doi: http://dx.doi.org/10.11606/issn.1679-9836.v100i4p413-416 Rev Med (São Paulo). 2021 July-Aug;100(4):413-6.

Late diagnosis of primary empty sella syndrome - a case report

Diagnóstico tardio de síndrome da sela túrcica vazia primária – um relato de caso

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Benincá PD, Marques GL, Sachetti LA, Soares LO. Late diagnosis of primary empty sella syndrome – a case report / *Diagnóstio tardio de síndrome da sela túrcica vazia primária – um relato de caso*. Rev Med (São Paulo). Rev Med (São Paulo). 2021 July-Aug;100(4):413-6.

ABSTRACT: Empty Sella syndrome can be asymptomatic and present itself only as a radiological finding, or be associated with different degrees of hypopituitarism and neurological symptoms. In most cases, it is an undiagnosed condition, which is recognized incidentally by imaging exams. This article highlights the importance of an accurate anamnesis and physical examination in order to diagnose less common syndromes through the report of a patient who had a late diagnosis of panhypotuitarism caused by primary empty sella syndrome (PES).

Keywords: pituitary gland, hypopituitarism, dwarfism, Empty Sella Syndrome.

RESUMO: A síndrome da Sela Túrcica Vazia pode ser assintomática e se apresentar apenas como um achado radiológico, ou estar associada a diferentes graus de hipopituitarismo e sintomas neurológicos. Na maioria dos casos é uma afecção não diagnosticada, sendo reconhecida de maneira incidental por exames de imagem. Este trabalho evidencia a importância de uma anamnese e exame físico apurados para diagnosticar síndromes menos comuns, através do relato de um paciente que teve o diagnóstico tardio de pan-hipotuitarismo ocasionado por sela vazia (SSV) primária.

Palavras chave: Hipófise; Hipopituitarismo; Nanismo; Síndrome da sela vazia.

INTRODUCTION

The Empty Sella syndrome, first described by Busch in 1951, is a clinical situation in which there is herniation of the arachnoid matter into the bone depression of the superior surface of the sphenoid bone, where the pituitary gland (hypophysis) is located.[1] Thus, this space is filled by cerebrospinal fluid (CSF), which compresses the pituitary against the floor of the sella turcica and leads to a radiological aspect of an empty space, resulting in different clinical presentations according to the degree of compression of the gland. [2,3]

The aim of this study is to report the case of a patient with a history of fatigue, asthenia and hyporexia and who had a late diagnosis of panhypotuitarism caused by PES. We intend to compare this case with literature available in aspects of clinic and epidemiology. Consequently, we expect to highlight the importance of an early diagnosis and management, which can avoid late manifestations of a rare syndrome.

CASE REPORT

A 54-year-old male patient was admitted to an emergency room complaining of fatigue, asthenia, hyporexia, nausea and abdominal pain, which started

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one week before the event. The symptoms were first treated as gastroenteritis, and an adrenal insufficiency was questioned at the time due to hyporexia, hypotension, asthenia and hyponatremia (Na of admission 122 meq/L). Hospitalization of the patient was chosen for a better evaluation of the hyponatremia.

During the hospitalization period, the diagnosis of panhypopituitarism was considered, and investigation was started. The previous history of the patient included thyroid endocrine disease with irregular use of levothyroxine. The patient also went through testosterone replacement therapy for 6 years due to hypogonadism, also with irregular use of the medication and without adequate follow-up of the condition. In addition, he had a history of infertility, having tried previous treatments without success. He denied any similar family history or previous cranial trauma. At the physical examination, he had short stature (Figure 1), gynecomastia and signs of hypogonadism, such as rarefaction of body hair and atrophic testicles. The basal cortisol of the patient at the time of the examination was of 1.12µg/dL, also leading to the diagnosis of secondary adrenal insufficiency.

Figure 1. Patient with short stature.

Subsequently, new blood tests were requested and presented the following results: sodium 117 mEq/L (reference range: 136-145 mEq/L), FSH 0.65 mUI/mL (reference range: 1.27-19.26 mUI/mL), LH less than 0.2 mUI/mL (reference range: 1.24-8.62 mUI/mL), TSH 0.02 mU/L (reference range: 0.3-4.2 mU/L), prolactin 6.3 ng/mL (reference range: 2.1-17.7 ng/mL) and ACTH 5,3 pg/mL (reference range 7-23 pg/mL).

