Case Report

Hypertensive emergency: A unique manifestation of a pituitary disorder

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ABSTRACT

Acromegaly a common pituitary disorder has significant adverse effects on well-being and survival. The slight increase in the prevalence of hypertension in acromegaly is well known and is proposed to be the direct effects of growth hormone. The hypertension for calculating the prevalence in most series was defined as diastolic more than 100 mmHg, but hypertensive emergency is rarely ever described in the literature. Growth hormone excess has been associated with renal manifestations such as hypercalciuria and nephrolithiasis, but never with renal failure. We present a case referred to a tertiary care nephrology center with malignant hypertension. This is the first case of a patient of acromegaly presenting with hypertensive emergency progressing to malignant nephrosclerosis and renal failure.

Key words: Acromegaly, hypertensive emergency, hypertensive nephrosclerosis

Introduction

Acromegaly is a disease well known for a delay of 7-10 years before a diagnosis is made.[1] The patients are known to present to internists, ophthalmologists, gynecologists, rheumatologists, and even dental surgeons before being taken over by endocrinologists.[2] The incidence of hypertension, but not of coronary artery disease, is increased and the blood pressure may be reduced following successful treatment. The association of hypertension with abnormalities of the renin – angiotensin – aldosterone system is difficult to interpret in acromegaly. The observation of hypertension in acromegaly as an independent indicator of mortality emphasizes the importance of treatment of hypertension in the management of acromegaly. The impact of aggressive treatment of this disorder on the overall mortality of the condition is not able to be evaluated from the present data, but is likely to be substantial.

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Our patient was referred to a tertiary care nephrology center and even underwent extensive investigations for the cause of hypertensive emergency and subsequent renal failure before acromegaly was diagnosed. The possible mechanisms of hypertension and renal involvement in acromegaly are discussed.

Case Report

A 46-year-old soldier presented with fever of 7 days duration and dysuria. His urine output was adequate and he gave no past history of urinary tract infection. However, there was a past history of hypertensive record 10 years ago but he had not been on any medications. He was found to be febrile with proportionate tachycardia and having a blood pressure of 220/120 mm of Hg. The fundus examination revealed changes of grade IV retinopathy [Figure 1]. Urinalysis revealed 6-8 pus cells and 3-4 RBCs per high power field and his creatinine was 4.5 mg/dl. The blood sugar was 120 mg/dl fasting and postprandial 184 mg/dl with glycated hemoglobin (HbA_1C) of 7.2 g/dl. Hemogram and other routine biochemical parameters were within normal limits. He was transferred to a nephrology center as hypertensive emergency with renal failure.

Further evaluation at the nephrology center revealed normal sized kidneys on ultrasound, proteinuria of 720 mg

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in 24 hours and sterile urine on culture repeatedly. With antihypertensives and antibiotics, the creatinine settled to 2.5 mg/dl. 99mTc-dimercaptosuccinate (DMSA) scan showed no evidence of scars and 99mTc-diethylenetriamene pentaacetate (DTPA) scan revealed a GFR of 23 ml/min. Various serological tests done to rule out secondary causes including viral markers (hepatitis B surface antigen, anti-hepatitis C IgM antibodies, anti-HIV 1 and 2 antibodies), connective tissue markers (ANA, anti-dsDNA, c-ANCA, and p-ANCA), and complement levels were all within normal range. MR urography showed no evidence of any structural genitourinary tract abnormality. A Doppler study revealed normal renal arteries. Normal serum catecholamine level and an iodine-131 metaiodobenzylguanidine (MIBG) scan ruled out pheochromocytoma. As a patient of unexplained renal failure with the suspicion of underlying primary renal pathology a kidney biopsy was performed that demonstrated malignant nephrosclerosis [Figure 2a and b]. The ECG and echocardiography revealed evidence of left ventricular hypertrophy.

