Case Study

Malignant hypertension in a young male: Sequelae and salvageability

Dilip Gude, Registrar, Internal Medicine, Ratan Jha, Chief, Department of Nephrology, Medwin Hospital, Hyderabad, India. E-mail: letsgo.dilip@gmail.com


Key Words: Malignant hypertension, retinopathy, nephropathy

Abstract
Malignant hypertension is a hypertensive emergency with devastating outcomes and boasts an incidence far more than that reported. Regardless of the etiology (secondary or essential) it has shown overwhelmingly alarming consequences. The end organ damage curtailed can be salvaged at least to a reasonable degree with prompt and aggressive management. We discuss a case of young male diagnosed of malignant hypertension who improved significantly after emergent and aggressive treatment.

Key messages:
Although the outcomes of malignant hypertension are nightmarish for a practicing clinician, immediate and dexterous handling of the case with intravenous and/or oral medications along with targeting the cause (if secondary hypertension) can be lifesaving and may even reverse the associated morbidity.

Introduction:
Malignant hypertension (MH) is a hypertensive emergency occurring in approximately 1% of patients with essential hypertension. It is an entity of significant morbidity and mortality (at-times despite treatment) and poses a major challenge for clinicians. Almost all the organ systems get affected in hypertensive emergencies causing a plethora of manifestations like cerebral infarction (24.5%), hypertensive encephalopathy (16.3%), pulmonary edema (22.5%) and congestive heart failure (12%).¹ Nephropathy following MH is not uncommon (5 and 10 years after presentation with MH, renal survival 84% and 72% respectively).² Malignant hypertensive retinopathy (grade 4) is a prognostic indicator with patients having a 3 year survival of only 6%.³ Prompt diagnosis and aggressive management can curb the irreversible end-organ damage. We discuss a case of MH with a conglomeration of such presentations yet improved considerably after adequate therapy.
Case report
A 23 year old obese male with a history of hypertension diagnosed 3 months ago, not on treatment presented with shortness of breath and blurred vision for 3 days. He gave history of recurrent headaches for which he took NSAIDS repeatedly. On examination his weight was 110kg, Body Mass Index -36.9. Heart rate -82/min, all the peripheral pulses felt equally, Blood pressure-206/160 mm of Hg (right upper limb); 198/150 mm (left upper limb); 190/150 mm (right lower limb),186/146 mm (left lower limb). Pallor was present. Cardiovascular, respiratory and abdominal exam were normal (no renal bruit noted). Examination of the eye revealed visual acuity-6/9 (Right); 6/18 (Left) and fundoscopy showed markedly edematous disc with hyperemia. Arteriolar attenuation, hard exudates, macula edema were also seen (Figure1) suggesting Grade IV hypertensive retinopathy. Arterial blood gas analysis was normal. Labs showed Hb-10 gms/dl, Total WBC-10,500/mm$^3$, Platelets-1.4Lakhs/mm$^3$. Peripheral smear showed normocytic normochromic anemia and no schistocytes were found. Plasma renin activity (basal) was 5ng/ml/h (normal 0.29-3.7ng/ml/h), Plasma aldosterone (supine, on low sodium diet) 25ng/dl (normal 4-45ng/dl), Plasma aldosterone concentration(PAC)/Plasma Renin ratio=5 and 24 hour urinary VMA was 3.8mg/day (normal 2-7 mg/day). Urinalysis showed protein 1+, blood1+, no WBC /casts. Spot protein / creatinine ratio-0.8 (normal <0.2); Serum creatinine-12.2 (normal 0.8 - 1.4 mg/dl) and Urea-220mg/dl (normal 5-20mg/dl); Sodium- 122 meq/l, Potassium -3.7meq/l, Chloride-82 meq/l; TSH -3.1 mIU/L(normal 0.5 -5mIU/L); serum PTH-42pg/ml (10-60pg/ml), serum Calcium -9.2mg/dl (8-10mg/dl). After renal function stabilisation, 24-hour urinary aldosterone level was 8mcg (Normally <12mcg after a salt diet in those without Conn's syndrome). Ultrasonography of abdomen showed grade II renal parenchymal changes; Duplex ultrasound for renovascular hypertension was inconclusive because of obesity. Magnetic Resonance angiography showed no evidence of renal artery stenosis. CT abdomen without contrast showed normal adrenals and normal sized kidneys. Radionuclide scan (technetium-99m-L, L-ethylenedicysteine) showed symmetrical reduction in renal function on either side. CT angiogram showed no evidence of coarctation of aorta. ECG and 2D Echo showed left ventricular hypertrophy. He received three sessions of hemodialysis followed by CT guided kidney biopsy which showed florid myxoid intimal thickening with onion skin skin lesions in interlobular arteries, widespread acute tubular damage, fibrinoid necrosis and glomerular ischaemic changes (Figure 2). He received four classes of antihypertensive drugs (nifedipine 60mg OD, clonidine 0.1mg TID, telmisartan 80mg OD and frusemide 20 mg OD). His blood pressure at the time of discharge was 136/82 mm of Hg. Lifestyle modifications including strict diet and exercise were advised. After 8 weeks his vision along with his renal parameters [S Creatinine -2.3mg/dl, Serum $K^+$ -4mEq/L with normal ABG (no metabolic acidosis)] improved considerably which was sustained at last follow up of 9 months with adequate BP control as well.

