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Pituitary apoplexy presenting as diabetic ketoacidosis: A great simulator?

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Abstract

Pituitary apoplexy is a life-threatening illness due to acute infarction of the pituitary gland. The most common symptoms associated with pituitary apoplexy are headache, nausea, vomiting, visual impairment, hypopituitarism, and altered mental status. Diabetic ketoacidosis is a common acute complication of diabetes mellitus and is itself associated with similar symptoms. We present the case of a 38 year old woman, who presented with altered mental status and biochemical alterations suggestive of diabetic ketoacidosis who was found to have a pituitary apoplexy. The low frequency of this condition coupled with an acute and usually dramatic presentation that includes non-specific symptoms makes it a diagnostic challenge. Pituitary apoplexy can simulate a wide range of neurological conditions.

CASE REPORT

INTRODUCTION

Pituitary apoplexy is a potentially life-threatening illness due to acute ischemic infarction or hemorrhage of the pituitary gland. The most common symptoms associated with pituitary apoplexy are headache, nausea, vomiting, visual impairment, hypopituitarism, and altered mental status (Briet *et al.* 2015; Chang *et al.* 2009). Secondary adrenal crises, however, represents the most critical complication to address and treat as it can cause a life-threatening refractory hypotension. In most of the cases pituitary apoplexy has been associated with a pituitary adenoma, but rarely has it been reported to occur in an otherwise normal pituitary gland. Its association with radiotherapy, diabetes mellitus, severe hypertension and pregnancy has also been described (Briet *et al.* 2015; Chang *et al.* 2009). The low frequency of this condition coupled with an acute and usually dramatic presentation that includes non-specific symptoms, makes it a diagnostic challenge even for an experienced physician.

On the other hand diabetic ketoacidosis (DKA) *per se* represents also, an acute, life-threatening complication of uncontrolled diabetes whose clini-

cal presentation, besides a prior diabetic syndrome, could be with non-specific signs and symptoms including neurological impairment that could easily mimic a primary neurological illness. The association between pituitary apoplexy and DKA has been seldom reported. Herein, we report the case of a patient with pituitary apoplexy and an associated moderate DKA.

CASE PRESENTATION

A 38-year-old woman arrived to the emergency room with an altered mental status. Besides obesity (body mass index=37.5) she was otherwise healthy. Three days before admission she complained solely of mild, sudden frontal headache. She denied having diplopia or any visual field impairment. The day before admission she progressively developed polydipsia, polyuria, nausea and vomiting, followed by alteration in her mental status. On examination she was lethargic and unresponsive. She had 7 points in the Glasgow Coma Scale. Her vital signs, including temperature, were normal. Pupillary reflexes and eye movements were normal and she had no positive meningeal signs. Osteotendinous reflexes were normal but she was found to have bilateral Babinski sign. Laboratory tests showed severe hyperglycemia (366 mg/dL), high anion gap metabolic acidosis (pH: 7.28, HCO_3: 14 mEq, Anion Gap: 17 mEq/L, Lactate: 2.1) and positive urine ketones, with no other abnormalities. Her hemoglobin A1c was 12.9%. A brain CT scan was reported to be normal. A diagnosis of a DKA with probable type 2 diabetes was diagnosed and immediately received intravenous fluids, potassium and IV insulin drip. After 24 hours, her metabolic abnormalities resolved and she regained normal mental status. However, she still complained of severe frontal headache; a lumbar puncture was performed and revealed multiple red blood cells, lymphocytic pleocytosis (180 cell count), high protein and normal glucose and lactate levels. Gram stain was negative as well as cultures, polymerase chain reaction for tuberculosis and herpesvirus type 1 and 2. We ordered a brain MRI with gadolinium that revealed sellar engorgement and hemorrhage both consistent with pituitary infarction (Figure 1). There was no clear evidence of an adenoma or an underlying alternative cause. Basal pituitary hormones were consistent with hypopituitarism; thyroid stimulating hormone 0.23 µUI/ml (normal range: 0.27–4.2); free thyroxine 0.64 ng% (0.93–1.7); free triiodothyronine 2.8 pmol/l (3.1–6.8); follicle stimulating hormone <0.100 mUI/ml (6.9–12.5); luteinizing hormone 0.18 mUI/ml (2.4–12.6); estradiol 9.73 pg/ml (postmenopausal <5–54.7); diluted prolactin 28.29 ng/ml (3.9–29.25) and a serum cortisol 0.64 µg/dl (2.3–11.9). The patient was diagnosed with a pituitary apoplexy. She denied any previous menstrual or other endocrine abnormalities. Her headache disappeared in the next 2 days. Due to the fact that with DKA treatment her neurological impairment improved completely and no focal neurological signs or symptoms (including