Considering the results of the tests above, an MRI was requested and demonstrated a decrease in the space occupied by the pituitary gland. Also, the sella turcica showed an intense cerebrospinal fluid (CSF) signal (Figures 2 and 3). Therefore, the diagnosis of panhypopituitarism due to PES Syndrome was confirmed, with an association of symptomatic hyponatremia and a history of lack of adequate treatment.

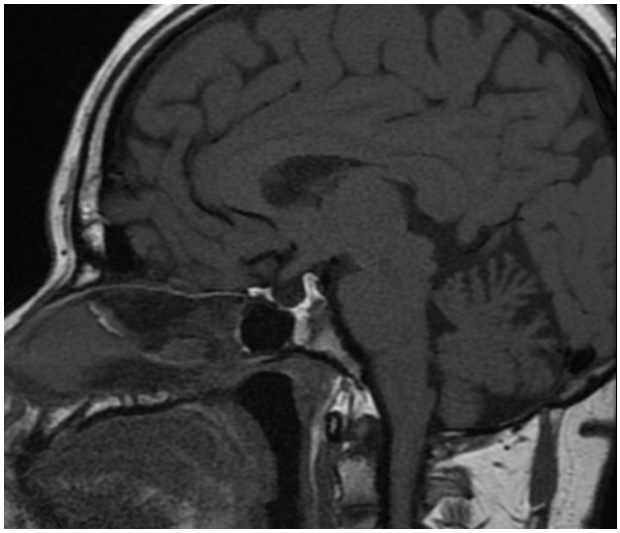

Figure 2. Sagittal Magnetic Resonance Imaging (MRI) of the patient's skull, showing the presence of CSF at the sella turcica.

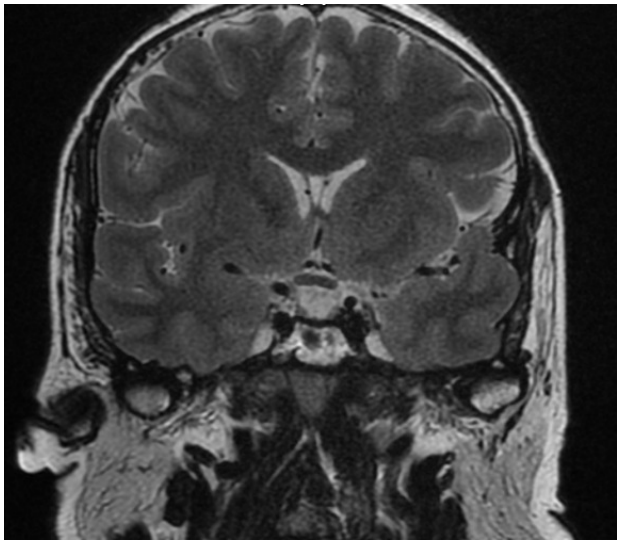

Figure 3. MRI of the skull of the patient in coronal plane, showing the presence of CSF at the site of the sella turcica.

During hospitalization, the patient needed high doses of intravenous hydrocortisone after the diagnosis of adrenal insufficiency was made, since he presented several episodes of headache and vomiting, even after the replacement of hypertonic saline solution due to hyponatremia. He was discharged with Prednisone (5mg twice a day, with a plan to gradually decrease the dose

of the medication), Levothyroxine (112mcg a day) and Testosterone Cypionate (one intramuscular ampoule every 15 days). One month after the episode, the patient returned with the following laboratory tests: sodium 135 mEq/L (reference range: 136-145 mEq/L), T4 1.14 ng/dL (reference range: 0.7-1.8 ng/dL), T3 0.77 ng/dL (reference range: 2.5-4.0 ng/dL), FSH 0.42 mUI/mL (reference range: 1.27-19.26 mUI/mL) LH 0.25 mUI/mL (reference range: 1.24-8.62 mUI/mL), prolactin 7.2 ng/mL (reference range: 2.1-17.7 ng/mL), total testosterone 708.96 ng/dL (reference range: 300-1,000 ng/dL), basal cortisol 5.26, ACTH 6.5 pg/mL (reference range: 7-23 pg/mL). Hormone replacements and regular follow up appointments were maintained.

