*SVOA Neurology*

ISSN: 2753-9180

ScienceVolks Open Access

Case Series

# Necrotic Apoplexy of Pituitary Adenoma; A Report of Three Cases

**Chafik HANDIS[1], Salim MEZIANI[1], Yacine FELISSI[1]*, Radhia AIT CHALAL[2], Leila AHMED ALI[3], Amel ADIMI[3], N Soumaya FEDALA[3] and Abdelhalim MORSLI[1]**

*[1]Mohamed Lamine Debaghine University Hospital, Department of Neurosurgery, Algiers University, Faculty of Medicine, Algiers, Algeria.*

*[2]Mohamed Lamine Debaghine University Hospital, National Centre of Medical Imaging, Algiers University, Faculty of Medicine, Algiers, Algeria.*

*[3]Mohamed Lamine Debaghine University Hospital, Department of Endocrinology Algiers University, Faculty of Medicine, Algiers, Algeria.*

***Corresponding Author:** Dr. Yacine FELISSI, Mohamed Lamine Debaghine University Hospital, Department of Neurosurgery, Algiers University, Faculty of Medicine, Algiers, Algeria.*

DOI: https://doi.org/10.58624/SVOANE.2023.04.083

***Received:** January 22, 2023* ***Published:** February 07, 2023*

## Abstract

Apoplexy is relatively a rare clinical expression or revelation of pituitary adenoma. Necrotic apoplexy is a subgroup with unique findings in its different aspects. Early surgical resection through the transsphenoidal route is the main modality for their management. We report three cases of patients with necrotic apoplexy. we reviewed the circumstances of revelation, the imaging features, surgical findings, and the results of histological analysis. The age of patients ranged between 22 and 53 years old. All patients complained of headaches and visual disorders. At the MRI evaluation, they had the same radiological features of necrotic apoplexy. They received endoscopic endonasal surgery for the resection and the histological analysis confirmed the presence of necrosis areas in the sampled tissues. Necrotic apoplexy is a rare and unique clinical entity. At the imaging, it appears as a solid sellar mass, iso to hyperintense in both sequences T1 and T2. during the surgical removal, the lesion is yellowish and poorly bleeding without hemorrhagic contents. The histological studies reveal large areas of necrosis in similar lesions.

***Keywords:** Apoplexy, necrosis, endoscopy.*

## Introduction

Pituitary apoplexy (PA) is a clinical presentation related to a hemorrhagic or infarction event of a pre-existing pituitary adenoma (1). It regroups several symptoms including visual acuity and field disturbances, hypopituitarism, nerve palsies, and even consciousness disorders (2). This situation is reported to be present in 2 to 12% of all pituitary adenomas(3). Therefore, this condition can be a possible evolution for adenoma or one of their revelation's ways. Despite that it's described as a major emergency, PA is described as the mechanism of spontaneous remission in secreting adenoma as it was reported in a few cases of acromegaly (4, 5).beyond all of these scenarios, PA could be subclinical without typical symptoms as headache or visual acuity deterioration (6).

Necrotic apoplexy (NA) is a subgroup of infarction PA with unique findings during the surgical resection or during reviewing histopathological reports of resected lesions (7). according to one significant retrospective study, NA is made mainly by two indispensable criteria that are: the first is the intraoperative finding of a specific aspect of the adenoma represented by a cheese-like aspect and poorly bloody mass and the second is the histological studies that will show mainly, large areas of necrosis (7). Our knowledge about NA lacks precision and this is due to the rarity of similar cases (8), therefore it remains interesting to analyze different aspects whether the pathophysiology or the efficient management of this pathology.

The work reports three cases of NA of PA with all the previously mentioned characteristics of definition. we have reviewed the clinical presentation, hormonal evaluations, and surgical management of these patients. this study is an additional reference for this rare entity within the pituitary pathology that must be further elucidated with larger series.

## Methods

### Type of study

This work is a retrospective analysis of patients that presented necrotic pituitary apoplexy between January 2019 and August 2022. All parameters of diagnosis were considered during the selection of patients. these candidates were operated on by the Department of neurosurgery at Mohamed Lamine Debaghine University Hospital in Algiers (Algeria).

### Data collection

The data were collected from the medical files of patients. we have considered the same parameters for each patient which were; patients' demographics, clinical presentation, investigations, the peroperative findings, and the results of histological reports.

### Studied population

We have included three (03) patients that presented all the diagnosis criteria of necrotic apoplexy. These criteria were mainly the radiological aspect of the lesion, peroperative findings during the removal, and finally the histological studies that reveals specific findings for this subgroup of apoplexy.

## Results

### Case 1

A 53 years old male with a previous history of allergic rhinitis and surgery for his femur bone a few years before. He had before his admission, subacute headaches, and severe visual decline. he remained conscious and didn't complain of another neurological deficit.

The clinical evaluation revealed a patient with features of acromegalic facies with an important enlargement of hands and feet with a dough-like consistency. he complained also of major headaches.

The hypophysiogram results were as follows: GH: 0.715 ng/ml, IGF1: 178 ng/ml, FT4: 7.75 pmol/l, TSH: 0.16 µIU/mL, PRL: 1.22 ng/ml, FSH: 0.672 IU/L, LH: 0.498 IU/L, morning cortisol: 36.42 nmol/L.

The neuroophthalmological examinations showed bilateral hyperemia in both eyes, a correct visual acuity, and inferior quadrantanopia more marked on the left eye.

Pituitary MRI showed a voluminous sellar lesion with a partial extension to the suprasellar cistern. this lesion appears isointense on T1 and hypo to hyperintense on T2 sequences. A peritumoral ring-like enhancement is noticed in sequences after gadolinium administration.

Surgery was planned and performed one day after a correct endocrinological assessment and administration of adequate doses of corticosteroids. The first goal was to relieve pressure on the optic pathways, especially the chiasm, and get the histological studies of the sellar lesion.

An endoscopic endonasal transsellar approach was performed on the patient following the classical phases of this approach. after the sphenoidotomy, we noticed a reduced space between the sphenoid and the sellar floor and this was due to an expanded morphology of the sella. after a circular dural opening, a giant yellowish mass we noticed. initially, tumoral sampling was performed using endoscopic tumoral forceps. the consistency of tissues was firm and poorly bleeding. no hemorrhagic components were encountered. The dorsum sellae was eroded by the tumor and both cavernous sinuses were not infiltrated. we didn't notice a herniation of the diaphragm in the operative trajectory. some abnormal and infiltrated gland was found on the right side of the sella and also crushed against the diaphragm. we completed the remaining resection using the angled telescopes. The postoperative course was uneventful with regression of headaches and the patient was discharged on day 3. The histological reports the appearance of an endocrine proliferation, the seat of extensive ischemic necrosis without hemorrhagic changes.

### Case 2

A 37 years old female without previous history, started to present gradually during 2 years an acromegaly-related dysmorphic syndrome. 3 months before surgery, she started to complain of headaches.

The biological evaluation demonstrated these hormonal levels; GH: 10ng/ml, IGF1:1039 ng/ml (both abnormally elevated), and thyrotropin and gonadotropin deficiencies were substituted.

The ophthalmological examinations demonstrated a bilateral temporal papillary palor more marked on the left side. the visual acuity was at;1/10, 4/10 in left and right eye respectively.

MRI evaluation showed a macro adenoma enlarging significantly the sella with an extension to the suprasellar space and compression of the chiasm. The lesion appears heterogeneous and mainly isointense in T1 and hypointense in the T2 sequence. in injected sequences, an enhancement only around the lesion was noticed.

She underwent an endonasal endoscopic resection of the adenoma. After performing a wide sphenoidotomy, the sella and dura were opened widely without noticing a significant tension during tumor resection. the lesion was mainly yellowish without bleeding except in a small compartment of it, where the color and the consistency were different from the rest of the lesion. Both of the cavernous sinuses were not infiltrated and their medial walls were inspected at the end of the resection. some parts of the tumor had a bad surgical plan with the herniated suprasellar cistern at the end of surgery. the postoperative course was good and the patient left the hospital 3 days after.

The histological analysis of tumoral samples found a largely necrotic adenomatous formation with the presence of fibrous reorganization.

**Case 3**

A 22 years old male, complained two months before surgery of severe headaches and vision deterioration which have significantly altered his quality of life. the patient became almost blind in one eye 24 hours before his admission to the department.

The basic ophthalmological assessment revealed a visual acuity of 3/10 in the left eye and blindness in the right one.

The hypophysiogram showed the following hormonal levels:

Morning cortisol: 179 ng/ml, FT4: 12 pmol/l, Growth hormone (GH): 7 ng/L, Prolactin (PRL): 27ng/ml.

Immediate MRI before admission showed a giant pituitary adenoma enlarging the sella and infiltrating the left cavernous sinus (KNOSP 4). The tumor showed a significant suprasellar extension and a compression of the optic chiasm and anterior communicating complex. the T1 sequences showed a mainly hypointense adenoma with a hyperintense rim around the lesions. the sphenoid mucosa was thickened. T2 sequences showed a heterogeneous aspect of the adenoma with a hemorrhagic part.

Endoscopic endonasal surgery was performed and the classic steps of the approach were followed. after the sphenoidotomy, we noticed an abnormally thickened mucosa of the sphenoid sinus. The sella was enlarged and asymmetric. The adenoma was yellowish without hemorrhagic parts. during the resection, one liquified component was aspirated. The sellar part was removed and the suprasellar cistern herniated into the sella. We couldn't the whole cavernous part of the tumor. The rest of the procedure was carried out on the usual method.

During the postoperative course, the visual acuity two days after surgery improved to 9/10 and 10/10 on the right and left eyes respectively.

The histological study of the resected tissue showed mainly a large apoplectic necrotic formation and the nuclei were slightly round and atypical. A hemorrhagic component was also noticed in another part of the tumor. The immunochemistry staining showed a negative aspect for GH, ACTH, FSH, LH, and TSH. for the prolactin, the studies revealed diffuse cytoplasmic positivity of tumor cells. The Ki67 was inferior to 1%.

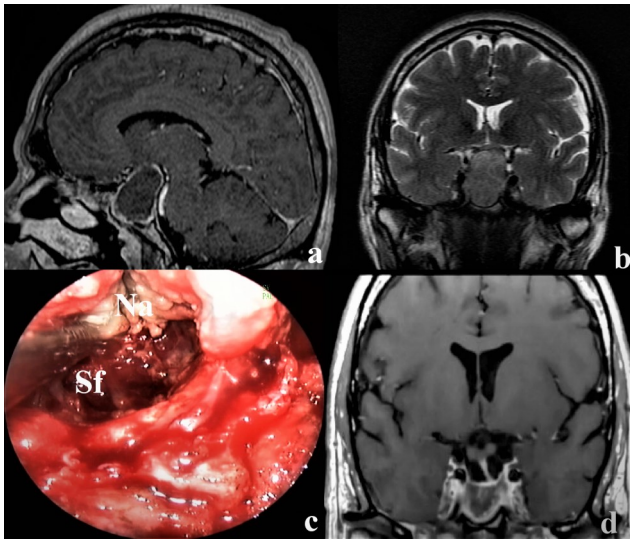


***Figure 1: Image a****: sagittal T1 with contrast that shows a solid sellar and suprasellar mass. the lesion is isointense with a ring enhancement around it, which is typical of necrotic apoplexy. we can notice also a thick ethmoidal sinus mucosa.* ***Image b:*** *coronal T2 section of preoperative MRI. The lesion is isointense without cystic or hemorrhagic contents.* ***Image c:*** *Peroperative endoscopic views of the lesion at the sellar phase during the resection. the lesion is yellowish and poorly bleeding (Na). the sellar's floor (Sf) is visualized after the removal of the inferior part of the lesion.* ***Image d:*** *coronal T1 section that shows total resection with a generous decompression of the optic pathways.*

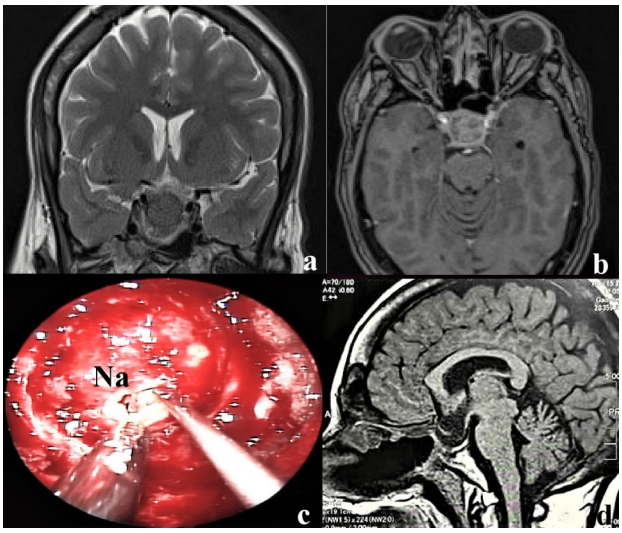


***Figure 2: Image a:*** *coronal T2 section of the MRI shows an isointense sellar lesion without cystic or hemorrhagic components.* ***Image b:*** *axial T1 with contrast MRI shows the typical perilesional ring enhancement of necrotic apoplexy.* ***Image c****: Peroperative endoscopic view at the beginning of the lesion (necrotic apoplexy NA), which looks yellow after the incision of the capsule.*

