Medical Sciences 2020 Vol. 8 (15), p. 156-163

e-ISSN: 2345-0592
Online issue
Indexed in *Index Copernicus*

Medical Sciences

Official website:
www.medicsciences.com

Diagnostic pitfalls of Empty Sella Syndrome: a case report

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Abstract

Empty sella is usually an accidental finding in visual brain examinations without clinical presentation. However, some of them diagnosed with empty sella syndrome experience a variety of symptoms. One of many concerning symptoms are headaches and visual disturbance which are caused by increased intracranial pressure. In rare cases increased intracranial pressure can result in critical conditions as in liquorrhea. In empty sella syndrome neuroendocrine system can be affected due to compression on the pituitary gland. Impairment of the neuroendocrine axis results in hormonal imbalance. Diagnosing empty sella syndrome is challenging for physicians. Due to the wide range of symptoms, patients are often examined by several specialists who only focus on the clinical manifestations of their field of expertise and an accurate diagnosis is made after years. In absence of clear diagnostic and treatment algorithms, patients with empty sella syndrome face many problems related to regular disease monitoring. There are no confirmed recommendations which specialist has to manage patients with empty sella syndrome. Currently, these patients are supervised by a multidisciplinary team consisting a neurologists, ophthalmologists, and endocrinologists. In this article, we report a case of empty sella syndrome with multiple diagnostic challenges.

Keywords: empty sella syndrome, empty sella, intracranial hypertension, hypophyseal axis.

Introduction

Empty sella (ES) most often is an incidental finding in brain imaging. Commonly it is asymptomatic, but in rare cases ES appears with serious endocrine, nervous system and visual symptoms and therefore is termed as empty sella syndrome (ESS). We report a case of ESS in a young woman with enigmatic medical history including multiple co-exiting diseases.

Case report

In 2011, 21-year-old patient presented with sudden onset anisocoria without any visual impairment or other leading symptoms. On fundoscopic examination bilateral edema of the optical nerve disc (OND) was observed. Two years later, patient complained about recurring frontal one-sided headaches. These symptoms were considered as migraine without aura. Magnetic resonance tomography (MRT) revealed haimoiritis and ethmoiditis, suprasellar cistern prolapse into sella turcica and normal sized hypophysis. In order to exclude sinusitis computerized tomography (CT) was performed. It showed a sphenoidal sinus cyst which could been the reason for frontal one-sided headaches. Therefore, transsphenoidal cystectomy was performed and headaches relieved until further notice. Around the same time patient developed endocrine symptoms. The patient noted rapid weight gain (about 14 – 15 kilograms per year) even though eating habits and physical activity have not changed.

Thyroid gland dysfunction was suspected but only euthyroid diffuse goiter was revealed. In addition, laboratory tests detected slight elevated hormone levels of prolactin (102 mIU/l) and cortisol (morning 1136 nmol/l, evening 1118 nmol/l) while adrenocorticotropic hormone (ACTH) was normal (morning 5,8 µmol/l). Patient was hospitalized for further examination with suspicion of Cushing‘s syndrome. Due to nearly normal cortisol levels (morning 762,51 nmol/l, evening 240,27 nmol/l),

normal ACTH (6,4 μmol/l) and only slight pathological Dexamethasone suppression test (54,8 nmol/l), diagnosis has not been confirmed. The patient was advised to discontinue oral contraceptives and repeat blood analysis. Slightly elevated cortisol (cortisol morning 1007 nmol/l and evening 642 nmol/l) and normal ACTH (8,8 μmol/l) were received.