Discussion:
Malignant hypertension (MH) is the most severe form of hypertension featuring high blood pressure with target-organ damage in association with bilateral retinal hemorrhages and/or exudates, and papilledema. With newer and more classes of
Impaired endothelial-dependant response to acetylcholine, increased circulating endothelial cells, endothelial progenitors and stiffness may be seen in MH. Ren2 gene mediated renin generation and upregulation of renin and the soluble prorenin receptor sPRR resulting in elevated (Angiotensin) ANG-II may be responsible for the maintenance of malignant hypertension and the associated reduction in renal hemodynamic function.

Glomerular damage (with higher glomerulosclerosis index), increased renal interstitial inflammation (macrophage accumulation) and increased proliferation in cortical tubules and vessels with histopathological evidence of arteriolar fibrinoid necrosis and onionskin lesions (seen in our patient) characterize MH. Although the pathologic appearance of progressive systemic sclerosis (PSS) overlaps with that of MH and thrombotic microangiopathy (TMA), MH tends to involve smaller vessels (afferent arterioles) whereas PSS may extend to interlobular and larger vessels, and TMA typically involves primarily glomeruli. Age, baseline creatinine level and systolic blood pressure are independent predictors of survival (follow up-mean proteinuria is an important renal prognostic indicator).

Before making a diagnosis of essential hypertension, one needs to exclude renal parenchymal diseases (such as glomeronephritis, glomerulosclerosis, systemic sclerosis, nephropathy related to IgA, reflux, diabetes, analgesic use, radiation and lupus), renovascular disease (RVD) and endocrine causes. Our patient was a non-diabetic, with no history of chronic analgesic abuse and urinalysis showing no evidence of glomerulonephritis. His biopsy excluded any form of glomerular or interstitial pathology (renal parenchymal cause of secondary hypertension). The radionuclide study showed no asymmetry of renal function in either kidney (which did not prompt us for a renal angiogram) and hence RVD was not considered. Endocrine workup was not warranted as he sported no cushingoid features, sonography and CT showed no evidence of adrenal abnormality. The work up for hyperaldosteronism was also not considered initially in view of high-renin hypertension. Pheochromocytoma was less likely owing to normal urinary VMA. The apparent hypokalemia at presentation was related to the use of diuretics and uremic vomiting though in the follow up his potassium was normal (4 mEq/L) all along. His arterial blood gases never showed metabolic alkalosis as well which typically characterizes endocrine hypertension. The apparent asymmetry in BP recordings with normal pulse may not be pathological as minor asymmetry in BP could stem from observer/cuff related artifacts and are of less clinical importance. Coarctation/reversed coarctation of aorta were ruled out owing to normal CT angiogram.

**Conclusion:** Malignant hypertension is an entity which needs thorough work up to exclude other secondary causes of treatable hypertension (Table-1). But an extensive battery of testing might not be warranted as clinical and laboratory clues
may help one narrow down to focused and specific tests which may be the need of the hour in resource poor countries. Our case also echoes that management of MH may represent an important remediable facet that apart from evading dialysis dependency in such conditions may result in lasting and significant improvement of renal dysfunction and that the cause of MH may not always be secondary even in the young.

Table-1

<table>
<thead>
<tr>
<th>Suspected cause of hypertension</th>
<th>Investigation to rule out the cause</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drug induced/related, e.g.</td>
<td>Negative history</td>
</tr>
<tr>
<td>• NSAIDs, coxibs,</td>
<td></td>
</tr>
<tr>
<td>• Glucocorticoid excess</td>
<td></td>
</tr>
<tr>
<td>• Sympathomimetics (decongestants, amphetamine)</td>
<td></td>
</tr>
<tr>
<td>Chronic kidney disease</td>
<td>Abdominal ultrasound and CT abdomen (normal sized kidneys) , kidney biopsy not showing chronic changes Estimated GFR (90 ml/min/1.73m²) at last follow up</td>
</tr>
<tr>
<td>Renovascular hypertension</td>
<td>MR angiography (negative)</td>
</tr>
<tr>
<td>Coarctation of the aorta</td>
<td>CT angiography (negative)</td>
</tr>
<tr>
<td>Pheochromocytoma</td>
<td>24 hour urinary VMA was 3.8mg/day (normal 2-7 mg/day).</td>
</tr>
<tr>
<td>Primary aldosteronism</td>
<td>Plasma renin (basal) was 5ng/ml/h (normal 0.29-3.7ng/ml/h); Serum aldosterone 25ng/L (PAC/Plasma renin ratio=5); Low 24-hour urinary aldosterone level (8mcg)</td>
</tr>
<tr>
<td>Thyroid/parathyroid disease</td>
<td>Normal TSH (3.1 mIU/L); serum PTH (42pg/ml), serum Calcium (8.9mg/dl)</td>
</tr>
</tbody>
</table>

Figure 1
References: