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Post-traumatic pituitary apoplexy: Case presentation and review of literature

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ABSTRACT

Pituitary apoplexy is a dramatic condition that can occur spontaneously or triggered by various precipitating factors. Head trauma is a rare but well-recognized cause of apoplectics events. We present the case of an 81-year-old woman, with negative past medical history and under antiplatelet agents, who experienced an isolated VI cranial nerve palsy 24 h after a mild head trauma. Early brain CT revealed an unknown pituitary lesion without signs of intralesional bleeding. Only late brain MRI imaging revealed pituitary apoplexy together with a subarachnoid hemorrhage. After aggravation of neurological condition the patient, undergo endoscopic transsphenoidal decompression of cranial nerves with rapid deficits improvement. Our aim is to share our experience and to propose the first critical review of all cases of post-traumatic pituitary apoplexy described in literature. We also try to suggest some management advice for post traumatic pituitary apoplexy.

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1. Introduction

Pituitary apoplexy (PA) is a rare event characterized by a rapid expansion of a pituitary adenoma after a hemorrhage or ischemia, and occurs in about 14–22% of patients [1]. Male-to-female ratio is 2:1, and most cases present in the V or VI decades of life [11]. PA is a dramatic condition that can be sometimes life threatening for the patient [9]. 70–81% of patients with PA had negative medical history for pituitary adenoma [9,15]. PA can be asymptomatic and recognizable only after performing neuroimaging, and is therefore called subclinical or subacute apoplexy [14]. Pituitary adenomas can develop silently, enlarge and then suddenly become symptomatic after triggering events such as head trauma, radiation therapy, sudden changes in intracranial pressure, dopamine agonists administration, hormone stimulation tests, lumbar puncture or spinal anesthesia [1,5,13]. Some authors argue that pituitary apoplexy is more prone to occur in large pituitary tumors (e.g. macroadenoma) whereas microadenomas (<1 cm in diameter) are less susceptible to bleeding [14]. Studies showed than about 70% of pituitary apoplexy occurred in nonfunctioning adenoma [10,15]. Furthermore, there is no evidence that a defined histological type of pituitary tumor is more susceptible to apoplectic events [3,15].

To date, only 12 cases of post-traumatic pituitary apoplexy are described in literature. In this report we want to share our experience in the management of post traumatic PA and propose the first critical review of all cases described in literature.

2. Case presentation

We report the case of an 81-year-old woman, which accidentally fell, in October 2015, from about 1.5 m height with subsequent mild head trauma and blunt contusion on her occipital bone. She was under lifetime prophylaxis with antiplatelet drugs. After she was admitted to the Emergency Department she underwent a brain CT scan which highlighted a left frontal contusion with subarachnoid hemorrhage (SAH), together with the evidence of an undiagnosed pituitary lesion (Fig. 1a, b). Neurological examinations were negative. Twenty-four hours later, she developed VI c.n. (cranial nerve) palsy with no evidence of diplopia or visual acuity loss. Visual field defects were not documented on manual visual field testing. A new brain CT scan showed that the pituitary lesion had enlarged in size, with presence of hyperdense foci, signs of potential intralesional hemorrhage (Fig. 1c). Imaging was compatible with pituitary apoplexy. A comprehensive hormone panel was performed which confirmed mild hypopituitarism (Prolactin 1.7 ng/ml, T3 1.93 mIU/ml, serum cortisol 2.9 ng/ml) and brain MRI (magnetic resonance) scan showed bilateral subdural hematoma together with left temporal and frontal contusions as well as an intrasellar-suprasellar lesion, of 30 mm × 20 mm size, with signs of recent bleeding (Fig. 1d). Brain MRI imaging evidenced how the sellar lesion exerted compression on chiasm and optic nerves, which were dislocated. In the first hours after PA diagnosis the only neurological sign manifested was the VI c.n. palsy and, considering patient's age and comorbidities, we adopt a “wait and see” approach. The patient's clinical conditions were constantly monitored and hormone replacement therapy was administered. After 4 days the patient complained of progressive loss of visual acuity (01/10 on right eye (R.E.) and 2/10 on left eye (L.E.)) and temporal hemianopsia was confirmed by Goldman visual field

