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Case Report

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Pituitary apoplexy secondary to dengue fever–induced–thrombocytopenia: A case report and review of literature

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ABSTRACT

Rationale: Pituitary apoplexy (PA) is a rare endocrine emergency that requires prompt diagnosis and management. Dengue fever-induced-thrombocytopenia may rarely predispose to PA.

Patient's Concern: A 58-year-old male patient having known pituitary macroadenoma presented to the emergency department with fever, a sudden onset severe headache, and altered sensorium.

Diagnosis: Pituitary apoplexy caused by dengue fever-induced-thrombocytopenia.

Interventions: Conservative management with fluids, mannitol, dexamethasone and symptomatic treatment.

Outcomes: The patient responded well to the treatment and was discharged uneventfully.

Lessons: Although dengue hemorrhagic fever is a rare cause of pituitary apoplexy, it should be considered if a patient presents with headache and altered sensorium, and prompt initiation of treatment is crucial to prevent fatality and neuro-ophthalmic deficits.

KEYWORDS: Dengue hemorrhagic fever; Pituitary adenoma; Apoplexy; Thrombocytopenia; Endocrine emergency

1. Introduction

Pituitary apoplexy (PA) is an acute catastrophic event caused by infarction or hemorrhage in the pituitary gland with or without pre-existing tumor that may lead to severe headache, vomiting, altered sensorium, diminished vision, and ophthalmoplegia[1]. PA may be induced by multiple precipitating factors including thrombocytopenia or may occur spontaneously[2]. Thrombocytopenia is an important feature of dengue fever, which may elicit PA. A review of the literature showed nine reported cases of dengue hemorrhagic fever-induced PA[1-8]. We report a case of PA due to dengue fever-induced-thrombocytopenia which was managed conservatively.

2. Case report

This study was approved by the Institutional review board, and informed consent was obtained from the patient.

A 58-year-old male patient presented to the emergency department with a history of fever of 102 °F, myalgia and retro-orbital pain for 5 d, a sudden onset of severe headache, left-sided hemiparesis, and altered sensorium for 1 d. There was no history of any petechial rash or spontaneous mucosal bleeding. He was diagnosed with pituitary macroadenoma (Figure 1A & 1B) 7 months ago after complaints of diminished vision and psychosis, yet had not undergone a complete hormonal workup. He was advised transsphenoidal surgery for treating the pituitary macroadenoma, but he refused and hence was not on any treatment. There was no history of smoking, alcohol use, or substance abuse. On examination, he had a pulse rate of 108 bpm (normal: 60-100 bpm), blood pressure of 100/64 mmHg (normal: 100-140/60-90 mmHg), respiratory rate of 22/min (normal: 13-19/min), SpO_2 92% (normal: ≥95%) at room air, altered sensorium with a Glasgow coma scale score of 10/15, disoriented, left-sided

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hemiparesis and left extensor plantar reflex, and the rest of physical examination was unremarkable. The pupils were reactive to light and normal in size. Visual acuity and field of vision could not be tested due to the altered sensorium.

Investigations showed thrombocytopenia (platelet counts 21 000/mm^3, normal: 50 000-150 000/mm^3) with positive dengue serology (both NS1 antigen and immunoglobulin M). Non-contrast computed tomography of the head was suggestive of pituitary macroadenoma with intratumoral hemorrhage and right temporal and capsulo-ganglionic (36 mm×38 mm) hemorrhage (Figure 1C & 1D). On hormonal evaluation, serum thyroid stimulating hormone was 0.23 mIU/L (normal: 0.34-5.60 mIU/L), serum FT4 was 0.55 ng/mL (normal: 0.61-1.12 ng/mL), serum prolactin was >200 ng/mL (normal: 2.64-13.13 ng/mL), 8:00 AM serum cortisol was 4.25 mcg/dL (normal: 5-25 mcg/dL), serum testosterone was 68 ng/dL (normal: 270-1 070 ng/dL) and luteinizing hormone was 2.2 mIU/mL (normal: 1.8-8.6 mIU/mL).