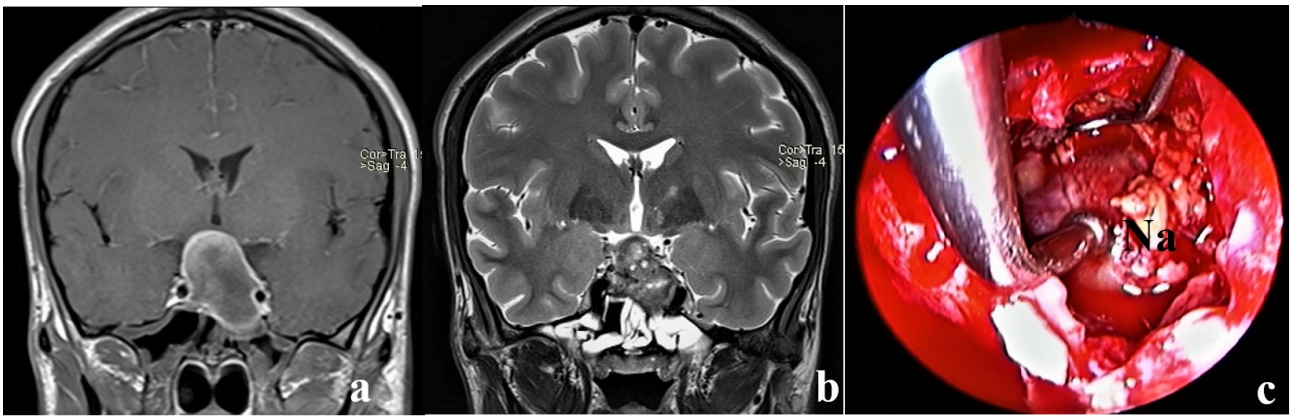


***Figure 3: Image a:*** *Coronal T1 section MRI with contrast that shows a predominantly hypointense sellar and suprasellar mass, with perilesional enhancement. The adenoma has a lateral extension to one cavernous sinus.* ***Image b:*** *coronal T2 section confirms a mainly isointense lesion, with an important thickening of the sphenoid mucosa (yellow star).* ***Image c****: peroperative endoscopic view showing the aspect of necrotic apoplexy NA during the sellar phase of resection.*

## Discussion

PA is rare and emergent in most cases condition. It's the result of a hemorrhagic or ischemic infraction of a preexisting pituitary adenoma. In some studies, (9, 10) their incidence ranges between 1 to 26%. In one large series of non-functioning adenomas, the apoplexy condition was present in 21% of cases (11). Necrotic apoplexy (NA) is a subgroup of this clinical condition with specific intraoperative and even histological parameters (7). In a recent Chinese study (7), NA was present in 4.8% of the studied population. Based on this same reference, the authors defined two specific and indispensable parameters for the definition of the NA; the presence of a coagulative necrosis zone in the histological studies and the cheese-like aspect of the lesion during surgical removal.

The males were slightly were mostly affected than women(12). In one word the age of affected patients ranged between 21 and 85 years(13). both of these parameters (age and sex) were concomitant with our patients, where we had 2 males and their ages ranged between 22 and 53 years old. In the largest study about this apoplexy (7), all patients complained of a headache at their first presentation and the intermittent scenario was mostly present in 17 candidates. 81% of patients in the same study, had disorders of their vision affecting the acuity and the field. Authors reported also the presence of nausea and vomiting (16 patients), and oculomotor palsies (47.6 %). All of our candidates complained of subacute headaches. we have noticed a deterioration of the visual acuity in two patients and the visual field in one case. Palsies of ocular movements were not present in our series and this was probably due to the absence of infiltration of the cavernous sinus.

