The Thickening of the Pituitary Stalk: about 25 Cases

Ali El Mahdi Haddam, Meskine Djamila, Farida Chentli, Soumeya Nora Fedala

1. Department of endocrinology bologhine hospital, Algeria
2. Department of endocrinology bab el oued hospital, Algeria

Corresponding author email: fedala16@gmail.com

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Summary

This is a retrospective study of 25 cases of thickening of pituitary stalk. All patients benefited from a clinical, biological (hormonal and non hormonal) and radiological exploration seeking etiology and scalability of their pathologies.

Results

A female predominance was found. The average is 42 years (4.5 to 60). Three children were observed in this series.

Methods

The most frequent reason for consultation was polyuria polydipsia syndrome (90%); It was associated with an amenorrhea galactorrhea syndrome in a little over two-thirds (63.2%) and epilepsy in one case.

Questioning revealed the former existence of extra-pituitary sarcoïdosis in five cases.

The hormonal exploration showed a post pituitary insufficiency in all cases; A central diabetes insipidus (CDI) is observed in three pediatric cases.

It was associated with hypopituitarism in 87.5% (n: 21/24) of cases: anterior pituitary Insufficiency (n: 10/24) thyreo-gonadotrope insufficiency (n: 11/24). Moderate hyperprolactinemia was observed in two thirds of cases (68.4%). CDI is observed in three pediatric cases.

The etiological exploration of the thickening of the pituitary stalk allowed to retain the following diagnoses: sarcoidosis 66.6% (n: 16/24)-lymphocytic hypophysitis 12.5% (n: 3/24) metastase cancer 12.5% (n: 3/24): vesicular thyroid carcinoma n: 1, breast cancer n: 2; cyst ratke 4.16% (n: 1/24) « idiopathic » 8.3% (n: 2/24). The cyst of ratkes and idiopathic forms were found in children. The evolution was marked in a child by the appearance of an autoimmune thyroiditis suggest the possible diagnosis of an autoimmune origin to the thickening of the pituitary stalk. No cause has been identified in the other case after a decline of ten years.

Keywords

Thickening; Pituitary stalk; Inflammatory; Tumor; MRI; Central diabetes insipidus; Anterior pituitary insufficiency

Introduction

We report in this regard the clinical, etiological and evolution of 25 cases followed in our service.

Material and Methods

This is a study of twenty-five patients (20 women and 5 men) with a thickening of the pituitary stalk followed in our department between 2000 and 2014.

The magnetic resonance imaging was shown for the etiological exploration of CDI with the exception of one case for which it was carried out to explore amenorrhea galactorrhea syndrome.

All patients received further questioning and a complete physical examination specifying the
circumstances of diagnosis, pathological personal or family history and looking endocrine and systemic abnormalities.

For each of our patients, we performed an anterior and posterior pituitary exploration. The pituitary growth hormone adrenocorticotropic function was evaluated by the insulin tolerance test (0.1u/kg/day): Dosage of cortisol base and after stimulation. The answer is considered normal when cortisol exceeded 500nmol/l.

Dosage of growth hormone (GH) before and after stimulation with insulin tolerance test (0.1 u/kg/day). Somatotropic function was considered normal when the peak GH over 20mu/l for children and 9mu/l for adults.

A static evaluation was performed for the other anterior pituitary functions:

- Dosages of free thyroxine (FT4) and pituitary thyroid stimulating hormone (TSH)
- Dosages of pituitary gonadotropins FSH and LH and peripheral hormonemia: estradiol (E2) in women and testosterone (T) in men for gonadotropic function.

In the presence of polyuria syndrome (diuresis>30 ml/kg/day), urinary density (DU) was performed (in the absence of osmometer for the calculation of plasma and urine osmolality). Hypotonic polyuria was evidenced by a lower DU<1 005.

The DU was then compared to the DU obtained after intranasal administration of an analog of the anti-diuretic hormone (DDAVP). CID was affirmed by the reduction of urine volume and the elevation of DU after DDAVP.