DISCUSSION

The Empty Sella syndrome can be classified as primary or secondary to other clinical conditions[4]. About 80% of the primary cases occur in obese, hypertensive and women[5] - as the pituitary gland doubles its volume during pregnancy[2], especially in case of multiple pregnancies[4]. Moreover, hypercapnia related to obesity (obesity hypoventilation syndrome – OHS) can chronically elevate cerebrospinal fluid pressure and induce herniation of the subarachnoid space[6,7]. Secondary causes, on the other hand, are broader and diverse, and their clinical presentation depends on the etiological factor[5]. It may be the result of surgical removal of pituitary adenomas, radiotherapy, or of medication use, as well as infectious, traumatic, autoimmune and vascular causes[2,4,8].

The clinical presentation of PES includes nonspecific headache, neurological symptoms, visual impairment, different degrees of hypopituitarism, and even intracranial hypertension; however, the syndrome may also occur in a scenario of total absence of symptoms[1]. Growth hormone (GH) deficiency is the most frequent alteration in patients with PES, occurring in 30 to 60% of cases[7]. Our patient had short stature, and his GH deficiency was quite prevalent. Other possible endocrine alterations are functional hyperprolactinemia (in 15% of cases) and varying degrees of hypopituitarism[9]; about 6% of patients also have hypogonadism. Isolated deficiencies of ACTH, TSH, ADH, and pan-hypopituitarism are uncommon. The reported patient had laboratory tests in accordance with the literature, presenting deficiency of different pituitary hormones.

When the patient went to the emergency room, his symptomatic hyponatremia was the initial concern of the medical team. It could be caused not only by adrenal insufficiency secondary to hypopituitarism, but also by other endocrine disorders; in this case, the hyponatremia with hyposmolarity is likely a consequence of hypothyroidism. A decrease in the cardiac output in these patients induces the release of ADH with consequent decrease in free water excretion, associated with intracellular sequestration of sodium[10], which could justify the hyponatremia in our patient, also enhanced by irregular use of levothyroxine.

Empty Sella Syndrome has a high prevalence in the female sex[6,11], which is not the case of our patient. Furthermore, a series of 142 cases showed 43 years old as an average age for diagnosis[11]. It is possible that the decrease of pituitary function developed gradually in our patient, which justifies his late diagnosis (at age 54).

MRI is the method of choice for diagnosis of PES[9]. The finding is often incidental, since most patients are asymptomatic and discover the disease when an imaging exam of the skull is requested for other clinical reasons[12]. Radiologically, the empty sella is defined as partial when less than 50% of the space is filled with CSF and the thickness of the pituitary gland is ≥ 3 mm, or defined as total when more than 50% of the sella is filled with CSF and the diameter of the gland is ≤ 2 mm[7,13]. The MRI of our patient showed an evident reduction of the pituitary gland, which was later confirmed by the radiology team as PES.

Most patients with PES are asymptomatic and do not require any specific treatment[8], but serial follow-up is strongly recommended[3]. In rare cases of visual impairment or cerebrospinal rhinorrhea, transesphenoid surgical treatment is necessary[4,8]. In Secondary Empty Sella syndrome, treatment should be directed to the underlying disease - if hypopituitarism is present, hormone replacement becomes necessary[14]. The reported patient received treatment according to the deficient hormones and was scheduled to regular follow-up appointments twice a year or annually according to his need of hormonal control.

CONCLUSION

In conclusion, we highlight the importance of a detailed clinical history and of the physical and laboratory findings to the diagnosis of uncommon syndromes. Our data emphasize that the development of hypopituitarism is generally not recognized in patients with Empty Sella syndrome and that the diagnosis of the condition may be delayed. In addition, a correct diagnosis is important for proper treatment of the pathologies associated with the syndrome and improvement of the overall well-being of the affected patients.

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Submeted: 2020, September 08
Accepted: 2021, May 20