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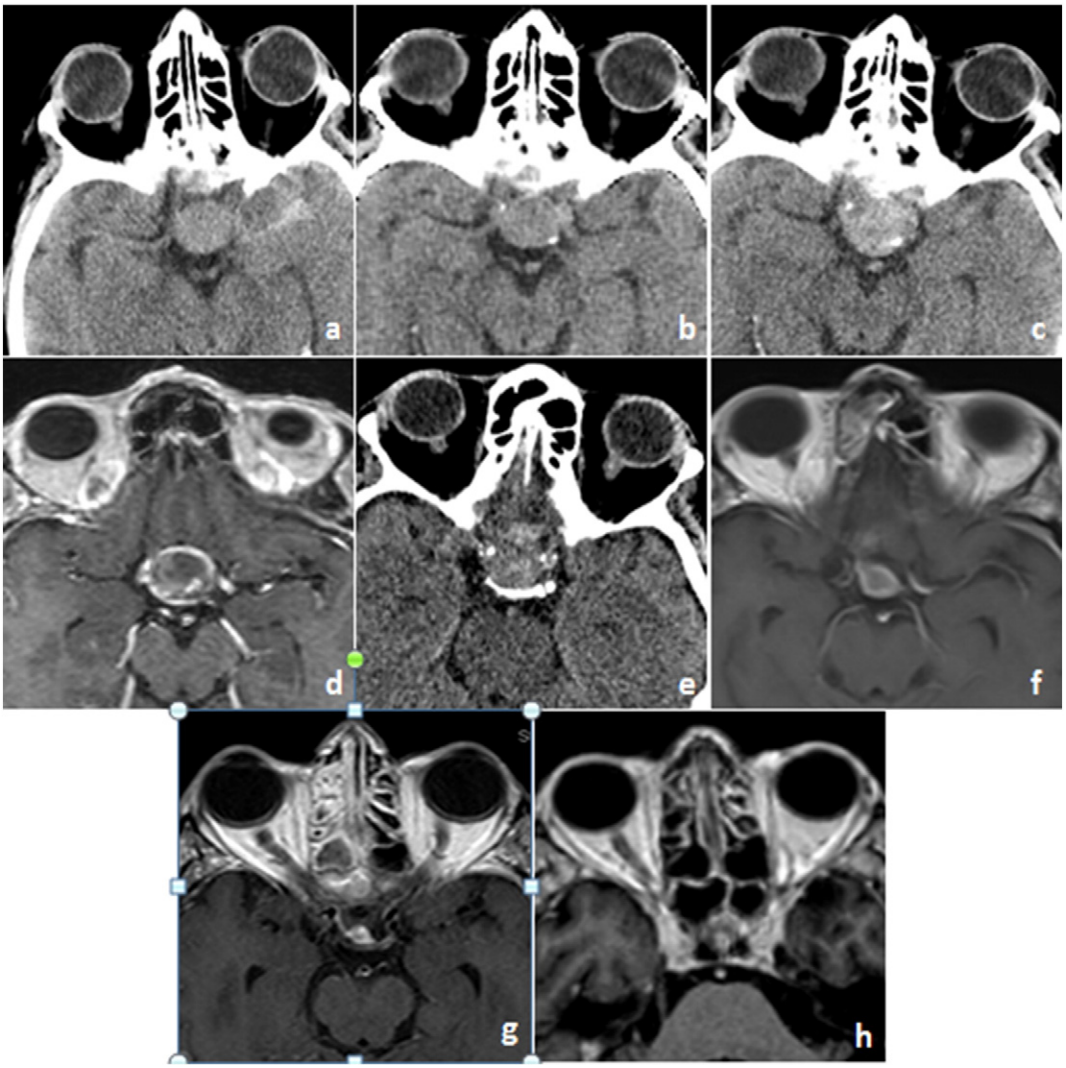

