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Case Report

Internal Medicine Section

Empty Sella Syndrome with Typical Facies: A Case Report

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ABSTRACT

Empty Sella syndrome with typical facies is a rare presentation of panhypopituitarism. Here, authors presented a case of 45-year-old male with a history of altered behaviour such as low mood, passivity, talkativeness with low-hoarse voice and spells of cries for three months. He also had headache, vomiting, abdominal pain, ataxic gait, and loss of libido. He had meningitis 10 years back since then he had multiple similar episodes. He had sparse thinned out hair, male pattern temporal balding, madarosis, brownish pigmentation of face and chest and dry coarse skin. Patient had hypotension but without hypoperfusion. Hormone levels including thyroid hormones, Follicle Stimulating Hormone (FSH), Luteinizing hormone (LH), total testosterone cortisol, and plasma Adrenocorticotropic Hormone (ACTH) were less than normal. Magnetic Resonance Imaging (MRI) brain suggested streak pituitary gland (empty sella). He was supplemented with required hormones. On follow-up, he improved significantly. Trio composite hypothyroidism, hypocortisolism, and hypogonadism have characteristic facies. This unique presentation of patient with blank look facies gives a hint of empty sella, thus leading the clinician to diagnose the disease through timely evaluation and work-up.

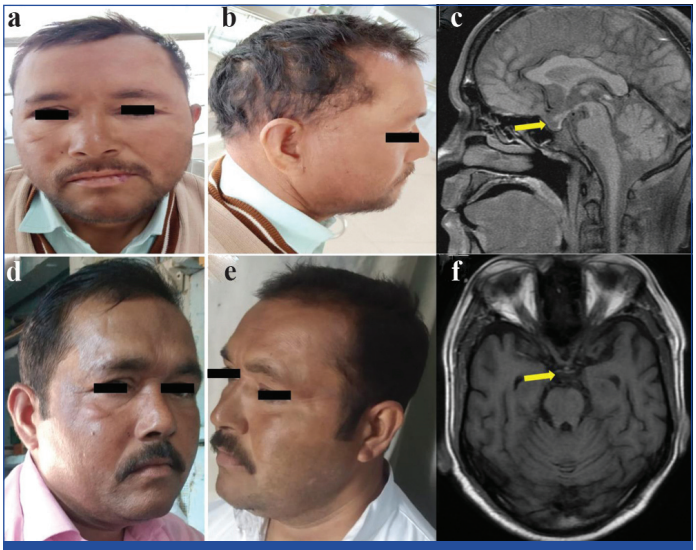
Keywords: Adrenal crisis, Hypogonadism, Hypothyroidism, Panhypopituitarism

CASE REPORT

A 45-year-old male presented with altered behaviour since three months in the form of low mood, increased talkativeness, spells of cries and loss of appetite. He also had a dull aching, holocranial, persistent headache for three months, worsened on lying down and gets temporarily relieved with oral analgesics i.e. 650 mg of acetaminophen in morning hours. Projectile vomiting occurs when the intensity of the headache increases. He had dull aching diffuse intermittent abdominal pain in all quadrants unrelated to food intake that increased three days prior to the initial presentation. He had a gait with a wide stance, slowing of speech and hoarseness of voice for one month. He also had a past history of orbital infection followed by meningitis 10 years back since which he had three similar episodes of altered behaviour with headache, each episode lasting for a duration of 3-5 months for which he took ayurvedic medications. In between these episodes, he led a normal social life except for the loss of libido. His illness was not properly evaluated until now and he was taking homeopathic and indigenous medications on worsening of symptoms. There was no history of diabetes, hypertension, any other co-morbidities or addictions. He was married for 15 years with two healthy kids. There was no history of similar illness in the family.