For each patient, we performed an assessment by including additional paraclinical exploration:

- The measurement of erythrocyte sedimentation rate and reactive ceruleoplasmin looking for an inflammatory condition.
- A specific assessment looking granulomatosis: intradermal to tuberculin and gastric intubation to search for the bacillus germ in favor of tuberculosis, calcium and phosphate levels and dosing converting enzyme whose elevation favored sarcoidosis.
- Determination of tumor markers and bHCG fetoproteins α in blood and cerebrospinal fluid in search of a germinoma.
- Autoimmunity assessment: measurement of non-specific and specific antibody organ for an autoimmune etiology (Nuclear antibodies, native DNA antibodies, endomysium antibodies, transglutaminase antibodies
- Réticule antibodies, TRAK, thyroperoxidase antibodies
- Thyroglobuline antibodies, GAD 65 antibodies, IA2 antibodies

Radiologically, magnetic resonance imaging of the hypothalamic pituitary region was performed on thin slices of 03 mm thickness, sagittal and coronal T1-weighted and T2 with and without gadolinium.

Pituitary stalk appears vertically or obliquely downward and forward, stretched between the top and middle pole of the pituitary and infundibulum of the hypothalamus. It is marked on the sagittal or coronal fine. The normal signal of the stalk is the same as that of the anterior pituitary before or after contrast agent injection. The pituitary stalk is considered thickened if it exceeds 2.5 mm especially in its middle or lower part (Tien, 1992).

Chest radiographs were performed in all patients completed by a CT when sarcoidosis suspicion; Skeletal radiographs completed the radiological exploration in children.

After exploration, patients have been substituted for the various deficiencies: DDAVP spray 5-10 ug/day for CDI, hydrocortisone per os 15-20 mg/day for the adrenocorticotropic insufficiency and levothyroxine 50-100 ug/day for thyrotropin insufficiency.

Patients with sarcoidosis or lymphocytic hypophysitis were put under treatment with anti-inflammatory corticosteroid dose of 1.5 mg/kg/day.

Patients were reevaluated clinically, biological and radiological every 06 months the first two years and then annually.

Results

A female predominance was seen with a sex ratio of six women for one man. The average age at diagnosis is 42 years (4.5 to 60). Three children were observed in this series. They were aged four and a half, six and eight years old.
The most frequent reason for consultation is polyuria polydipsia syndrome (90%); this is associated with an amenorrhea galactorrhea syndrome in a little over two-thirds (63.2%) and epilepsy in one case.

Questioning revealed the former existence of extra-pituitary sarcoidosis in five cases.

The hormonal exploration showed a post pituitary insufficiency in all cases; DIC was associated with hypopituitarism in 87.5% of cases: anterior pituitary Insufficiency (10/24) thryeo-gonadotrope (11/24); Moderate hyperprolactinemia was observed in two thirds of cases. A DCI is observed in three pediatric cases.

The etiological exploration of the thickening of the pituitary stalk allowed to retain the following diagnoses:

- Sarcoidosis (66.6%)
- Lymphocytic hypophysitis (12.5%)
- Metastase cancer (12.5%; vesicular thyroid carcinoma n: 1, breast cancer n: 2)
- Cyst of ratkes (4,1%)
- Idiopathic (8,3%)

The cyst of ratkes and idiopathic forms were found in children.

Corticosteroid therapy in patients with lymphocytic hypophysitis and sarcoidosis allowed:

- Normalization of inflammatory balance sheet, calcium and phosphate levels and angiotensin-converting enzyme in all cases where they were high (50%).

The disruption of the inflammatory balance sheet observed in all cases of sarcoidosis and lymphocytic hypophysitis has normalized after steroid therapy.

It is the same for the elevation of converting enzyme and serum calcium observed in half of the cases of sarcoidosis.

It was observed a normalization of hyperprolactinemia, gonadal function and GH deficiency in all cases. Diabetes insipidus and the other pituitary deficits persisted.