Fig. 1. Early after head trauma axial brain CT scan (a) and 6 h later brain CT scans (b); 24 h axial brain TC scan; recognition of pituitary apoplexy and first manifestation of symptoms (c); 36 h later T1 contrast enhanced axial brain MRI scan: aggravation of neurological condition (d) and 48 h later post-apoplexy CT axial scans (e). Postoperative axial T1 contrast enhanced brain MRI axial scans (f). Early (g) and long term follow up T1 contrast enhanced brain MR axial scan (h).

examination. At that point, surgical treatment was mandatory (Fig. 1d, e). The patient underwent endoscopic trans-sphenoidal surgery in order to decompress optic nerves (Fig. 1f). Histological and immunohistochemical examinations showed extensive necrosis with fibrosis and inflammatory granulation infiltration. The lesion express diffusely synaptophysin together with Ki-67 in 3% of cells, whereas ACTH, prolactin, CKCAM5.2, FH, TSH, GH were not expressed. At that point, the pituitary apoplexy was confirmed. After surgical decompression, visual acuity progressively improved. The patient underwent brain MRI imaging that documented a satisfactory decompression of chiasm and optic nerves. Clinical evaluation at 30 and 60 days documented recovery of visual acuity (4/10 in R.E. and 4–5/10 in L.E.) as well as of visual field impairment. Long-term MRI follow-up did not document any further complications (Fig. 1g, h).

3. Discussion

In 1932 Van Wagenen reported the first two cases of post-traumatic pituitary apoplexy and since 1983 no other cases have been described [2]. In addition, Dr. Harvey Cushing described a similar case in which the pathological examination documented a pituitary tumor with extensive blood infiltration in a patient died after head trauma [2]. In our review of literature, including our case report, we identified 13 post-traumatic pituitary apoplexy cases from 1983 to 2016 (Table 1). 9 patients were men, with a male to female ratio of 2:1, which is also the reported ratio for PA in literature. Age ranged from 30 to 85 with a mean age of 58.7 years. All patients were unaware of the presence of the pituitary tumor. In 2 cases patients complained of symptoms compatible with GH over secretion and in one case symptoms of increased serum prolactin levels were manifest.

To date the pathophysiological mechanism underlying post traumatic pituitary apoplexy has not been established [4]. The pituitary gland is perfused by its portal venous system, which passes down the hypophyseal stalk. It is well described how the particular pattern of vascular supply contributes to the occurrence of pituitary apoplexy [3]. Dandy et al. suggest that pituitary massive hemorrhagic infarcts can be consequent to traumatic shearing forces that cause the destruction of the pituitary stalk and lead to the consequent blockage of pituitary portal vascularization [2]. Several authors support that if the trauma involves the occipital region, as occurred in 9 cases (Table 1), shearing-rotational forces are more susceptible to tear the fragile junction between the intra-sellar portion, that is relatively firm, and the supra-sellar portion, that lies freely within the supra-sellar cistern [1]. Others authors argue that after a head trauma an intralesional hemorrhage can occur, such event alter the venous vascularization pattern encouraging ischemic-hemorrhagic occurrences. This hypothesis can explain the

Table 1
Literature review summary of post traumatic pituitary apoplexy.