During repeat clinical examination, a clinical suspicion of acromegaly was raised on the basis of large fleshy and moist hands, subtle prognathism with a prominent occipital protuberance. His voice was also noted to be hoarse. There was no constriction of field of vision. Endocrine assay revealed unsuppressible growth hormone (GH) levels after the glucose tolerance test (basal, 30 minutes and 60 minutes values of 59.4, 59.3, and 41 ng/ml, respectively). The corresponding IGF-1 basal, 30 minutes and 60 minutes values were 370, 372, and 446 ng/ml, respectively. The thyroid function tests and gonadotrophin levels were normal. The calcium level, the calcium – phosphate product, and the serum parathyroid hormone (PTH) levels (adjusted for the GFR) were within normal limit conclusively ruling out the secondary HPTH. A work-up for MEN syndromes was negative including contrast-enhanced computed tomography (CECT) chest/abdomen and colonoscopy. MRI brain confirmed a pituitary macroadenoma of 12 mm size [Figure 3a and b]. The patient was offered trans-nasal, trans-sphenoidal resection of the tumor under GA. Histopathology of the resected specimen was consistent with pituitary macroadenoma. He postoperatively had cerebral salt wasting with polyuria and hyponatremia. He was managed with fluid/salt management; however he did not need vasopressin. Following the surgery the hypertension was better controlled with antihypertensives and levels of GH reversed back to normal. Left radiocephalic AV fistula at 3 months after the first surgery. He still has kidney failure (CKD stage IV) but does not need dialysis.

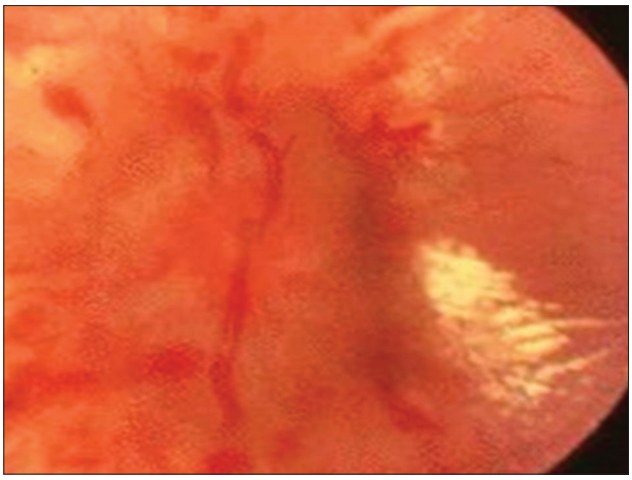

Figure 1: Fundus microphotograph showing grade IV hypertensive retinopathy

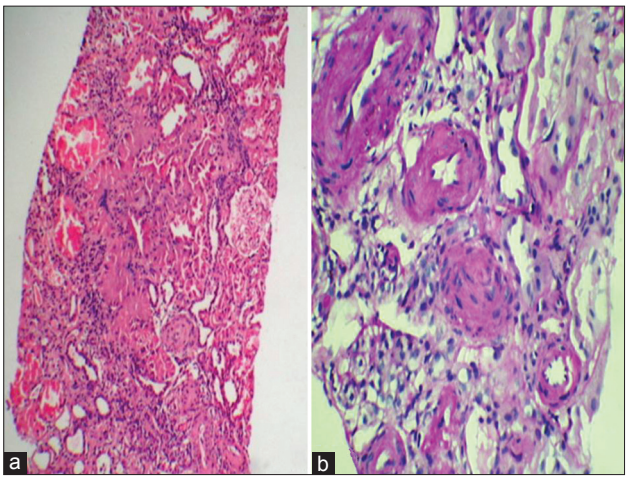

Figure 2: Renal biopsy on histopathological examination revealing normal glomeruli, with no inflammation and sclerosis on low power field (a – ×100) and arteriolar sclerosis. On high power field (b – ×1000)