In 2017 repetitive transient vision dysfunction occurred and headache returned. The patient was hospitalized for detailed examination. MRI revealed enlargement of sella turica partially filled with cerebrospinal fluid (CSF) and compressing hypophysis the fundus of sella turcica. During the year, complains of visual dysfunction became worse accompanied by impediment of vision field, blurred vision and amaurosis fugax alternately of both eyes at night time. Neuroophthalmological examination revealed bilateral edema of OND. Based on complains of headaches, visual impairment, both sided papilledema and MRI findings lumbar puncture was considered. Elevated intracranial pressure (40 mmH_20) was measured. In absence of inflammatory or other pathological signs in CSF and due to triad of ophthalmological, neurological and endocrinological symptoms, in MRI detected ES, condition assessed as ESS. Therefore, benign intracranial hypertension was treated with acetazolamide 500 mg per day, unfortunately treatment was not effective. Patient repeatedly presented with progressive vision dysfunction. Treatment with intravenous mannitol was induced. Patient refused further examination and was released with recommended outpatient treatment including acetazolamide which later was discontinued in consequence of renal insufficiency.

Endocrinological symptoms progressed further by the time. In 2018, patient complained of irresistible weight gaining, dry skin, dandruff and falling hair, irregular menstrual cycle and constantly elevated blood pressure. The patient was examined for imbalance of hypophyseal axis hormones. Laboratory tests detected reduced levels of somatotropin (0,18 mU/l) and insulin-like growth factor (10,9 nmol/l) and use of growth hormone analogues was recommended. Although cortisol levels were normal (morning 409 nmol/l, cortisol in 24h urine 336,3 nmol/l), clinical appearance of Cushing syndrome remains. Based on elevated aldosterone-to-renin ratio (ARR: 159) aldosterone suppression test was considered and ARR of 61 was evaluated as marginal. Since partial adrenal gland failure cannot be ruled out, in purpose to avoid severe hypercortisolism, hydrocortisone was prescribed to use before stressful situations. In addition, because of ovarian cyst and persisting anovulation in medical history, polycystic ovarian syndrome was diagnosed.

According to anamnesis, in 2006, patient was involved in a car accident, after which she suffered from bone fractures and contusions including head. At this time Neurosurgical pathology was excluded. After trauma patient had no complains until 2013. Further, in 2011, patient suffered from acute kidney failure due to chronic pyelonephritis and interstitial nephritis. Besides that, partial adrenal failure without known cause was diagnosed.

To sum up, over a few years gradually progressing triad of neurological, ophthalmological and endocrinological clinical symptoms and MRI finding of ES were considered to be ESS. The cause for this remains unclear. It is to be questioned whether endocrinological symptoms emerged due to elevated intracranial pressure or vice versa – endocrinological or other conditions, in this case related to head trauma or sinus operation, could have caused intracranial hypertension. Congenital disorders were not suspected.

Literature review

Empty sella syndrome (ESS) defines with an unclear pathogenesis until nowadays. It is known that incomplete formation of the sellar diaphragm, upper-sella and pituitary factors could be determining formation of empty sella (ES) and an ESS in a following. Upper sella factors are persistent or intermittent intracranial hypertension, CSF pulsatility, obesity and systematic arterial hyperstension, and pituitary factors are compensatory pituitary hypertrophy to primary hormonal deficit, pregnancy, lactation, menopause, hypophysitis [1]. According to pathogenesis ES is classified into primary (PES) and secondary empty sella (SES).

Etiopathogenesis

About 22 – 77% of PES cases present with insufficient sellar diaphragm [1]. The main cause is an anatomic defect of the diaphragma sellae that might be congenital. However, no clear genetic association is known [2]. PES occurs when increased intracranial pressure causes herniation of subarachnoid space which leads to compression of the normal pituitary gland. As a consequence, cerebrospinal fluid (CSF) accumulates in the sella turcica [3] resulting in enlargement of the sella turcica and pituitary gland flattening [4]. SES appears as a consequence of pituitary gland damage or injury [5]. Most commonly SES is the result of the pituitary gland atrophy previously due to pituitary adenoma, Sheehan's syndrome, craniocerebral trauma, after radiotherapy or diseases resulting in glandular infection or infarction. Further, this leads to CSF accumulation in the sella turcica [3]. Pulsation of CSF to the pituitary gland or pituitary stalk provoke glandular dysfunctions [2, 6].