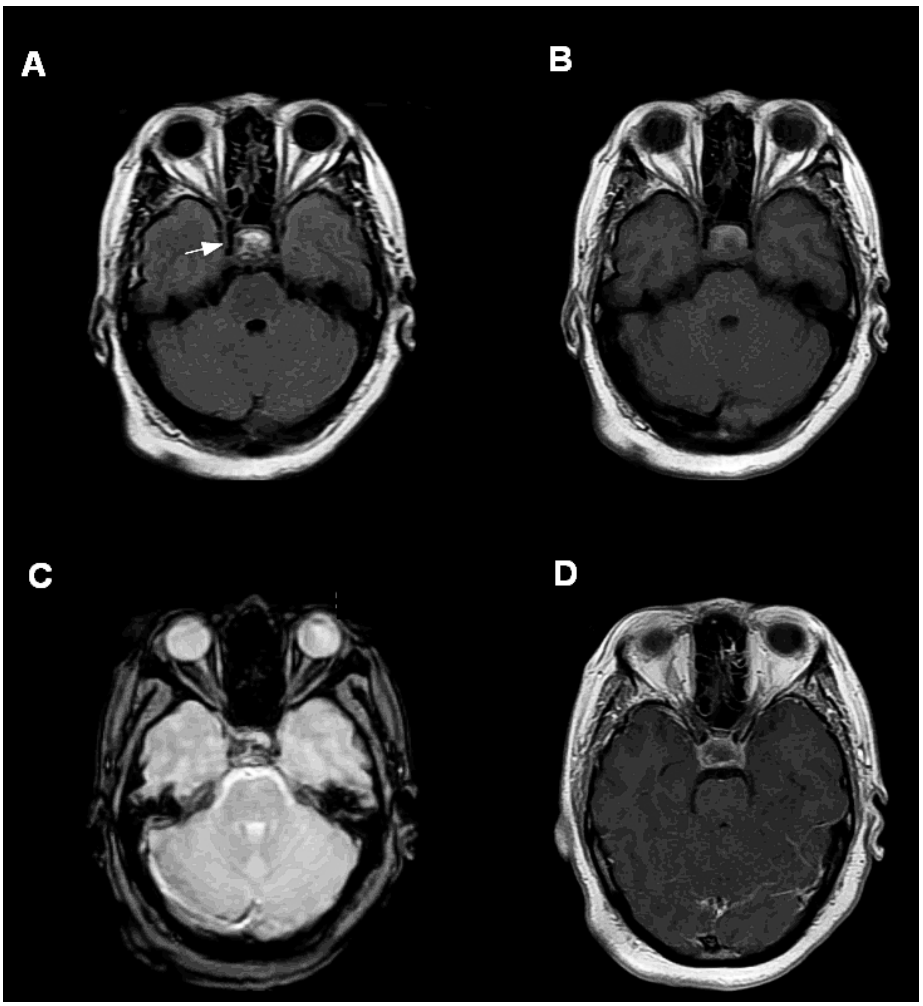

Fig. 1. MRI findings. T2-FLAIR sequence showed an enlarged sellar space, with a heterogeneous hyperintense lesion (A, arrow), suggestive of acute bleeding, edema and infarction. The lesion was hyperintense on T1 (B) and hypointense on Gradient Echo (C), indicative of hemorrhage. There was no nodular contrast enhancement (D).

visual abnormalities) were documented, she was managed medically with active surveillance and hormone replacement therapy that included hydrocortisone, levothyroxine and insulin. She was discharged 10 days after admission with no neurological sequelae with further plans to investigate the underlying cause of the pituitary apoplexy.