Several works in the literature reviewed the MRI appearance of PA(14-16). the intensity of the lesion was different according to its age; acute (before 7 days), subacute (7 to 14 days), and chronic (after 14 days)(7). According to the same work (7), authors had defined radiological features for this subgroup of apoplexy and are represented by the homogeneous solid aspect of the tumor, an iso to hyperintense signals in both sequences (T1, T2) with the irregular presence of rim enhancement around a hypointense mass and finally the important thickness of the mucosa of the sphenoid and ethmoidal sinuses. For our patients, we have noticed most of the previously revealed parameters. the adenoma was solid in all cases and they appeared isointense, homogeneous in both T1 and T2 sequences. The ring enhancement aspect was also present in all of our patients. The mucosa of the sphenoid sinus had an abnormal thickness that was confirmed during surgical resection. in one interesting study (17), the authors evaluated the grade of apoplexy, the patient's vision, and the endocrinological evolution according to the sphenoid sinus mucosal thickening and concluded that a thickened mucosa is correlated to worse apoplexy grade and worse endocrinological and visual status.

The portal system and hypophyseal arteries (superior and inferior) supply the pituitary gland. in a more detailed concept, the infundibulum and the pars tuberalis are supplied by the superior hypophyseal which is a branch of the internal carotid artery. the posterior gland receives blood from the inferior hypophyseal artery. consequently, a significant blood flow is present within these structures. conversely, a relatively low flow is existing in the anterior hypophysis that receives the blood supply from the long and short portal systems. Both of these systems seem sensitive to volume and pressure modifications(18). some factors were defined as favoring the PA as; cranial trauma, angiographic and dynamic tests as well some drugs as dopamine agonists or antiplatelets (13).

We have considered the results of the largest series (7) when evaluating the results of the histological findings. the Hematoxylin and eosin staining revealed large pink and acellular necrotic zones. the same authors defined what they call a ghost cell present in histological studies, which were outlined cells however without any material. Our main results were the presence of a large necrotic adenomatous formation with extensive necrosis which is concomitant with the previously cited study. the encountered preoperative aspect was the cheese-like and poorly bleeding lesion in all of the candidates, where we could achieve a gross total resection.

Conservative and surgical management were both reported to be therapeutic options in PA (19, 20). In the presence of severe visual disorders in our case, endoscopic endonasal surgery was adopted for the removal of the adenoma in the three cases. According to the previously cited work (7), early surgical removal with sufficient hormone replacement therapy previous to surgery is the adequate management for NA cases. we have operated on all three cases because they were symptomatic and presented some visual acuity or field disorders.

## Conclusion

PA is an emergent scenario during the management of patients with pituitary adenoma. most of them are hemorrhagic, however, the necrotic subgroup is sufficiently studied because of the reduced series reported in the literature. the revelation is made on subacute symptom as headaches or visual disorders. The imaging is specific and predicts even long-term evolution. transsphenoidal surgical resection is an efficient modality to relieve the pituitary gland and optic pathways. the histological studies combined with specific radiological features are the constant diagnosis parameters.

**What is already known on this topic:**

- NA is a subgroup of pituitary apoplexy with specific preoperative and histological features.
- The radiological characteristics of NA are related to the consistency of the lesion and another pathophysiological phenomenon that affects the sella and the surrounding structures.
- The thickening of the sphenoidal and ethmoidal mucosa are predictors of severe apoplexy and worse endocrinological and visual outcomes.

**What this study adds:**

- The NA could be the origin of the normalization of hormonal levels in a patient with functional adenoma as it was the first case.
- Despite radiological features of worse apoplexy and endocrinological outcomes, our patient (case 3) remained without replacement therapy after surgery.

## Limitations of the study

The limitation of the study is mainly the reduced number of participants and this is also related to the scarcity of these circumstances in the pituitary disease. To our knowledge, only 21 patients were included in the largest study found in the literature. we don't have long-term follow results, especially the replacement therapy, which has a significant impact on the prediction of the prognosis and the recovery of pituitary functions after surgery. The retrospective aspect of the study is also another limitation of this work.

## Conflicts of interest

The authors certify that there is no conflict of interest with any financial organization regarding the material discussed in the manuscript.

## Funding

The authors report no involvement in the research by the sponsor that could have influenced the outcome of this work.

## Authors contributions

All authors contributed equally to the manuscript and read and approved the final version of the manuscript.