Authors		Age (years)	Sex	Medical history	Dynamics of trauma	Delay (time)	Symptoms	Imaging	Treatment	Post-operative	Hormonal replacement therapy	Follow up (months)	Antiplatelet medications
Haruaki U et al. [4]	1999	60	F	X	Fell down stairs with occipital trauma	1 h	Lethargic, VI. PL on RE, MM on LE	CT + RM	TSS + TSS	RI	X	1	n.d.
Haruaki U et al. [4]	1999	66	M	X	Fell from a 4-m-height with back trauma	15 h	Lethargic, MM	CT + MR: pituitary apoplexy	CT	RI	X	4	n.d.
K. Kayayurt et al. [1]	2015	68	M	X	Fell with occipital trauma	2 h	OP	MR: pituitary apoplexy	n.d. (surgical)	OP	Yes	3	X
Ravi Dev et al. [3]	2007	40	M	X	Head-on collision of motorcycle with a road divider	7 h	MM in RE; 2/10 in LE; hemianopsia	CT: hematoma in sella and supra-cellar region + hematoma in the basi-frontal region	TTS	2.5/10 in RE, 5/10 in LE, hemianopsia	X	n.d.	n.d.
Horie N et al. [12]	2002	56	F	X	Traffic accident	n.d.	Lethargic	MR: pituitary apoplexy	Fronto-temporal CT	No	X	n.d.	n.d.
Itoyama Y et al. [7]	1999	45	M	X	Fell from a 2 m height with right frontotemporal trauma	3 h	Anisocoria, OP, VI hemianopsia	CT: SAH due to pituitary apoplexy AGF: vasospasms	NST	7/10 in RE, 3/10 in LE	Yes	>27	X
Holness RO et al. [2]	1983	39	M	X	Head injury with fracture of right patella	<1 h	1/10 on LE; MM on RE, hemianopsia	CT: pituitary apoplexy	Frontal CT + RT	Mild recovery on LE. 5/10 RE, hemianopsia	X	3	X
Smidt MH, et al. [6]	2007	30	M	X	Fell of a truck	3 w	OP, 5/10 RE; 8/10 LE	CT + MR: pituitary apoplexy	TTS	RI	Yes	5	n.d.
Lin Chang et al. [11]	2009	85	M	X	Fell, minor parietal trauma	6 d	HD	MR: pituitary apoplexy	NST	RI	Yes	n.d.	Yes
N. Tamasawa [8]	1988	34	M	X	Fell from the back of a truck	2 d	VI	CT: no pituitary apoplexy RM: signs of hemorrhage	NST	RI	Yes	2	n.d.
Mohammad Sami Walid et al. [5]	2009	80	F	X	Fell in the yard	<1 h	No VI	CT + RM: SAH due to pituitary apoplexy	NST	RI	Yes	48	Yes
Bao Xi ling et al. [9]	2007	79	M	X	Fell, head occipital trauma	6 h	No VI	CT + RM: SAH due to pituitary apoplexy	NST	HD	Yes	18	n.d.
Present case	2015	81	F	X	Fell from 1.5 m height + occipital trauma	24 h	OP	CT + MR: pituitary apoplexy	TSS	RI	Yes	6	Yes

Legend: VI: visual impairment; HD: hormonal deficits; RE and LE: right and left eyes respectively; OP: ophtalmoparesys; NST; non surgical treatment; TTS: transsphenoidal surgery; CT: craniotomy; RI: restitutio ad integrum; MM: motu mano; PL: perceive light; SAH: subarachnoid hemorrhage; AGF: intracranial angiogram; X: no.

delay in post-traumatic PA onset and symptoms manifestation [4]. Other authors suggest that also, arterial vasospasm may have a role in post-traumatic PA, but the pathophysiological mechanism have still to be clarified [3].

It is well known how anticoagulants and antiplatelet agents, especially in elder patients, can facilitate and worsen adverse vascular events. After head trauma, owing to anticoagulant/antiaggregant therapy, small bleedings that should be silent turn instead into massive ischemic-hemorrhagic events, as described in 3 cases (Table 1) [6].

Most common symptoms of PA are headache (63–100%) [10,15], nausea (80%) [10], vomiting (20–77%) [15], visual acuity deterioration (56–75%) [10,15], ophthalmoparesis (45–68%) [15], hypopituitarism, dizziness, confusion and even coma (13–77%) [10,15]. Symptoms may have an acute or delayed onset with a wide variability of clinical manifestations. In 43% of PA cases, involvement of multiple cranial nerves (c.n.) was described. The III c.n. is the most frequently affected, followed by abducens nerve (VI c.n.) in 5% of cases [1]. Hypopituitarism occurs in 70% to 80% of patients and usually becomes persistent, necessitating lifetime hormone replacement therapy [10] whereas diabetes insipidus incidence accounts for 4% for transient and 2% for persistent deficits [8]. ACTH (adrenal) deficit become manifest in 67% of cases, TSH (thyroid stimulating hormone) deficiency in 45%, gonadal hormones in 82% and PRL (prolactin) in 26% [15]. The most dangerous consequence of pituitary apoplexy is sudden death, attributable to the onset of acute adrenal insufficiency [10].