DISCUSSION

Its rarity and the absence of preceding symptoms make the diagnosis of pituitary apoplexy challenging. Sudden headache and an altered mental status raise the suspicion of intracranial hemorrhage, and subsequent imaging often reveals the diagnosis. As mentioned earlier pituitary apoplexy is often associated with adenomas as they can lead to apoplexy when their growth overcomes their arterial supply, when there is a compression of vascular structures, other intrinsic factors that can lead to vasospasm (such as local inflammation), or after starting drug therapy for symptomatic adenomas (e.g. dopaminergic agonists for prolactinomas) (Briet *et al.* 2015; Chang *et al.* 2009). It is worth to mention that non-functioning adenomas and prolactinomas have been associated in a greater extent to apoplexy than other types of pituitary tumors (Briet *et al.* 2015; Chang *et al.* 2009).

In non-adenoma pituitary apoplexy, other precipitating factors have been described. Diabetes has been classically considered to predispose to pituitary apoplexy because of degenerative changes in the gland's microvasculature, but there is no evidence from observational studies that diabetes is more common in patients with pituitary apoplexy (Biousse *et al.* 2001). However, it is known that DKA may precipitate an apoplectic episode (Biousse *et al.* 2001).

DKA is a life-threatening acute diabetes complication that can occur in patients with both type 1 and 2 diabetes mellitus. Diagnostic criteria for DKA includes the blood glucose >250 mg/dL, arterial pH of ≤7.30, bicarbonate level of ≤18 mEq/L, adjusted for albumin anion gap of >10–12, and usually along with a history of polyuria, polydipsia, weight loss, vomiting, dehydration, weakness, and altered mental status (Kitabachi *et al.* 2009), signs and symptoms that can easily be mistaken with those of a pituitary apoplexy. Headache is a non-specific symptom also commonly associated with hyperglycemic crises, and in the setting of DKA it constitutes a symptom that could be related to cerebral edema. Meningeal irritation, dura-mater compression, enlargement of sella turcica walls and involvement of the trigeminal nerve in the cavernous sinus can lead to headache in pituitary apoplexy, while an altered mental status could be due to sub-arachnoid hemorrhage, increased intracranial pressure, obstructive hydrocephalus or most commonly, adrenal insufficiency, all feared and life-threatening complications (Briet *et al.* 2015; Chang *et al.* 2009).

There are other reports of patients with pituitary apoplexy who presented with DKA. Weng *et al.* (2008) reported the case of a 28 year old woman who presented with altered mental status and hyperglycemia. She was diagnosed with DKA, but her hyperglycemia was ultimately attributed to hypercortisolism associated with an apoplexy of an adrenocorticotropic hormone (ACTH) producing pituitary adenoma (Cushing disease). She had no metabolic acidosis but had positive serum ketones. Later, Jiang *et al.* (2013) reported the case of a 49 year old male who presented with DKA and pituitary apoplexy. He had a growth hormone (GH) producing adenoma, and his uncontrolled diabetes was possibly due to acromegaly associated insulin resistance. In both these cases, their metabolic disturbances were possibly precipitated by secreting adenomas, as both GH and ACTH excess are known to be associated with uncontrolled diabetes mellitus and ketoacidosis.

In conclusion, our patient presented with signs, symptoms and biochemical characteristics typical of DKA, and her mental status alterations completely resolved after metabolic treatment. A diagnosis of pituitary apoplexy was only possible after a persistent headache that prompted additional testing. Pituitary apoplexy can present with headache, nausea, vomiting, weakness and visual abnormalities, all common and non-specific symptoms that can be associated with a wide variety of conditions, leading to misdiagnoses such as meningoencephalitis (Chibbaro *et al.* 2007), subarachnoid hemorrhage due to a ruptured aneurism (Chen *et al.* 1988), and DKA, among others. Pituitary apoplexy appears to act as another great simulator of central nervous system disease.

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