According to the UK PA guideline, when having a PA score of 3/10, a patient should be managed conservatively[9]. Our patient was managed with oxygen therapy, intravenous fluids, 5 units of platelet transfusion, antibiotic, mannitol, and steroid (dexamethasone 4 mg intravenous 8 hourly with gradual tapering). The patient was also started with a tablet of thyroxin 50 mcg daily and a tab of cabergoline 0.5 mg half tablet weekly. He responded well to the conservative treatment with improvement in oxygen saturation and sensorium and started to take orally on the 5th day of admission. The patient was discharged with a prescription of thyroxine 50 mcg peroral daily, prednisolone 5 mg peroral daily, and tab cabergoline 0.5 mg half tablet peroral weekly. A follow-up visit after two weeks showed significant improvement in clinical condition with residual left-sided hemiparesis.

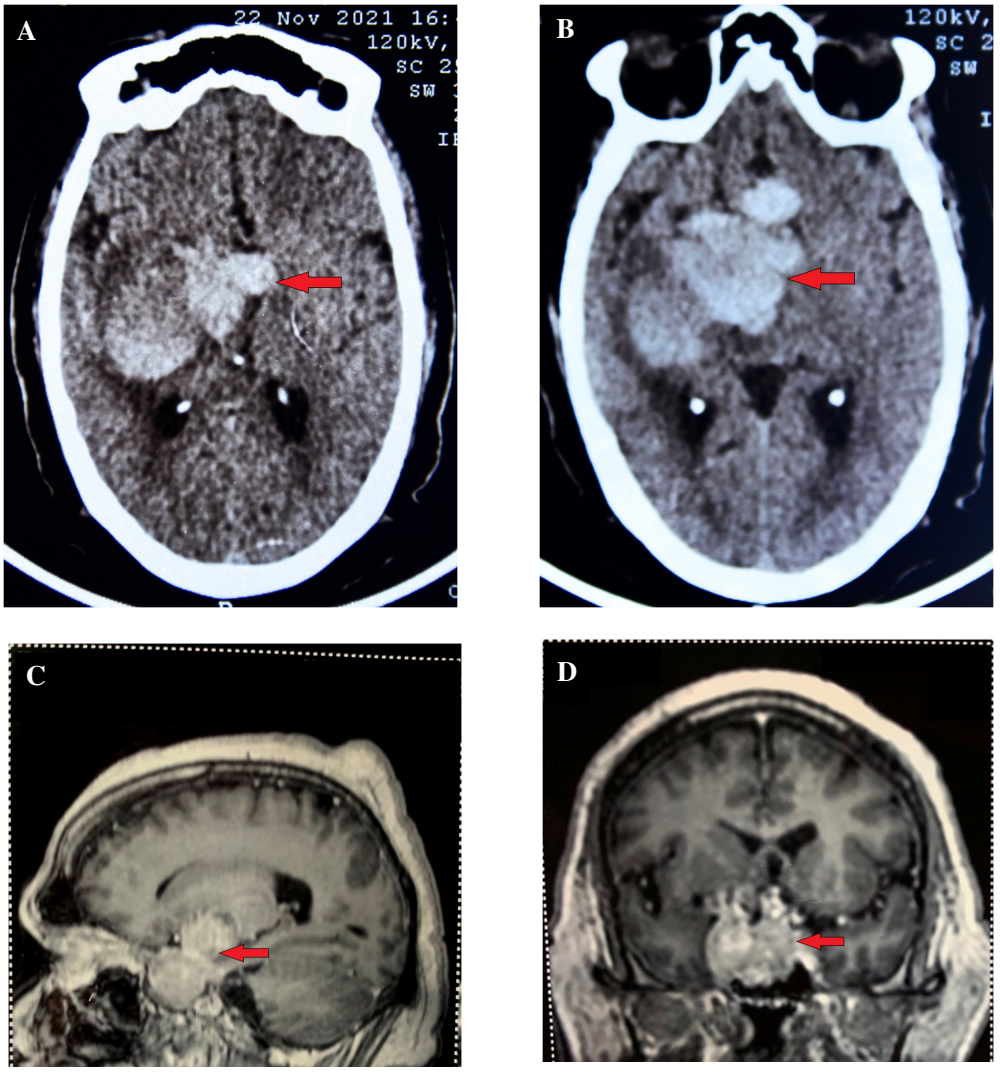

Figure 1. A & B: T1W magnetic resonance imaging of brain sagittal and coronal section showing lobulated sellar-suprasellar mass (35 mm× 60 mm × 55 mm) suggestive of pituitary macroadenoma (arrows). C & D: Non-contrast computed tomography head showing iso to hypodense mass (28 mm× 41 mm× 42 mm) mass suggestive of pituitary macroadenoma with intratumoral hemorrhage and right temporal and capsulo-ganglionic (36 mm× 38 mm) hemorrhage (arrows).

Table 1. Summary of cases of pituitary apoplexy induced by dengue hemorrhagic fever.

Authors and year	Ref	Age/ Sex	Clinical manifestations	Platelet counts (cells/mm^3)	Hormonal profiles	Imaging	Management	Follow–up
Tan *et al*. (2014)	[1]	53/M	Acute onset left 3rd, right 6th cranial nerves palsy, right temporal hemianopia	16000	Hyperprolactinemia, thyrotropin, and gonadotropin deficiency	37 mm×24 mm×31 mm hemorrhagic pituitary adenoma with bilateral cavernous sinus extension	Transsphenoidal surgical decompression (two surgeries)	Prolactin normalized, other pituitary hormones deficits and right eye visual defects persist
Wildenberg *et al*. (2012)	[2]	40/M	Headache, vomiting, features of acromegaly	98000	Acromegaly, hypogonadotropic hypogonadism	Intrasellar mass with areas of bleeding	Transsphenoidal surgery 20 d after apoplexy	Acromegaly persists, other hormones normal
