

# An Unusual Presentation of Apoplexy in Nelson's Syndrome: Case Report

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## Abstract

Nelson syndrome is a complication of bilateral adrenalectomy performed in some cases of Cushing's disease. In this paper, we report a case of a thirty-six-year-old man with a history of bilateral adrenalectomy for Cushing's disease five years previously, presented with sudden onset of severe headache, visual disorders, and cranial nerve palsies. The radiological investigation showed a pituitary macroadenoma measuring 33x29x47mm with apoplexy and extension to the left cavernous sinus which was removed through an endonasal endoscopic approach and the histological examination was concomitant with an ACTH-secreting pituitary adenoma. The present work aims to describe a rare presentation of pituitary apoplexy in Nelson's syndrome patient. This fact would be interesting and must be kept in neurosurgeons' minds during their daily activity to ameliorate the management of similar cases.

**Keywords:** Cushing disease, Nelson's syndrome, apoplexy, endonasal endoscopic approach.

## Introduction

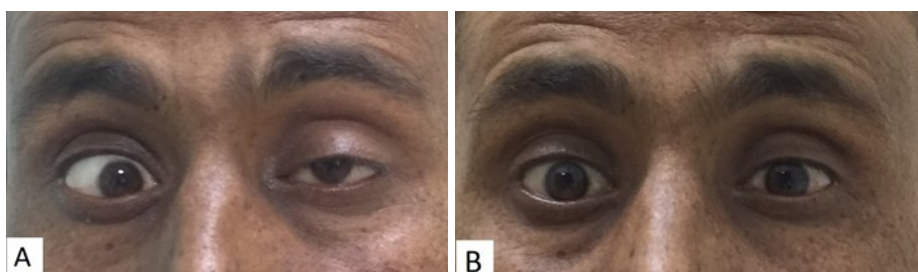
Nelson's syndrome is a relatively common complication of total bilateral adrenalectomy for refractory Cushing's disease (CD). It's observed in 8-47% of similar patients.<sup>1-4</sup> It was first described in 1958 by Don Nelson, its clinical presentation is made of skin hyperpigmentation and a high level of corticotrophic hormone (ACTH) with corticotrophin adenoma.<sup>5</sup> Pituitary apoplexy is a rare endocrine emergency resulting from hemorrhage or an infraction of a pituitary adenoma. The first clinical case was described by Brougham et al in 1950.<sup>6</sup> The incidence of apoplexy in pituitary adenomas is between 1% and 26% on the largest series.<sup>7,8</sup> Apoplexy remains even unusual in corticotrophin-producing adenomas. Usually, the reports of apoplexy are in corticotrophin microadenomas, however, descriptions of pituitary apoplexy in a corticotrophin macroadenoma are unusual,<sup>9</sup> and remain even extremely rare in Nelson's syndrome. In this report, we review a case of Nelson's syndrome with an unfamiliar presentation of acute spontaneous apoplexy.

## Case Report:

A 36-year-old man was referred to our department with complaints of sudden onset of severe headache, visual field defects, and eyelid ptosis on the left side. After a detailed study of his medical history, we found that he was diagnosed with Cushing syndrome 5 years previously. The syndrome was revealed after the investigation of significant obesity with typical biological data of negative low and high-dose dexamethasone tests and high levels of ACTH. At this stage of assessment, the radiological imaging did not reveal a pituitary adenoma. After a multidisciplinary discussion, His clinical status justified bilateral adrenalectomy combined with a hormonal substitution treatment. made of glucocorticoids. Unfortunately, the clinical follow-up was interrupted after that. The current physical examination revealed significant skin hyperpigmentation, and several palsies of cranial nerves; right sixth nerve palsy, and a left Cavernous sinus syndrome made of ophthalmoplegia, proptosis, conjunctival congestion, and trigeminal sensory loss [Figure 1A].

The visual acuity was at 1/10 on both eyes. Pituitary MRI revealed a heterogeneous pituitary lesion classed grade IV E in Hardy classification,<sup>10</sup> measuring 33x29x47 mm. The lesion was mainly hemorrhagic, marked by a hyperintensity on the T1 sequence. It had extensions into the suprasellar, both cavernous sinus more important to the left, and didn't show any enhancement in the T1+GADO sequence [Figure 2]. The endocrinological assessment showed that ACTH level was >2000 pg/ml and 08:00 hours cortisol was at 1490 nmol/L. we noticed also a gonadotropin deficiency.