## References

1. Cardoso ER, Peterson EW. Pituitary apoplexy: a review. Neurosurgery. 1984;14(3):363-73.
2. Semple PL, Webb MK, de Villiers JC, Laws ER, Jr. Pituitary apoplexy. Neurosurgery. 2005;56(1):65-72; discussion -3.
3. Briet C, Salenave S, Bonneville JF, Laws ER, Chanson P. Pituitary Apoplexy. Endocrine reviews. 2015;36(6):622-45.
4. Imaki T, Yamada S, Harada S, Tsuchiya M, Sano T, Demura H. Amelioration of acromegaly after pituitary infarction due to gastrointestinal hemorrhage from gastric ulcer. Endocrine journal. 1999;46(1):147-51.
5. Wichers M, Kristof RA, Springer W, Schramm J, Klingmüller D. Pituitary apoplexy with spontaneous cure of acromegaly and its possible relation to Gd-DTPA-administration. Acta neurochirurgica. 1997;139(10):992-4.
6. Garg MK, Pathak HC, Singh G. Subclinical pituitary apoplexy with preserved pituitary functions. Indian J Endocrinol Metab. 2014;18(1):122-3.
7. Wang Z, Gao L, Wang W, Guo X, Feng C, Lian W, et al. Coagulative necrotic pituitary adenoma apoplexy: A retrospective study of 21 cases from a large pituitary center in China. Pituitary. 2019;22(1):13-28.
8. Fanous AA, Quigley EP, Chin SS, Couldwell WT. Giant necrotic pituitary apoplexy. Journal of clinical neuroscience : official journal of the Neurosurgical Society of Australasia. 2013;20(10):1462-4.
9. Ranabir S, Baruah MP. Pituitary apoplexy. Indian journal of endocrinology and metabolism. 2011;15 Suppl 3 (Suppl3):S188-96.
10. Mohanty S, Tandon PN, Banerji AK, Prakash B. Haemorrhage into pituitary adenomas. Journal of neurology, neurosurgery, and psychiatry. 1977;40(10):987-91.
11. Nielsen EH, Lindholm J, Bjerre P, Christiansen JS, Hagen C, Juul S, et al. Frequent occurrence of pituitary apoplexy in patients with non-functioning pituitary adenoma. Clinical endocrinology. 2006;64(3):319-22.
12. Ahmed M, Rifai A, Al-Jurf M, Akhtar M, Woodhouse N. Classical pituitary apoplexy presentation and a follow-up of 13 patients. Hormone research. 1989;31(3):125-32.
13. Möller-Goede DL, Brändle M, Landau K, Bernays RL, Schmid C. Pituitary apoplexy: re-evaluation of risk factors for bleeding into pituitary adenomas and impact on outcome. European journal of endocrinology. 2011;164(1):37-43.
14. Goyal P, Utz M, Gupta N, Kumar Y, Mangla M, Gupta S, et al. Clinical and imaging features of pituitary apoplexy and role of imaging in differentiation of clinical mimics. Quantitative imaging in medicine and surgery. 2018;8(2):219-31.
15. Dubuisson AS, Beckers A, Stevenaert A. Classical pituitary tumour apoplexy: clinical features, management and outcomes in a series of 24 patients. Clinical neurology and neurosurgery. 2007;109(1):63-70.
16. Waqar M, McCreary R, Kearney T, Karabatsou K, Gnanalingham KK. Sphenoid sinus mucosal thickening in the acute phase of pituitary apoplexy. Pituitary. 2017;20(4):441-9.
17. Liu JK, Couldwell WT. Pituitary apoplexy in the magnetic resonance imaging era: clinical significance of sphenoid sinus mucosal thickening. Journal of neurosurgery. 2006;104(6):892-8.
18. Biagetti B, Simò R. Pituitary Apoplexy: Risk Factors and Underlying Molecular Mechanisms. 2022;23(15):8721.
19. Maccagnan P, Macedo CL, Kayath MJ, Nogueira RG, Abucham J. Conservative management of pituitary apoplexy: a prospective study. J Clin Endocrinol Metab. 1995;80(7):2190-7.
20. Ayuk J, McGregor EJ, Mitchell RD, Gittoes NJ. Acute management of pituitary apoplexy--surgery or conservative management? Clin Endocrinol (Oxf). 2004;61(6):747-52.

**Citation:** Handis C, Meziani S, Felissi Y, Chalal RA, Ali LA, Adimi A, Fedala NS, Morsli A. Necrotic Apoplexy of Pituitary Adenoma; A Report of Three Cases. *SVOA Neurology* 2023, 4:1, 06-12.