

Case Report

Hyperprolactinaemia in a Patient with Acute Ischaemic Stroke

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Abstract - This is a case report of a 47-year old man with an unknown medical illness, presented with neurological deficits typical of clinical stroke. The Magnetic Resonance Imaging (MRI) findings were an acute left middle cerebral artery (MCA) territory infarction and an incidental finding of a sellar mass likely pituitary origin. The pituitary hormones showed markedly hyperprolactinaemia with the level of 21146 ng/ml (n 4.04 – 15.2 ng/ml), low Follicle-stimulating hormone (FSH) with a level of 0.929 IU/L (n 1.5-12.4 IU/L), and low luteinizing hormone (LH) with a level of 1.11 IU/L (n 1.7-8.6 IU/L). Other investigations of serum cortisol, growth hormone (GH), thyroid-stimulating hormone (TSH), platelet count and coagulation profiles were normal. The patient was treated conservatively in the ward for acute ischaemic stroke and later was started on dopamine agonist cabergoline for hyperprolactinaemia.

Key words-- Pituitary, prolactin, macroadenoma, stroke.

I. INTRODUCTION

Hyperprolactinaemia is a condition of raised prolactin level in blood due to functional or physiological, pathological, factitious or analytical, and idiopathic in origin. It is defined as the fasting level of serum prolactin above 20 ng/ml in men and above 25 ng/ml in women at least 2 h after waking up [1]. Physiological hyperprolactinaemia level, for example, during pregnancy or lactation, physical exertion, hypoglycaemia, sexual intercourse, and high protein diets, are typically less than 50 ng/ml [1]. Serum prolactin level 500 ng/ml and above is diagnostic of a macroprolactinoma [1]. This present report describes the unusual, very high

prolactin in a patient presented clinically with acute ischaemic stroke.

II. CASE

A 47-year-old Malay gentleman with no known medical illness previously, non-smoker, noted by family members showing a sudden onset of right-sided body weakness. It was associated with facial asymmetry, inability to talk and ambulate. However, he was still able to understand the conversation and obey simple commands. Otherwise, there was no clinical manifestation of hyperprolactinaemia, no fever, and no trauma. He is single and mentally challenged

since young but still independent. There is no history of substance abuse.

On examination, Glasgow Coma Scale was 11/15 with Eye of 4, Verbal of 1, Motor of 6, pink, not tachypnoeic, pupils were reactive bilaterally, and hydration was fair. His vital signs, especially blood pressure (BP), were unstable with a BP of 244/142 mmHg, heart rate of 82 beats per minute with a regular rhythm, respiratory rate of 17 breaths per minute, afebrile with good oxygenation with SPO₂ of 99% under room air. Neurological examinations showed expressive aphasia, right hemianopia, right facial nerve palsy, and absence of gag reflex. Cerebellar signs were negative. Motor function examinations of right upper and lower limbs showed hypertonia, power of 2/5, normal reflexes, and upgoing plantar response. Sensory functions of the right upper and lower limbs were reduced.

The blood investigation results are presented in Table 1.

TABLE I
BLOOD INVESTIGATION RESULT(S) AND COMMENT(S)

Test	Result	Reference interval	Comment
*Prolactin	21146	4.04-15.20 (ng/ml)	Markedly elevated
*FSH	0.929	1.5-12.4 (IU/L)	Low
*LH	1.11	1.7-8.6 (IU/L)	Low
*Testosterone	0.15	8.64-29.0 (nmol/L)	Low
Total protein	85	65-83 (g/L)	Slightly elevated
Albumin	45	38-44 (g/L)	Slightly elevated
Sodium	135	135-145 (mmol/L)	Lower limit of normal
Potassium	3.5	3.5-5.0 (mmol/L)	Lower limit of normal
Uric acid	105.9	210-420 (umol/L)	Low
Triglycerides	2.09	< 1.7 (mmol/L)	Elevated
Total cholesterol	9.11	3.6-6.3 (mmol/L)	Elevated
Low-density lipoprotein (LDL)	7.27	< 2.6 (mmol/L)	Elevated
High-density lipoprotein (HDL)	0.89	< 1.04 (mmol/L)	Low
HbA1c	9.6	< 6.5 (%)	Uncontrolled
Renin activity	18.55	Supine early morning: 0.32-1.84 (ng/ml/h) Upright 2 h: 0.60-4.18 (ng/ml/h)	Elevated
Aldosterone	227.8	Supine: 33.24-436.28 (pmol/L) Upright: 36.84-641.00 (pmol/L)	Normal
Erythrocyte sedimentation rate (ESR)	78	1-15 (mm/60 min)	Elevated
C-reactive protein (CRP)	35	< 10 (mg/L)	Elevated

*Investigated following MRI findings.

Other investigations such as full blood count, coagulation profiles, liver enzymes, renal function, serum osmolality, urine osmolality, thyroid function, cortisol, GH, and Venereal Disease Research Laboratory (VDRL) were normal.