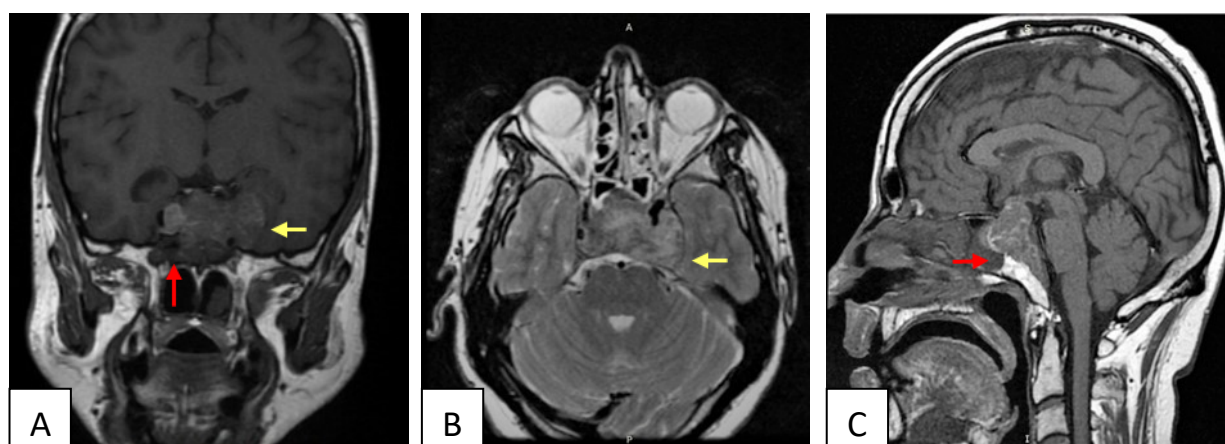
An urgent endoscopic endonasal surgery was performed on the patient to relieve hemorrhagic compression on the optic chiasm but also obtaining tumoral tissue for histological studies. During the sellar phase of surgery, the main component of the lesion was hemorrhagic confirming then "the apoplectic event". It was aspirated carefully with meticulous visualization of critical neurovascular structures. We had tissue samples for further histopathological analysis. The hemostasis was performed and goals of surgery have been achieved for the patient. The pathological and immunohistochemistry studies showed strong staining for ACTH; this was concomitant with a pituitary corticotrophin adenoma. Histological evidence of tumor infarction was also reported. The immediate postoperative course was uneventful with a full recovery of the left cavernous sinus syndrome and the right sixth nerve palsy [Figure 1B]. The further ophthalmological assessment found that the visual acuity was at 6/10 and 2/10 on right and left eyes respectively, however endocrinological evaluation showed a persistently high level of ACTH. A hormonal substitution treatment was carried out for the patient by the endocrinologists. Meanwhile, the patient received replacement therapy with glucocorticoid (hydrocortisone 30 mg/hr). Post-operative imaging performed one month later showed a subtotal removal of the tumor with a residual part in the left cavernous sinus [Figure 3]. observation with radiological screening was planned for the patient.



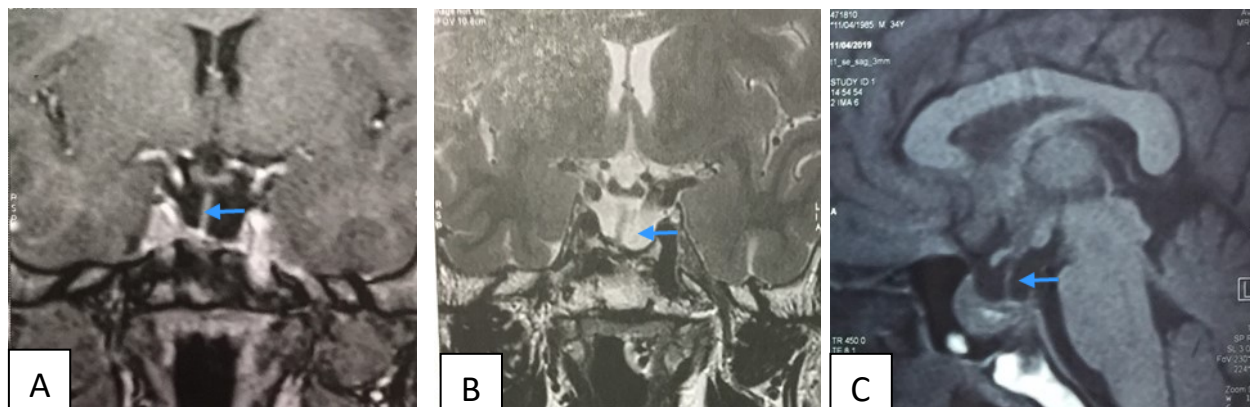
**Figure 1: Photograph showing**

*A: Eyelid ptosis on the left side and right sixth nerve palsy.*

*B: Recovery of the right sixth nerve palsy and left ptosis.*



**Figure 2: preoperative MRI; A: T1 weighted coronal slide, B: T2 weighted axial slide C: T1 weighted sagittal slide.** showing a pituitary macroadenoma, with hyperintense T1 signifying hemorrhage (red arrow), associated with suprasellar, left temporal extension, and invasion into left cavernous sinus (yellow arrow).