Clinical features

ESS can lead to endocrinological and neuro-ophthalmological symptoms. 40% of patients may experience headaches and occasionally neurological dysfunction such as visual field disturbance, mostly bitemporal hemianopsia or hemifield slide phenomena, as a consequence of elevated intracranial pressure [2, 7, 8, 9]. In our presented case visual impairment occurred primarily and progressed constantly. Headache as well presented in a very beginning but its differential diagnosis was more complicated due to other conditions. Present intracranial hypertension helped to confirm ESS diagnosis. According to literature, liquorrhea can occur due to pulsative movements of CSF that may erode into sphenoid sinus [1, 10]. All endocrinological symptoms are associated with hypothalamic–pituitary–endocrine axis suppression on level of the pituitary gland. Therefore, in ESS pituitary gland secretion can be insufficient. About 20% of patients present with hormone disorders which can be the first and only sign of ESS. They are mostly revealed by menstrual irregularities, galactorrhea, hirsutism and sterility [11]. Ghatnatti et al, 2012, identified hyperprolactinemia as most common endocrine abnormality [12]. There is no exception in this case. Endocrinological abnormalities were noticed through infertility and symptoms of partial adrenal gland failure. Laboratory test could not confirm the diagnosis. Furthermore, PES is often associated with obesity and high blood pressure. Even 50% of females are overweight or obese [6, 13]. These clinical features have great importance in the presented case. Some rare cases present psychiatric manifestations in ESS but relation between ESS and psychiatric symptoms is not determined yet and ES is usually only incidental finding [14, 15].

All this considered, ESS diagnosis is made based upon identification of characteristic symptoms, a detailed patient history, a thorough clinical evaluation and specialized imaging techniques. If ES is diagnosed even though there are no symptoms, it is usually a coincidental finding [16]. ES is confirmed through magnetic resonance (MR) or computerized tomography (CT) in patients with

contraindications to MR [1]. Radiological findings are distinct between partial ES (sella turcica is filled with CSF up to 50 %) and complete ES (filled with CSF more than 50 %) [3, 17]. Pituitary function should be checked as well in asymptomatic patients because in 52% incidental cases hypopituitarism associated with ESS is revealed by measuring hormone levels [2, 10, 18].

Treatment

Treatment should be arranged according to specific symptoms and their severity. Patients are usually treated multidisciplinary by a team including a neurologist, endocrinologist and ophthalmologist [1]. Intracranial hypertension and therefore following symptoms should be corrected in first stage of treatment. If overweight or obesity is considered as main cause of intracranial hypertension, weight loss is actively suggested for the patients as the most important part of treatment [19]. First choice of medication to reduce intracranial pressure are osmotic diuretics, such as acetozolamide or escin [1]. Invasive procedures such as placing a lumboperitoneal shunt can be effective if visual impairment is progressive and very severe as well when non-invasive treatment is not effective [16, 20].

Hormonal imbalance is commonly treated by endocrinologists adjusting precisely combined hormonal therapy. Any hormone deficiency should be replaced in a slow progression. Treatment begins with hydrocortisone, followed by levothyroxine. After successful substitution sexual hormones can be added. If hyperprolactinemia occurs, dopamine agonist drugs can improve symptoms [1, 21].

ESS is usually a benign condition and does not determine life expectancy. But prognosis and quality of life depends on hormone deficiency and hormonal treatment [4]. Patients with absent symptoms and incidental diagnosed ES, should be monitored for hormonal imbalance or visual impairment [21]. Although, sometimes patients can not specify their well-being and abnormal conditions seem to be fine as long as specialists ask particular questions and make detailed examination. While ESS occurs with many symptoms, it remains unclear which specialist should fully take care of these patients.

Conclusion

Empty sella is usually an incidental finding in brain visual examinations. Although, empty sella can occasionally present with clinical triad of neurological, ophthalmological and endocrinological symptoms that are considered as empty sella syndrome. Variety of symptoms make diagnosis confirmation challenging. The treatment as well require a multidisciplinary team. Unfortunately, diagnostic and treatment algorithms remain unclear.

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