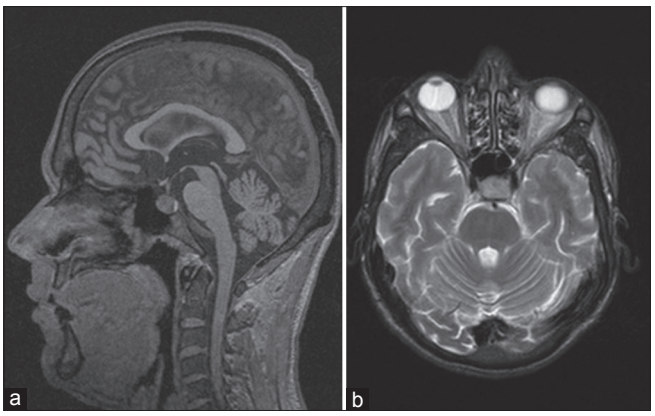

Figure 3: (a and b) Sellar mass on both sagittal and coronal sections suggestive of pituitary macroadenoma with no erosions of sellar margins and no impingement onto optic chiasm

Discussion

Acromegaly is a disorder with an insidious onset and varied clinical manifestations. Well-described esoteric

presentations are visual field defects, dental malocclusion, menstrual irregularities, infertility, osteoarthritis, and cranial nerve abnormalities. Hypertensive emergency leading to renal failure as a presenting feature or consequence of acromegaly has never been described in the literature.

It is common for acromegalics to have high blood pressure (18-60% in different clinical series).[3] Hypertension in acromegaly is ascribed to a direct antinatriuretic action of GH and hyperinsulinaemia and insulin resistance that may be resulting in increased sodium reabsorption with increased sympathetic activity.[4] The contribution of the renin – angiotensin – aldosterone system to hypertension is controversial. A total of 31% of acromegalics have low renin hypertension that is similar to the prevalence in nonacromegalics with essential hypertension. Recent evidence from animal models suggests epithelial sodium channel mediated transport in the distal renal tubule as a direct consequence of GH levels with resulting sodium retention.[5] An increased IGF level results in arteriolar thickening and has been proposed to be another mechanism of secondary hypertension in acromegaly. Hypertension is a serious manifestation of acromegaly and is known to contribute to cardiovascular morbidity and mortality.[6] However, progression of hypertension to malignant nephrosclerosis has not been previously described in acromegalics. The temporal association and the lack of any other underlying renal abnormality strongly argue in favor of an etiological role played by the GH secreting eucortisolic, euthyroid pituitary adenoma in the causation of secondary hypertension. This was further proven by the subsidence of the hypertension on resection of the tumor with return of the GH levels to normalcy.

Kidneys in acromegalics have been documented to have increased longitudinal and transverse diameters, higher creatinine clearance, and urinary calcium excretion, association with microalbuminuria and micronephrolithiasis.[7] Our patient had clear histopathological evidence of the ravages of uncontrolled hypertension on the renal microvasculature. The past history of hypertension, hypertensive retinopathy, and evidence of left ventricular hypertrophy suggest that the patient had long-standing hypertension that went into an accelerated malignant phase. It is possible that the patient had essential hypertension that has taken accelerated course due to the effects of high GH levels. This emphasizes the importance of controlling hypertension in acromegalics.

The patient had symptoms of dysuria and fever at presentation with pyuria; however the culture reports were negative repeatedly. Despite thorough evaluation, no predisposing factor could be found to predispose to infection other than hyperglycemia. Enhanced activation of vitamin D resulting in absorptive hypercalciuria is known to contribute to urolithisiasis.[8] Hypercalcemia is rare and is consequent to associated hyperparathyroidism.[9] Our patient had no evidence of renal stones despite extensive evaluation. Since our patient had evidence of hypercalciuria, the only explanation we can speculate on is that the sterile pyuria may be due to micronephrolithiasis.

Finally, it was a good general examination and sharp clinical acumen that clinched the diagnosis. The unusual presentation with hypertensive emergency, renal failure, and symptoms of urinary tract infection had resulted in expensive investigations and even invasive biopsy to be performed because of the lack of clinical suspicion in the first place.

Conclusion

Hypertensive emergency progressing even to malignant nephrosclerosis can be a rare manifestation of acromegaly. The importance of control of hypertension in acromegalics cannot be overemphasized. Though hypertension is treatable but the secondary effects are rarely reversible. There is no substitute for a thorough unbiased clinical examination in medicine.

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