Wildenberg *et al*. (2012)	[2]	38/M	Prolactinoma on cabergoline presents with bitemporal hemianopia	79000	Hypogonadism, prolactin decreased on cabergoline	Pituitary mass with areas of bleeding	Transsphenoidal surgery	Visual field defects improved, hypogonadism persist
Kumar *et al*. (2011)	[3]	31/F	Vision loss, headache, vomiting	45000	Hypothyroidism	Pituitary macroadenoma (16 mm×22 mm) with acute bleeding	Transsphenoidal decompression of tumor	Residual bitemporal field defects
Mishra *et al*. (2015)	[4]	43/M	Headache, vomiting, diminished vision	47000	Normal hormonal profile	23 mm×21 mm×20 mm sellar and suprasellar mass with bleeding	Urgent transsphenoidal decompression of tumor	Visual acuity improved, residual visual field deficits
Balaparame-swara Rao *et a*l. (2016)	[5]	45/M	Severe headache, vomiting, and loss of conciousness	27000	Normal hormonal profile	Pituitary apoplexy (sellar and suprasellar lesion) and obstructive hydrocephalus	External ventricular drains for hydrocephalus; follow by trans-sphenoidal decompression	Vision normal. Anterior pituitary deficits present
Sree Harsha Varma *et al*. (2017)	[6]	39/F	Fever, melena, vision loss, altered sensorium	11000	Hypothyroidism, Hypogonadotropic hypogonadism	Pituitary adenoma with apoplexy	Urgent decompression of tumor	Symptoms subsided
Singh *et al*. (2018)	[7]	48/F	Fever, headache, vision loss	17000	Hypothyroidism, low prolactin	Pituitary apoplexy (sellar and suprasellar lesion)	Transsphenoidal decompression of tumor	Visual acuity improved, hypocortisolemia persist
Thomas *et al*. (2019)	[8]	85/M	Fever, headache, right 3rd cranial nerves palsy, altered sensorium	9000	Low FT4, cortisol and prolactin	Pituitary macroadenoma (24 mm× 22mm) with apoplexy	Medical management (Thyroxine, steroid)	Drastic improvement
Present case (2022)	-	58/M	Fever, headache, altered sensorium, left-sided hemiparesis	21000	Low cortisol, low FT4, and high prolactin	Pituitary macroadenoma (28 mm× 41 mm×42 mm) with apoplexy	Medical management (Thyroxine, steroid)	Improvement with residual left hemiparesis