**Figure 3: post-operative MRI images, A: coronal slide of injected T1, B: T2 WI coronal slide, C: T1 sagittal slide.** Note the subtotal removal of the pituitary macroadenoma, with visualization of the pituitary stalk (blue arrow).

## Discussions

Nelson's syndrome is classically defined by the presence of a pituitary adenoma associated with elevated ACTH levels and cutaneous hyperpigmentation in patients with Cushing's disease following bilateral Adrenalectomy.<sup>5</sup> On studies the prevalence of this syndrome ranges from 8% to 47%.<sup>1-4</sup>

The adrenalectomy induces a loss of cortisol inhibition allows the pituitary tumor to secrete high amounts of ACTH with a consequent clinical expression of hyperpigmentation of the skin and mucosa. The origin of the overproduction of ACTH is variable either due to the occurrence of an adenoma in cases in which no adenoma was visible on previous MRI or as a result of the progression of a pre-existing adenoma.<sup>11</sup>

The time of appearance between the bilateral adrenalectomy and Nelson's syndrome in series ranges from 2 months to 24 years.<sup>11,12</sup> Our patient presented this syndrome about 5 years after adrenalectomy, which corresponds to the average in the literature.<sup>13</sup>

The indications of adrenalectomy currently are: patients with non-operable pituitary adenomas or non-controlled symptoms after adenoma resection, a failure of anti cortisolic drugs or their contraindication, patient with biochemical evidence of CD without pituitary lesion, or life-threatening symptomatic CD.<sup>14</sup>

Pituitary tumor apoplexy is a rare and underdiagnosed neuroendocrine syndrome and potentially life-threatening disorder resulting from a hemorrhagic infarction with enlargement of a pre-existing adenoma. The epidemiological studies reported a prevalence of 1.6 to 12.8 %.<sup>15,16</sup>

Clinically, it is characterized by a sudden onset of headaches which was the commonest complaint, followed by an ophthalmoplegia and visual impairment.<sup>16,17</sup> This presentation was similar in our patient, this is due to the localization of the hemorrhagic event close to the optic chiasm and cavernous sinus.

Several factors were considered as predisposing to the onset of apoplexy and most frequent are: arterial hypertension, previous irradiation of the gland, anticoagulant therapies, thrombocytopenia, and even trauma in some cases.<sup>18,19</sup> Another important factor that was also reported is the discontinuation of steroid treatment. This may lead to apoplexy especially in corticotrophin pituitary adenoma. The origin of this consequence is the triggering of an important tumor activity after the hormonal negative feedback.<sup>18</sup> Our patient was lost to follow up with probable discontinuation of exogenous steroids, which may have precipitated this apoplexy.

The ideal therapeutic modality for this syndrome is surgical resection of the corticotrophin pituitary adenoma via a transsphenoidal approach and less commonly, via a transcranial route for complex forms.<sup>20</sup> The main aim of this strategy is to relieve optic pathways and decompress the cavernous sinus as well. Our patient was operated on through an endoscopic transsphenoidal approach and the postoperative course was excellent.

After the development of radiological diagnosis and micro neurosurgical techniques, the need for bilateral adrenalectomy for hypercortisolism has decreased, a parallel decrease in the incidence of Nelson's syndrome and their rate among apoplectic pituitary adenomas can be expected.<sup>18</sup>

## Conclusion:

Nelson syndrome is defined as progressive enlargement of the pituitary adenoma and an increase in adrenocorticotrophic hormone after bilateral total adrenalectomy for Cushing's disease and can be life-threatening. Pituitary apoplexy is an uncommon presentation of Nelson's syndrome. The appropriate management of apoplexy is the surgical removal of the blood and decompressing the gland, the cavernous sinus, and the optic chiasm. The transsphenoidal approach seems ideal in achieving these goals.

This case showed that an aggressive form of apoplexy can be encountered in Nelson's syndrome and that surgical treatment with endocrinological support can lead to a favorable result.

## Conflict of Interest

The authors declare no conflict of interest.

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