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Polyarteritis Nodosa Renal Crisis with Malignant Hypertension

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Abstract- A case of 28 years female with no significant past medical history presented with malignant hypertension. She was found to have Polyarteritis nodosa involving the kidney on angiography. She was treated successfully with steroids and cytotoxic drugs and made uneventful recovery. Her kidney function remained stable and her BP was controlled on Po medications. Even though she was negative for hepatitis B infection, the association was strongly confirmed in about 10% of patients. PAN should be suspected in any patients with multisystem involvement with hypertension and minimal findings in urinalysis. Polyneuropathy and high ESR are also red flags for PAN.

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I. Case History

28 years Caucasian female without any significant past medical history was admitted to the hospital for severe frontal headache of one month duration. Family history is significant for hypertension in her father and granduncle. In the week proceeding presentation to the hospital, she had taken 6-8 (60 mg) pseudoephedrine tablets for head cold. Her blood pressure was 248/177 mmHg. Her eye examination showed retinal hemorrhage, cotton wool spots, and papilledema. Otherwise, her physical examination was unremarkable. Her renal ultrasound revealed bilateral symmetrical kidneys of 11.2 cm size, with mild medical-renal parenchymal disease.

Captopril renogram was suggestive of bilateral renal artery stenosis which was ruled out by angiography. Routine laboratory was within normal limits with serum creatinine 1 mg/dl, and 24-hour creatinine clearance of 112 ml/min.

Tests for hepatitis B, C, and RF, ANA, anti-DNA and ANCA were negative. Her ESR was 10 mm/hr. Renin level at 8 am in the supine position was 26 μU/ml (normal <5). The 24-hour urine catecholamine were collected in the second day of admission were found to be within normal limits.

ECG showed LVH, and CXR and CT of head were normal.

A diagnosis was made by angiography of the kidneys and the patient was treated with

- High dose steroids (1000 mg methyl-prednisone IV daily for three consecutive days).
- Prednisone 1 mg/kg/day PO x 3 weeks, the prednisone was then tapered slowly.
- Cyclophosphamide 0.6 g/M^2 monthly IV for 6 months.
- Hypertension became controlled, average BP 132/80 mmHg within 2-3 weeks.
- The patient was initially stabilized with IV nitro-prusside and Labetalol and then switched later to oral regimen consists of Lisinopril 20 mg/day, Hydrochlorothiazide 12.5 mg daily, and Labetalol 400 mg three times daily.
- Her renal function remained stable throughout the treatment course.

II. Discussion

Poly- arteritis nodosa (PAN) is a systemic vasculitis characterized by necrotizing inflammatory lesions affecting predominantly medium and small muscular arteries, resulting in micro-aneurysmal formation, thrombosis, rupture with hemorrhage, and organ infarction (1-3).

PAN is a rare disease with an incidence of 4.6 cases/million in England to 77 cases/million in hyper-endemic areas for hepatitis B. PAN affected both sexes and has been diagnosed in all racial groups.

The etiology of PAN remained unknown and hepatitis B, hepatitis C, and Hairy cell leukemia are associated with some cases of PAN (4-7). The current incidence is $<10\%$ because of hepatitis B vaccination.

In contrast to microscopic polyangitis (MPA), PAN is not associated with anti-nuclear cytoplasmic antibodies (ANCA) and does not affect the glomeruli. PAN is acute multisystem disease with relatively short prodrome. For unknown reasons PAN spars the lungs.

Skin manifestation of PAN may include tender erythematous nodules, purpura, livedo reticularis, ulcers, and vesicular eruption (8-10). The erythematous nodule resembles erythema nodosum, but biopsy of these nodules reveals necrotizing vasculitis in the walls of the medium sized arteries.

Renal involvement by PAN frequently, leads to renal insufficiency and hypertension. Incomplete luminal narrowing of the inflamed arteries leads to glomerular ischemia but no inflammation or necrosis. Renal ischemia usually leads to activation of the renin-angiotensin system (2). Thus, the urinalysis, when abnormal, shows only sub-nephrotic and minimal proteinuria and sometimes hematuria, but red cell casts (indicative of glomerulitis are usually absent (1,11).

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Neurological disease of PAN includes asymmetric polyneuropathy affecting radial, ulnar, peroneal etc. These neuropathies are usually mixed motor and sensory occurring in up to 70% of patients (8,12-14). Central nervous system is involved in 5-10% of patients with PAN (8,15-17).

Gastrointestinal disease is an early symptom in patients with PAN including mesenteric arteritis (18), Weight loss, malabsorption, bowel infarction with perforation may also occurs (19).

Muscle weakness and myalgia with elevated CPK may trigger suspicion of inflammatory myopathy. Muscle biopsy has an approximately 50% sensitivity for the diagnosis of PAN (20,21). Orchitis with testicular tenderness (22), eye involvement with ischemic retinopathy (23,24), and splenic infraction may occurs.

The diagnosis of PAN may be difficult due to non-specific signs and symptoms, multi-system involvement and the rarity of the disease. However, the sedimentation rate is elevated in about 90% of patients. The clinical manifestations of PAN are illustrated in table-1.

Table-1: Clinical manifestation of PAN

Clinical Feature	Percentage
Fever, malaise, weight loss	70%
Pain and peripheral neuropathy	70%
Myalgia	30-73%
Arthralgia and polyarthritis	20-50%
Abdominal pain	34%
Depression	8%
Renal involvement (CKD, HTN), activation of RAAS may lead to malignant HTN	25-70%

Tissue biopsy of the affected organs and or angiography may clinch the diagnosis. The palpable purpuric lesions seen in PAN are identical to vasculitis associated with small vessels disease (e.g IgA vasculitis, ANCA- associated vasculitis, and mixed cryoglobulinemia) (25).

Due to sampling error the diagnosis of PAN may be missed on renal biopsy, but renal angiography may be diagnostic with specificity of 95%.

PAN has a 5 year survival of <10% if untreated. Treatment of PAN consisted of high doses steroids and intra-venous pulse cyclophosphamide. This treatment achieves a 5-year survival of 82%.

- 115 patients with PAN, (4.2%) had severe hypertension during the 1 year of presentation of the disease. Renal insufficiency, gastrointestinal disease, and positive hepatitis B were present in the majority of these patients (4).
- Many patients with PAN reported in the literature had isolated renal involvement with severe hypertension (8).

III. Conclusion

PAN should be suspected in any patients with multisystem involvement with hypertension and minimal findings in urinalysis. Polyneuropathy and high ESR are also red flags for PAN. PAN is rare disease especially after wide spread vaccination for hepatitis B. Steroids and cytotoxic medications remain the foundation of treatment of PAN.

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