The Magnetic Resonance Imaging (MRI) scan showed left middle cerebral artery (MCA) territory infarction with an aggressive sellar mass likely pituitary origin measuring 3.5 cm x 4.7 cm x 4.9 cm. No evidence of left MCA compression by the mass. No evidence of haemorrhage (Figures 1 and 2).

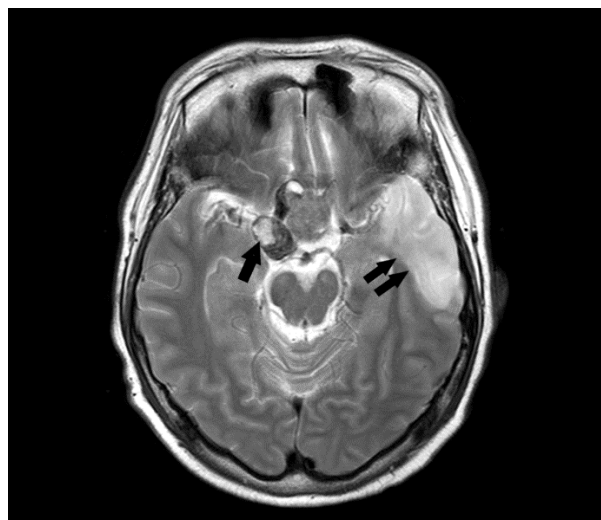


Fig 1. MRI image (axial view) showing sellar mass (single arrow) and left MCA territory infarction (double arrow).

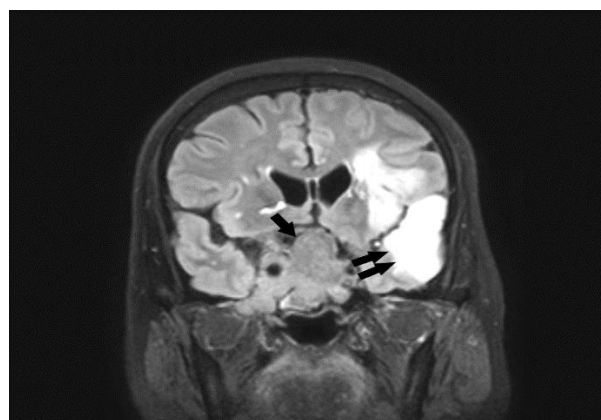


Fig 2. MRI image (axial view) showing sellar mass (single arrow) and left MCA territory infarction (double arrow).

The Polyethylene Glycol (PEG) precipitation was used to screen for macroprolactinaemia. The result is presented in Table 2.

TABLE 2.
PERCENTAGE OF RECOVERY POST PEG PRECIPITATION RESULT
AND COMMENT.

Test	Result (%)	Reference [2] (%)	Comment
Percentage of recovery post PEG precipitation	45.8	<40 predominant macroprolactin	Indeterminate
		>60 predominant monomeric prolactin	
		40-60	
		indeterminate	

III. DISCUSSION

A prolactinoma is suggestive if the serum prolactin level is greater than 250 ng/ml. A level of 500 ng/ml or greater is diagnostic of a macroprolactinoma [1]. Drugs, for example, risperidone and metoclopramide, may cause raised prolactin levels above 200 ng/ml [1]. Among the causes of hyperprolactinaemia, pituitary tumours account for 50% of cases and required thorough investigations [1]. Macroprolactinaemia, which is the factitious or the analytical cause of hyperprolactinaemia, needs to be ruled out in patients with a lack of clinical symptoms. This form is biologically inactive and does not require treatment [1][2]. PEG precipitation was done in this patient to screen for macroprolactinaemia. However, the result was indeterminate, while confirmation using Gel Filtration Chromatography (GFC) method is required [2]. Unfortunately, the GFC method is not available in the setting of this case. Thus, the presence of macroprolactinaemia, in this case, is still possible.

Studies show that prolactin levels are significantly increased in stroke patients in comparison with control subjects (without a past history of ischemic vascular disease) with the value of 11.8 and 6.6 ng/ml, respectively [3]. Thus, the macroprolactinoma must be considered as a differential in this case. A macroprolactinoma is a prolactinoma measuring more than 1 cm in size, commonly occurs in man as an incidentaloma, and typically associated with serum prolactin level of 500 ng/ml and greater [1][4] as occurred in this case. The prolactin level reported in this case was 21146 ng/ml, approximately 2 to 4 times above the levels of previously published case reports of prolactinoma and stroke, which were 8997 ng/ml [5] and 4700 ng/ml [6], respectively. The size of the tumour generally determines the degree of prolactin secretion [6]. The larger the tumour size, the greater the prolactin secretion. Macroincidentalomas were reported in 0.2% of patient underwent Computerized Tomography (CT) or MRI scans for central nervous symptoms (CNS) [4].

Hyperprolactinaemia is also a predisposing factor to thrombosis based on various studies [3][7]. Thus, there is a possibility that the marked hyperprolactinaemia in this patient leads to the occurrence of ischaemic stroke confounded by uncontrolled diabetes mellitus (elevated HbA1c), hypertensive emergency and hyperlipidaemia (lipid profiles showed predominant hypercholesterolaemia).