PA symptoms usually become manifest after few hours, with a mean delay of presentation of 14 days, whereas in some cases even 2 months. In the reviewed series of post-traumatic apoplexy, the mean delay after head trauma was 11 h, with in 2 cases a delay of six days and 3 weeks (Table 1).

PA could be misinterpreted as bacterial meningitis, subarachnoid hemorrhage, viral meningo-encephalitis or migraine, [6,11] as occurred in 2 of reviewed cases. The high temperature in consequence to PA could be referred as a sign of infections, but is in fact a typical finding in patients with PA. Furthermore ophthalmoparesis, a frequent sign of PA, can be wrongly referred as ocular motility disturbances associated with meningitis. It is therefore advisable to mind about the possibility of pituitary apoplexy when mental alteration and meningismus appear together, even without visual or other cranial nerve deficits [11].

A full clinical and instrumental diagnosis requires adequate neuroimaging, a complete ophthalmological examination, and a full hormonal panel [10]. Head CT scan represents the gold standard for head trauma but CT imaging can highlight a PA only in 25–28% of cases. It is well known that pituitary adenoma, which is isodense to brain parenchyma, is difficult to diagnose on CT even in case of hemorrhage. In the reported cases series CT scans failed to recognize post-traumatic PA in 6 (50%) of cases [1,4,6,8,9,11].

Brain MRI imaging is more sensible and allows recognition of PA in nearly 100% of patients [1]. In the suspect of PA, MRI imaging should be preferred.

Sometimes post-traumatic PA accompanies subdural hematomas, as occurred in 4 cases [7,8]. In one case of post traumatic PA arterial vasospasm occurred as consequence of SAH, in that case the author suggest to perform cerebral angiography when patients with pituitary apoplexy exhibit rapid neurological aggravation [7] (Table 1).

The combination of endoscopic trans-sphenoidal surgery and hormone replacement therapy is considered the standard treatment in case of pituitary apoplexy [9]. Surgery within the first days is recommended when visual impairments or neurological deficits are manifest, even without acute clinical deterioration. Early surgical decompression is related to an improved neurological outcome. Indeed, patients with progressively improving neurological deficits, particularly with only isolated cranial nerves deficit, could benefit from conservative treatment with subsequent clinical-radiological follow up [10], as we had first intended to do with our patient. If apoplectic events are so dramatic as to be associated with an intra-parenchymal hemorrhage, some authors argue that surgical evacuation can be obtained through endoscopic trans-sphenoidal approach if such hematoma affects the frontal-basal regions, or by craniotomy in other cases [3]. If a surgical approach is chosen, total tumor resection is not mandatory but a prompt decompression of cranial nerves involved is advisable [1,8]. In the reported cases series, craniotomy was performed 3 times whereas endoscopic trans-sphenoidal surgery was performed in 6 cases. Four cases were managed conservatively and integration of hormone deficits was administered, with hormone replacement therapy (Table 1). The recovery rate in patients with neurological deficits that undergo early surgery was 73%. This percentage drops to 43% in case of delayed surgery [1] (Table 1).

4. Conclusion

Pituitary apoplexy after a head trauma is a rare event that could manifest acutely or silently with delayed presentation of neurological signs, because of the occurrences of a symptoms-free time interval between trauma and bleeding. Furthermore, pituitary apoplexy does not always show the typical signs of hemorrhage but may also mimic meningitis or subarachnoid hemorrhage syndromes. It is therefore essential for a physician to be extremely cautious in case of elderly patients admitted to the Emergency Department following an head trauma, especially if under antiaggregants/anticoagulants agents, even if they don't exhibit neurological deficits. We suggest performing adequate diagnostic investigations and being aware that head CT scan do not always allow recognition of PA. Furthermore, in case of unexplained neurological deficits, always perform brain MRI scan. It is therefore advisable to warn the patient on potential signs of pituitary apoplexy in case of recognition of unknown pituitary adenoma. As already suggested in literature, we believe that in every case of post head trauma PA case even without acute and progressive deficits (visual acuity deterioration, visual field defects) early trans-sphenoidal surgery through endoscopic route is the mandatory choice for treatment. An accurate recognition and intervention, as described in our case, allows a restitutio ad integrum in most cases and avoid unpleasant consequence for patients.