3. Discussion

We report a case of PA in a 58-year-old male due to dengue fever-induced-thrombocytopenia. PA is a catastrophic disorder manifested as a sudden onset of intrapituitary hemorrhage and/or infarction, generally within a pre-existing pituitary tumor[9]. The incidence of PA in pituitary tumors is about 2%-12% around the world[9]. The important risk factors for PA are cerebral angiographic procedures, systemic hypertension, surgeries, head injury, coagulopathies, and drugs (gonadotropin-releasing hormoneanalogs, dopamine receptor analogs, *etc*.)[10]. The proposed pathophysiology for PA include reduced blood flow resulting in infarction, acute increase in blood flow, stimulation of the pituitary gland from dynamic tests, and coagulopathies from thrombocytopeniaor anticoagulation[9].

Our patient had dengue fever-induced-thrombocytopenia, which precipitated apoplexy. In dengue hemorrhagic fever and dengue shock syndrome, hypotension and hypovolemia may trigger apoplexy in patients with pre-existing pituitary adenoma[2].

The clinical presentation of PA is highly variable and is largely depending on the extent of hemorrhage, necrosis, and edema. Clinical manifestations include headache, nausea, vomiting, diminished visual acuity, visual field defects, ocular paresis, and altered mental status[9]. Our patient presented with headache, altered sensorium, and left-side hemiparesis. PA is an endocrine emergency and the most common hormonal deficiency is corticotrophin deficiency, occurring in up to 80% of cases, resulting in severe hemodynamic instability and hyponatremia[10]. PA can also result in other hormonal deficits like growth hormone, thyrotropic, and gonadotropic deficiency[9]. A comparison of the present case with previously reported cases of dengue fever-induced PA is shown in Table 1.

Computed tomography brain is a suitable choice of imaging. PA can be managed both conservatively and by surgical debridement as per the UK guideline suggests[9]. Medical management is aimed at hemodynamic stabilization, correction of electrolyte imbalance, and parenteral steroids to correct secondary adrenal insufficiency that occur from acute corticotrophin deficiency[9,10]. PA is an endocrine emergency and glucocorticoid should be started immediately to prevent hemodynamic instability, neurological complications, and mortality[10]. Transsphenoidal surgical decompression should be considered if the patient has a progressive neuro-ophthalmic deficit and deterioration of consciousness[9,10]. Our patient was managed medically with supportive treatment including steroids and thyroxine and showed significant improvement with residual left-side hemiparesis.

In conclusion, dengue hemorrhagic fever-induced PA is rare and requires a high index of suspicion. Clinicians should strongly suspect PA in patients with or without pituitary adenoma and dengue hemorrhagic fever who develop a rapid onset of severe headache and neuro-ophthalmic deficit and should be managed urgently to prevent adverse clinical outcomes.

Conflict of interest statement

The authors report no conflict of interest.

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Authors' contributions

HRN: concept, design, intellectual content, literature search, data acquisition, manuscript preparation; RA: literature search, editing, and review; BM: intellectual content, data acquisition; RPA: clinical studies, data acquisition, manuscript editing, and review.

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