On examination, he was conscious, oriented with delayed response to commands. His vitals were as follows: pulse rate was 110 beats/minute, regular and low volume Blood Pressure (BP) of 60/30 mmHg with saturation maintained at room air. On head to toe assessment, he had sparse thinned out hair, male pattern temporal balding, madarosis, dry coarse skin with brownish pigmentation on face and chest [Table/Fig-1a,b]. Systemic examination including per abdominal examination was unremarkable except for an ataxic gait with a wide stance. From the brief history and general examination findings, a possibility of myxoedema coma was kept. But the detailed history was suggestive of co-existing hypogonadism.

His routine blood investigations were done, which was suggestive of normocytic normochromic anaemia (haemoglobin was 7.3 mg/dL) with pereipheral smear showing normocytic normochromic picture, leukocyte count were 4.12×10^9/L, platelets were 1.48×10^9/L with normal liver and kidney functions and mild hyponatremia (130.2 mmol/L). Hormonal profile was suggestive of multiple pituitary hormone deficiencies with FSH was 1.07 (normal range, 1.4-19.3 IU/mL), LH was 0.31 (1.5-9.3 IU/mL), total testosterone was <0.2 (8.4-28.7 nmol/l), Thyroid Stimulating Hormone (TSH) 1.34 (0.4-3.8 microU/mL), free Triiodothyronine (T3) <1 (4-7.4 pg/L), free Tetraiodothyronine (T4)- <0.4 (0.7-1.9 ng/dL), cortisol at 8 AM was 1 (10-20 mcg/dL), plasma ACTH 9.68 (10-46 pg/mL). This was suggestive of panhypopituitarism. MRI brain with a focus on pituitary fossa suggested absent pituitary gland [Table/Fig-1]. A final diagnosis of panhypopituitarism with Addison's crisis probably as a sequel of meningitis was kept.



[Table/Fig-1]: Face and MRI images of empty sella syndrome case. (a) and (b) shows typical hypothyroid facies with a blank look in a case of panhypopituitarism. (d) and (e) shows normal facies after starting hormonal treatments. (c) and (f) shows sagittal and axial sections of brain MRI T1 images depicting typical empty Sella (arrows).

Symptomatic treatment, Intravenous (IV) fluids, and inotropes were started accordingly along with hydrocortisone 50 mg 6th hourly and thyroxine 75 microgram daily based on clinical suspicion of myxoedema and adrenal crisis. After confirmation of panhypopituitarism, he had continued thyroxine and hydrocortisone 50 mg 6th hourly during hospitalisation. During discharge, methylprednisolone 32 mg daily was continued and then tapered off over next eight weeks by reducing the dose to half every two weeks along with thyroxine

75 microgram daily for six months and testosterone (testosterone enanthate 100 mg Intramuscular (IM) once weekly) for six months. The initial symptomatic treatment with antipsychotic risperidone 0.5 mg once daily for seven days was later withdrawn after steroids and hormone supplementation and after recovery of the symptoms. He was discharged in stable condition. He was clinically improved in the following visits, especially the typical face of hypopituitarism changed to normal face, libido has improved, and has completely normal mentation [Table/Fig-1d,e].

DISCUSSION

Empty Sella is a radiological finding when Cerebrospinal Fluid (CSF) fills the Sella turcica and pituitary gland tissue is limited to the sellar walls and floor [1]. It constitutes signs and symptoms, suggestive of single pituitary hormonal deficit to panhypopituitarism depending on the extent of compression. Thus, a patient can present with acute adrenal insufficiency or profound hypothyroidism, with symptoms suggestive of pituitary mass lesion or sometimes with non specific symptoms like fatigue and malaise [2]. Among the various aetiologies, of late, infectious/inflammatory conditions are increasingly being recognised [3]. Pituitary tumours are the most common cause (61%) of empty Sella; infectious diseases are a relatively rare cause. But the most common long-term complication of meningitis is sensory neural hearing loss, not empty sella syndrome [4]. Panhypopituitarism, a well-known, yet rare, acute as well as chronic sequel of meningitis, but empty sella syndrome, secondary to meningitis has been studied only in a few case reports [5].