Another possibility of cerebral ischaemic or infarction in this case is pituitary apoplexy (PA), but the incidence is rare.

PA is defined as a rare endocrine emergency due to infarction or haemorrhage of the pituitary gland and is mostly associated with a pituitary adenoma [8]. The incidence of apoplexy in pituitary adenoma is between 1 and 26%, while the PA is the first presentation of an underlying pituitary tumour in 80% of patients [8]. The major neurological signs in the case of PA causing cerebral infarction are hemiplegia (52.2%), facial paralysis (10.9%) and dysarthria (13%) [9]. The MCA is the affected cerebral blood vessel in 25% of cases [9]. The main pathophysiological mechanisms include the compression of cerebral blood vessels by the pituitary tumour and vascular spasm secondary to tumour haemorrhage [9]. The diagnosis can be confirmed by clinical symptoms and imaging, particularly CT or MRI [9]. This case showed all the neurological signs with evidence of MCA territory infarct. However, no evidence of MCA compression by the pituitary tumour and no evidence of the tumour haemorrhage on MRI examination; thus, PA was less likely.

This patient previously was mentally challenged, which suggests the possible occurrence of CNS lesion causing cognitive impairment. However, previously no clinical manifestation of hyperprolactinaemia and the patient was unmarried, therefore unable to justify any fertility issue. Prolactinoma patients suffer from cognitive impairment, especially executive and memory functions, mainly due to endocrine disorders caused by functioning prolactinoma rather than the tumour mass effect [10].

Follicle-stimulating hormone (FSH) and luteinizing hormone (LH) levels were low in this patient due to suppression of gonadotropin-releasing hormone (GnRH) secretion from the hypothalamus by prolactin. Low LH level leads to low testosterone level as LH is responsible for stimulating testosterone production from the Leydig cells of the testes. Low endogenous levels of testosterone may be related to reduce cognitive ability [11][12]. In the brain, testosterone can be metabolized to dihydrotestosterone and bound to androgen receptors, or it can be converted to oestradiol by the enzyme aromatase. Both androgen and aromatase receptors are found in the brain's key regions, which involve learning and memory [11]. Other anterior pituitary hormones, for example, growth hormone (GH) and thyroid-stimulating hormone (TSH), were normal in this case.

Sodium and potassium levels in this patient were at the lower limit of the reference range. Hyponatremia in stroke patients can be due to Syndrome of Inappropriate Anti-diuretic Hormone (SIADH) or Cerebral Salt Wasting Syndrome (CSWS) [13], dietary restriction or diuretic induced. Hypokalaemia is also a common electrolyte imbalance in stroke patients [14]. Serum potassium is associated with an increased incidence of stroke as it serves as a marker for sodium consumption [15]. High sodium consumption, which is a risk factor for hypertension, will lead to low aldosterone release and thus result in hyperkalaemia [15]. Hyperkalaemia, in turn, will cause cardiac arrhythmia, which is a risk factor for cerebral embolism. This patient showed normal urine sodium concentration, normal serum and urine osmolality, and clinically no hyper or hypovolemic state features, making the diagnosis of SIADH or CSWS unlikely. The possible

explanation for the serum sodium and potassium levels in this patient was secondary to dietary restriction as a measure to control hypertension [13].

The uric acid level was reduced in this patient. This can be due to poor intake of purine during food post brain injury. However, total protein and albumin levels were slightly increased in this patient. High serum albumin level in acute stroke patients decreases the risk of poor outcomes [16]. Hyperreninaemia with normal aldosterone, in this case, was due to a hypertensive emergency. Elevation of both Erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) were secondary to the inflammatory process.

In our case, the incidental finding of a pituitary mass during a clinical stroke presentation is a challenging process, with no prior hyperprolactinaemia manifestation. Therefore, a multidisciplinary approach is required in the management of this patient. A non-functioning pituitary adenoma is a more accurate diagnosis for this patient as he was asymptomatic. The patient was treated conservatively in the ward for acute ischaemic stroke, and later dopamine agonist cabergoline was used for hyperprolactinaemia. Cabergoline treatment in macroprolactinomas as the primary therapy is considered effective and successful in normalizing the prolactin level and reducing the size of tumour mass [17]. However, the patient defaulted on the follow-up, and thus, the effects of cabergoline treatment could not be determined in this case.

IV. CONCLUSIONS

This is a case of acute ischaemic stroke in a middle-aged man with significant risk factors (uncontrolled diabetes, dyslipidaemia and hypertension). However, an incidental finding of macroprolactinoma on imaging warrants extended investigations which could incur more cost. Therefore, a multidisciplinary approach is required to decide on the management of markedly raised prolactin without clinical manifestation.

CONSENT TO PARTICIPATE

Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

CONFLICT OF INTERESTS

The authors declare that there is no conflict of interest.

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