Figure 1 Patient has a central diabetes insipidus related to an autoimmune hypophysitis

Figure 2 A Saggitale section of Pituitary Metastasis in MRI B: Coronal section of Pituitary metastasis in MRI

- Radiographically, a complete disappearance of the lesions in the pituitary stalk was noted in the majority of cases (85.7%). In the other patients (14,3%) a partial reduction was observed.

Complete disappearance in the majority of cases versus partial reduction in 85.7% (incongruence).

The evolution was marked in a child by the appearance of an autoimmune thyroiditis suggest the possible diagnosis of an autoimmune origin to the thickening of the pituitary stalk.

- No cause has been identified in the other case after a decline of ten years.

**Discussion**

Diseases of the pituitary stalk could be described through advances in CT, but most of MRI. They require appropriate imaging technique and are recognized for superior thickening 25-30 mm
especially in its middle or bottom. Axial, sagittal and frontal sections allow to visualize the pituitary stalk that in the normal state has a diameter of 1 to 1.5 mm (Tien, 1992). The thickened pituitary stalk is very often revealed to diabetes insipidus opportunity. Other endocrine and neuro-ophtalmic manifestations can be associated to it. Frequently, the installation of diabetes insipidus is brutal and it is usually permanent (HIGUCHI, 1993; HONEGGER, 1997). It was observed in our patients.

Its Importance varies from one subject to another. It can be moderate or severe. It can be linked to a arginine vasopressin deficiency Vasospressine, loss of neurosecretory neurons or dysfunction of osmoreceptors. A hypopituitarism is possible and focuses on gonadal function, thyroid stimulating but also somatotropic function. Indeed, the hypopituitarism more or less dissociated may be up panhypopituitarism (Scaranini, 1989; Vasile, 1997). Hyperprolactinemia can be observed. It is related to an inhibition of the prolactin secretion by inhibiting the hypothalamic pituitary axis. It usually remains below 100ng/ml (Ghafoori, 2015). Others hypothalamic disturbances can be observed other hypothalamic can be observed as hypersomnia, thermoregulation disorders and polyphagia.

Hypothalamic manifestations may be encountered type of insomnia, drowsiness and thermoregulation disorders (unclear, unrelated).

With the pituitary insufficiency, tumor symptoms can be observed that can evoke a neurosurgical emergency. Patients may suffer from headaches, nausea, blurred vision and oculomotor impairment that have to perform quickly a hypothalamic magnetic resonance imaging (Di lorgi et al., 2014).

The causes of thickening pituitary stalk are multiple. Tumor lesions should be considered from the outset particularly among children and adolescents because they determine the prognosis and treatment. In adults, inflammatory causes or granulomatosis are the most common. In fact, the hypothalamic-pituitary inflammatory conditions are rare and represent 0.38% to 1% of the pituitary lesions operated (Can et al., 1998).

They reach both sexes without predilection with an average age of 19-58 years. Granulomatous lesions are secondary to such a specific lesion sarcoidosis, histiocytosis Langherans or tuberculosis. Idiopathic cause remains a diagnosis of exclusion when other aetiologies are eliminated (Tazi, 2000).

Disorders of the central nervous system are rare (5% of cases) during sarcoidosis (unclear). But when it is reached, the hypothalamus and pituitary are often affected. In over 95% of cases of "neurosarcoidosis" other organs (lungs, lymph nodes) are also affected. The granulomatous hypophysitis mainly affects the anterior lobe but can extend to the posterior pituitary, the pituitary stalk or even the hypothalamic region (Vasile, 1997).

The lymphocytic hypophysitis is an autoimmune disorder characterized by anterior infiltration pituitary cells by lymphocytic infiltration. It is very characteristic as it occurs in the majority of cases in late pregnancy or postpartum. However, it has also been reported in pre-menopausal and in male patients (Bet, 1997; Beressi, 1999) Clinical signs are rapidly progressive and dominated by headache associated with partial ante-pituitary insufficiency predominant on the HPA axis and gonadotropin. A total hypopituitarism can be objective. Diabetes insipidus is rarely reported (Rohmer, 1997). There are no distinctive radiological signs between lymphocytic and granulomatous hypophysitis. For some authors, raising the sellar diaphragm is evocative of lymphocytic origin (Jan and Destrieux, 2000; Khare, 2015).