Hypothalamic-pituitary dysfunction is a well-recognised complication of acute infectious diseases of the central nervous system (meningitis and encephalitis), which may occur in the acute phase or in the late stage [6]. In this case study, MRI brain and sella revealed most of the sella filled with CSF. The pituitary gland appeared to be thinned out with concave upper borders, characteristics of empty Sella turcica [7]. Metadata shows that only less than 1% of individuals with empty sella present with symptoms and the majority are men [8]. Thus present case falls into that rare category of an adult male presenting with panhypopituitarism, mostly due to empty sella turcica, which was postulated to be due to the sequel to meningitis that patient developed 10 years earlier. A review of the literature was done, which is described in detail in [Table/Fig-2] [4,5,7,9-22] on the development of hypopituitarism and Empty Sella syndrome as a sequel to meningitis in adults, which revealed that hypopituitarism is well-known, yet rare manifestation and sometimes considered as a post-encephalitic syndrome, as adequate hormonal work-up is not done in follow-up period. However, the literature only revealed one similar case report of empty sella as a sequel to meningitis in one Japanese patient [4].

Serial No.	Publication year	Citation	Type of study	Age (years/ Mean±SD)	Clinical findings	Duration from meningitis	Conclusion
1	1968	Summers VK et al., [9]	Case report	20	Hypopituitarism	14 years	Hypopituitarism can develop long after Tuberculosis meningitis.
2	1969	Haslam RH et al., [10]	Case report	17	Hypopituitarism	12 years	Intracranial calcification in hypothalamic or pituitary tissues after recovering from tuberculous meningitis, may results in various endocrine disturbances.
3	1978	Hägg E et al., [11]	Case report	43 and 53	Panhypopituitarism	Both case: 3 year	Endocrine insufficiency should not be misinterpreted as an ordinary post meningoencephalitic syndrome.
4	1980	Kupari M et al., [12]	Case report	23, 39 and 54	Hypoglycaemia, hypocortisolism, and GH deficiency	First case: 3 year, Second, Third case: 3 days	Hypopituitarism may not only appear in the very acute stage of the illness but also much later. Recognition of this rare complication of meningoencephalitis may be of vital importance to the patient.
5	1984	Ew K et al., [13]	Case report	53	Panhypopituitarism	7 days	CT during meningitis may show inflammatory changes in pituitary –hypothalamic area raising suspicion of pituitary dysfunction.
6	1989	Muraoka A et al., [5]	Case report	58	Panhypopituitarism	At presentation	Acute meningoencephalitis can present with Empty Sella syndrome.
7	2001	Ogunrin AO et al., [4]	Case report	15	Empty sella syndrome with CSF rhinorrhoea	5 years	Empty Sella syndrome can present as long term sequelae of complicated meningitis.
8	2008	Tanriverdi F et al., [14]	Prospective study	35.3±13.3	(28.6%) had isolated GH deficiency	Mean: 20 months	Pituitary dysfunction is a more common sequel of acute bacterial or viral meningitis, but large study to be done for prevalence analysis.
9	2010	Dhanwal DK et al., [7]	Prospective study	28.4±10.3	Hypocortisolism (42.7%), (30.7%) central hypothyroidism, hyperprolactinemia (49.3%)	At presentation	Hypothalamic-pituitary hormonal dysfunction is common in newly diagnosed patients with tubercular meningitis.
10	2010	Tsiakalos A et al., [15]	Prospective study	38±15.2	Isolated corticotropic deficiency-12.5%, isolated somatotropic deficiency 6%, both corticotropic and somatotropic deficiency 12.5%	12 months	Isolated or combined pituitary deficiencies, which could present at the acute phase and/or occur at a later stage, can develop in a considerable proportion of patients after infectious meningitis.
11	2011	Dhanwal DK et al., [16]	Prospective case series	28.97±11.306	Adrenal insufficiency (23.3%), hyperprolactinemia (30.0%), hypogonadism (23.3%)	At presentation	Hypothalamic-pituitary hormonal dysfunction is not uncommon in newly diagnosed patients with acute nonmycobacterial meningitis.
12	2012	Tanriverdi F et al., [17]	Prospective study	40.9±15.9	GH deficiency (42.8%), ACTH deficiency (7.1%), FSH/LH deficiency (7.1%), combined FSH+GH (28.6%), GH+ACTH (14.3%)	12 months	Risk of hypopituitarism, GH deficiency in particular, is substantially high in the acute phase, after 6 and 12 months of the acute infectious meningitis.