Conflict of interest

The authors declare that they have no conflict of interest.

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Ethical approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. This article does not contain any studies with human participants performed by any of the authors.

Informed consent

Informed consent was obtained from all individual participants included in the study.

References

[1] K. Kayayurt, Ö.L. Gündogdu, Ö. Yavaşi, Y. Metin, E. Ugras, Isolated abducens nerve palsy due to pituitary apoplexy after mild head trauma, Am. J. Emerg. Med. 33 (10) (2015) 1539.
[2] R.O. Holness, F.A. Ogundimu, R.A. Langille, Pituitary apoplexy following closed head trauma. Case report, J. Neurosurg. 59 (4) (1983) 677–679.

[3] R. Dev, S.K. Singh, M.C. Sharma, P. Khetan, A. Chugh, Post traumatic pituitary apoplexy with contiguous intra cerebral hematoma operated through endonasal route—a case report, Pituitary 10 (3) (2007) 291–294.
[4] H. Uchiyama, S. Nishizawa, A. Satoh, T. Yokoyama, K. Uemura, Post-traumatic pituitary apoplexy—two case reports, Neurol. Med. Chir. 39 (1) (1999) 36–39.
[5] M.S. Walid, Hemorrhage from a pituitary macroadenoma after a minor trauma, J. Clin. Med. Res. 1 (5) (2009) 305–306.
[6] M.H. Smidt, A. van der Vliet, P. Wesseling, J. de Vries, T.B. Twickler, P.E. Vos, Pituitary apoplexy after mild head injury misinterpreted as bacterial meningitis, Eur. J. Neurol. 14 (7) (2007) e7–e8.
[7] Y. Itoyama, S. Goto, M. Miura, J. Kuratsu, Y. Ushio, T. Matsumoto, Intracranial arterial vasospasm associated with pituitary apoplexy after head trauma—case report, Neurol. Med. Chir. 30 (5) (1990) 350–353.
[8] N. Tamasawa, K. Kurahashi, T. Baba, R. Hishita, S. Murabayashi, H. Kashiwamura, K. Takebe, Spontaneous remission of acromegaly after pituitary apoplexy following head trauma, J. Endocrinol. Investig. 11 (6) (1988) 429–432.
[9] Y.J. Bao, X.G. Li, Z.T. Jing, S.W. Ou, A.H. Wu, Y.J. Wang, Pituitary apoplexy complicated with subarachnoid hemorrhage caused by incidentaloma following a head injury: case report, Chin. Med. J. 120 (24) (2007) 2341–2343.
[10] W.L. Bi, I.F. Dunn, E.R. Laws Jr., Pituitary apoplexy, Endocrine 48 (1) (2015) 69–75.
[11] C. Lin, T. Jen-Ho, Y. Muh-Yong, J. Cherng-Lan, H. Sheng-Huang, Pituitary apoplexy following mild head injury mimicking bacterial meningitis, J. Chin. Oncol. 25 (2) (2009) 137–141.
[12] N. Horie, Y. Tokunaga, N. Takahashi, S. Furuichi, K. Mori, S. Shibata, A case of pituitary apoplexy with severe consciousness disturbance following mild head trauma, No To Shinkei 54 (8) (2002) 697–701.
[13] E. Chng, R. Dalan, Pituitary apoplexy associated with cabergoline therapy, J. Clin. Neurosci. 20 (12) (2013) 1637–1643.
[14] D.H. Jho, B.M. Biller, P.K. Agarwalla, B. Swearingen, Pituitary apoplexy: large surgical series with grading system, World Neurosurg. 82 (5) (2014) 781–790.
[15] R.N. Nawar, D. AbdelMannan, W.R. Selman, B.M. Arafah, Pituitary tumor apoplexy: a review, J. Intensive Care Med. 23 (2) (2008) 75–90.