In the presence of neurosarcoïdosis, it is important to initiate rapidly corticosteroids associated with hormone replacement therapy in order to preserve the functional prognosis and sometimes vital of the patient. Corticosteroids may be effective. Although they do not usually allow recovery of pituitary function, they can reverse the damage and decrease the risk of compression of neighboring structures (Dubas, 2001).

Langerhans cell histiocytosis represents 60% of large stems. It may be the first manifestation of the patient whose diagnosis may sometimes be worn for several years after the revelation of the CDI. In half of cases, there is a hypopituitarism. Bone manifestations may go unnoticed or may occur more than 20 years after the revelation of diabetes insipidus (Marchand, 2011).

These chronic conditions occur in a context of multisystem disease. Histiocytosis is sometimes revealed in a neurohypophysis location responsible for DI in 50% of cases with MRI thickening of the
pituitary stalk. Lung damage is seen in 60% of cases. Bone involvement is also possible (Fahrner, 2012; Howard, 2015).

The non-adenomatous tumors most often reported are the germinoma thechoristoma, and pituitary metastases (Reddy, 2015).

Germinomas is mainly seen in children and adolescents, as they are the first cause of DI. However, this etiology was not found in our series. Visual disturbances and slower speed of growth velocity can also be noticed. Sometimes the lesion is visible only several months after the onset of DI, making diagnosis difficult. Brain MRI, tumor markers and ophthalmic examination should be repeated every 3-6 months during the first 3 years of the onset of diabetes insipidus (Reddy, 2015). So the absence of etiology in our patients, requires us to regularly monitor.

Thickening of the pituitary stalk, especially if there is an increase in the intrasellar content and/or progressive pituitary insufficiency must practice a neurosurgical biopsy.

In germinoma, the tumor begins with a thickening of base stalk to extend up to the stem and the bottom to the pituitary. It joins in the absence of high signal intensity on T1 of the posterior pituitary. Looking for another location of the midline or pineal particular a brain or spinal cord dissemination is the rule. The increase in the blood of fetal proteins and hCG is highly evocative (Loto, 2014; Fukuoka, 2015)

Pituitary metastases are a rare cause of pituitary lesion. In asymptomatic form, majority of them are found at several known systemic cancer with metastatic sites (case of our patients). More rarely, they may be indicative of the cancer disease. Diabetes insipidus is the most frequent revealing symptom (70% of cases VS 100% in our study) due to the frequent posterior pituitary location of the tumor, the invasion of the anterior pituitary being by continuity (Fujimori et al., 2014; Ismail et al., 2014)

This distinction is explained by differences in blood supply between the anterior and posterior pituitary. The anterior pituitary gland receives its blood supply from a capillary bed after the Rathke pouch that would be a natural filter metastatic hematogenous spread. While the post pituitary has a direct systemic arterial vasculature. 51% of cases of pituitary metastases are located in the posterior pituitary. The adenohypophysis failure is mainly due to hypothalamic damage and frequently associated with the compression of the pituitary stalk which prevents the passage of hypothalamic hypophysiotropic hormones (He et al., 2015).

Other even rarer etiologies have been reported as choristoma of the posterior pituitary.

Tuberculomas isolated pituitary and Syphilis (Bachelot, 1996; Spinner, 2013; Pruthi, 2014).

In all cases a careful analysis of clinical, biological and radiological controls should be realized in order to find an etiologic diagnosis.

In the absence of known injury, regular monitoring shall be indicated in search of elements moving towards the origin of the achievement of the pituitary stalk.

Conclusion
The thickening of the pituitary stalk is secondary to several causes that need to be known and sought systematically. Endocrine manifestations of thickening of the pituitary stalk are variable. They are dominated by the DIC and hyperprolactinemia. When no etiology is found, regular clinical, biological and radiological controls are required.

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