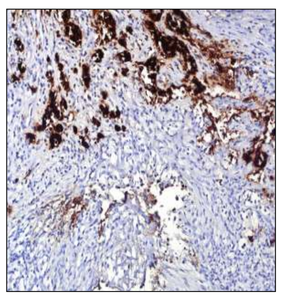


HE,20x

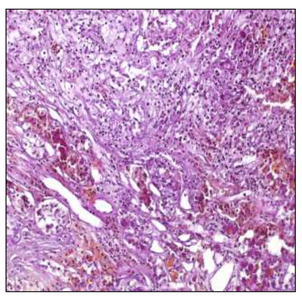
Immunohistochemistry



CD68, 20x

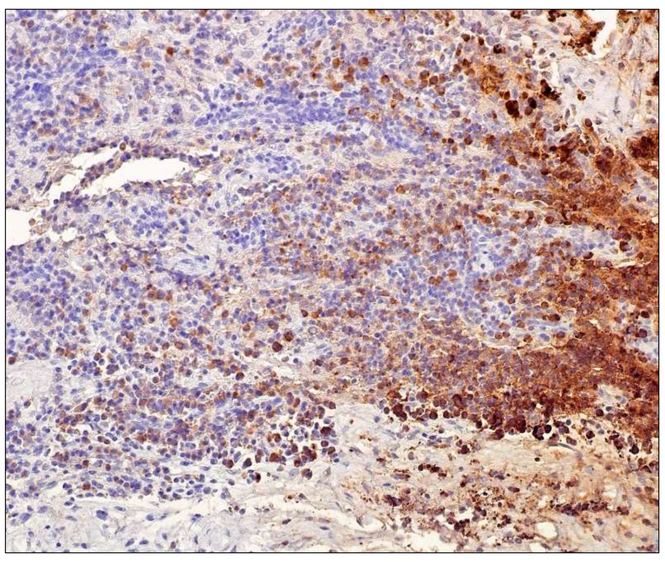


GH, 20x



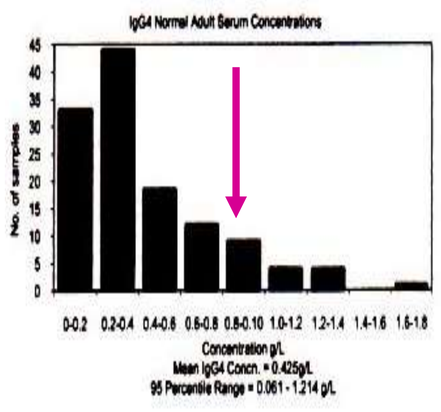
PAS, 20x

	Preoperative	Postoperative 1.	Postoperative 2. (headache)	Postop. 3. (1year)	Postop. 4. (2year)
TSH (mIU/L)	1.3	1.61	1.32	1.4	2.15
fT4 (pM/L)	14.7	14.7	10.5	14.9	14.9
ACTH (pg/mL)	7.78	6.49	3.38	6.36	3.41
Cortisol (nM/L)	444	445	96	445	562
FSH (IU/L)	2.4	3.1	3.3	1.4	2.1
LH (IU/L)	3.7	4.2	2.8	1.2	1.6
PRL (mIU/L)	197	88	202	151	129
Testosterone (nM/L)	7.36	3.87	3.44	2.05	12.24 (onT)
SHBG (um/L)	19,4	16.5	15.7	13.1	10.1
hGH (ng/mL)	0.13	0.07	0.05	0.15	4.2
IGF1 (ng/mL)	<25	<25	163	137	75.5



IgG4 immunostaining,20x

Patient's serum IgG4= 815 mg/l (0,815 g/l)



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