13	2013	Spinner CD et al., [18]	Case report	46	Panhypopituitarism	2 weeks	Neurosyphilis can present with pan hypopituitarism, syphilis exclusion strongly recommend in HIV-patients.
14	2019	Malik S et al., [19]	Retrospective descriptive study	53.8 ± 14.7	Hypopituitarism	2.7 years	Tuberculosis can be a rare cause of empty Sella syndrome.
15	2019	Kim Y et al., [20]	Case report	45	Panhypopituitarism	2 weeks	The clinical presentations of hypopituitarism are usually non specific and the recognition of these patients remains the challenge, and it can develop over a varying time period depending on aetiology.
16	2019	Agrawal VM and Giri PJ [21]	Case report	40	Headache, decreased vision, 3rd cranial nerve palsy	3 months	CNS tuberculoma, to be kept as differential in panhypopituitarism.
17	2020	Jalil F et al., [22]	Case report	65	Panhypopituitarism,	3 months	Patients with pituitary abscess and meningitis can develop acute deterioration and panhypopituitaris, and require long term hormone replacement.
18	2021	Present case	Case report	45	Panhypopituitarism	3 months	Characteristic blank look facies gives a hint of empty sella.

[Table/Fig-2]: Review of literature involving hypopituitarism being a sequel of meningitis in adults.
GH: Growth hormone; CNS: Central nervous system; CT: Computed tomography; ACTH: Adrenocorticotropic hormone; FSH: Follicle-stimulating hormone; LH: Luteinizing hormone; HIV: Human immunodeficiency virus

Clinical manifestations of hypopituitarism are variable dependent on the degree and severity of hormone deficiency. As it is associated with increased mortality and morbidity early diagnosis and prompt treatment are necessary. The facial features in panhypopituitarism are not described in the literature. Typically in isolated hypothyroidism, dry, pale, and cold skin due to decreased capillary flow, sweating, and thermogenesis; thick skin, periorbital oedema, and mucosal thickening (macroglossia) with dysphonia due to generalised myxoedema or cutaneous mucinosis due to the accumulation of hyaluronic acid and glycosaminoglycans in the skin; and permanent alopecia, thinned hair, and lateral loss of eyebrows due to keratosis pilaris of follicles; all these cause the characteristic hypothyroid facies, which were evident in present study. Simultaneously, palmoplantar keratoderma, which may become generalised and convert into xeroderma is also part of hypothyroidism [23]. Hypocortisolism patients usually have poor skin turgor, increased skin pigmentation, and neuropsychiatric presentations [24]. Similarly, male hypogonadism presents with temporal hair recession, fine facial wrinkles, deep voice, depressed mood, increased irritability, difficulty concentrating, lack of masculinity, reduced energy and stamina, and loss of libido [25]. If all facial features are combined it looks more often like a 'blank look'. All features dramatically respond to replacement therapy. Long-term endocrinological follow-up of hypopituitarism patients is important to monitor hormonal replacement regimes and to avoid under or over-treatment [26].

CONCLUSION(S)

Panhypopituitarism due to empty sella turcica is a rare long term sequel of meningitis. Characteristics facies of the blank look may give a hint of empty sella. With proper supplementation of hormones, the symptoms are completely reversible including loss of libido.

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