Case Report

Polycythemia Secondary to Pheochromocytoma

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Abstract

Polycythemia, also known as polyglobulia, is a clinical condition characterized by an increased number of red blood cells (RBC) or haematocrit concentrations in the peripheral blood. It can either be primary (polycythemia vera) or secondary, which can be congenital or acquired; the most common causes include obstructive sleep apnoea, obesity, hypoventilation, Pickwickian syndrome, Chronic obstructive pulmonary disease (COPD), and lastly, pheochromocytoma.

Here we present a case of a 54-year-old male with a four-day history of altered state of consciousness (ASOC), right-sided body weakness, and respiratory difficulty. After a thorough history, examination, and investigation, he was diagnosed as a case of polycythemia secondary to pheochromocytoma. Early diagnosis and intervention are critical to saving the patient's life.

Keywords: Polycythemia, pheochromocytoma, tumor, management.

Introduction

Pheochromocytoma is a rare tumor of the adrenal gland /chromaffin tissue. Functional tumor leads to excessive secretion of catecholamines and is responsible for 0.1% of cases of hypertension.[1] About 80% occur in the adrenal medulla, while 20% occur elsewhere in the body and are known as paragangliomas. About 40% are inherited, and 15% show features of malignancy.[2] Paraneoplastic syndromes are commonly seen in certain tumors. Polycythemia secondary to pheochromocytoma is due to the production erythropoietin (EPO) that normally stimulates erythropoiesis to increase blood cell production.[3] Polycythemia due to underlying pheochromocytoma is a rare occurrence. We present a case of pheochromocytoma presenting with signs and symptoms of polycythemia diagnosed on a complete blood picture.

Case Report

A 54-years-old male patient was referred to the Emergency department of Holy Family Hospital Rawalpindi from a primary healthcare facility with a four-day history of altered state of consciousness (ASOC), right-sided body weakness, and difficulty breathing. On presentation, the vitals of the patient was as follows: Blood Pressure (BP): 210/130 mmHg, Pulse: 82/min, Respiratory rate (RR): 22/min, Temp: A/F, O_2 Saturation: 89% at room air. On examination, the patient had a Glasgow Coma Scale score (GCS) of 11/15, right-sided planter up going and left-sided down-going, right-sided upper limb and lower limb power of 3/5 for each limb, pupils normal bilaterally and reactive to light, no signs of meningeal irritation, in all four limbs mascular tone was normal, cranial nerves could not be assessed as the patient was unconscious. Occasionally, coarse crepitus was auscultated bilaterally in the chest; the rest of the systemic examination was unremarkable. Lab investigations were done in the ER department (see Table 1), and the results showed some derangements viz. Hemoglobin: 18.8 g/dL, HCT: 60, WBC: 15.5 cells/microliter, Urea: 67 mg/dL, Creatinine: 1.5 mg/dL. Serum electrolytes, Serum total bilirubin, Coagulation profile, and ECG were within normal. Plain CT Brain showed left middle cerebral artery infarct with apparently no mass effect and midline shift. Chest X-ray (CXR) showed bilateral infiltrates. Bedside funduscopic examination of the patient showed a bilateral hyperemic disc with tortuous vessels, bilateral hemorrhages, and Grade-II papilledema, indicating hypertensive retinopathy. Initially, differentials of malignant hypertension, aspiration pneumonitis, and cerebrovascular accident (CVA) were made.

The patient had a history of CVA 3 years back with complete recovery, and hypertension was diagnosed at that time. For the management of hypertension, oral antihypertensive medication was prescribed, but the patient was poorly compliant.

The patient was shifted to the high dependency unit (HDU) of the medical ward and managed with an antiplatelet drugs regimen, i.e., aspirin, IV antibiotics, PPI, antihypertensives, IV fluids, nebulization with Atem and Clenil, and oxygen inhalation. Good nursing care, chest and limb physiotherapy were provided. Nasogastric tube feeding was started. Phlebotomy and venesection with 450 ml blood volume were performed.

Initial complete blood count (CBC) showed a raised Hb and HCT, suggestive of polycythemia. Serial CBC on the following days also showed the same trend. Secondary causes of polycythemia, i.e., hypoxia, smoking, diuretic use, high altitude, obesity, and alcohol access, were ruled out. Further workup for polycythemia was done, which included JAK-2 V617F mutation, and was found absent. Twenty-four hours urine VMA levels were measured, which were markedly raised, i.e., VMA= 42.3 mg/24 hours (Normal= 13mg/24 hours). The test was repeated, and levels were found elevated again, i.e., 43.1 mg/24 hours. Suspicion of polycythemia secondary to pheochromocytoma was made. When serum creatinine and urea were within normal limits, CT abdomen was performed, which showed a left-sided adrenal mass, suggestive of pheochromocytoma. Serum erythropoietin levels were measured, which were found to be elevated. Thus, confirming pheochromocytoma as the source of polycythemia.

Surgical consultation of the patient was sought, but surgical removal of the pheochromocytoma could not be carried out due to the critical condition of the patient. GCS and clinical condition of the patient gradually deteriorated, and eventually, the patient succumbed to his illness.

Table 1: Laboratory Investigations of the Patient during Hospital Stay

Parameters	*Test Dates*				
	22/6	**23/6**	**24/6**	**25/6**	**26/6**
RBC (x1012/L)	8.5	7.2	-	9.1	-
Hb (mg/dL)	18.8	17.7	-	19	-
HCT	60	56	-	63	-
MCV (fL)	89	-	-	62	-
MCH (pg)	29	-	-	288	-
TLC (x103/microliter)	15.5	16.2	-	15.2	-
Neutrophils (%)	89	86	-	81	-
Lymphocytes (%)	6.7	8.7	-	11.6	-
Platelets (x103/microliter)	257	231	-	183	-
PT/APTT	27/55	-	-	13	28/ 51
Urea (mg/dL)	67	55	40	43	46
Creatinine (mg/dL)	1.5	1.1	0.8	0.9	0.9
Serum Total Bilirubin	0.8	-	-	0.5	0.7
Na+	140	-	-	145	142
K+	3.5	-	-	4.6	3.7
Ca2+	9.3	-	-	-	-
DIC Profile	Normal (assessed on 28/6)				

Discussion

Polycythemia, as a paraneoplastic syndrome, due to benign or malignant conditions is common; the common tumor conditions involving polycythemia include renal cell carcinoma, cerebellar hemangioblastoma, ovarian carcinoma, leiomyoma, hepatocellular carcinoma, and pheochromocytoma.[4] Pheochromocytoma usually follows "Rule of 10s": 10% are malignant, 10% extra-adrenal, and 10% are malignant. Pheochromocytoma has a rare association with neurofibromatosis, von Hippel Lindau syndrome, and multiple endocrine neoplasia 2 (MEN-2).[5-6]

Clinical features in polycythemia stem from greater viscosity of blood due to an increased number of RBCs and involve headache, pruritis, dizziness, and visual deterioration.[7] While common signs and symptoms in pheochromocytoma arise from catecholamine production causing vasomotor instability, hypertension and its complication like stroke, hypertensive retinopathy, myocardial infarction and left ventricular failure.[8] Other features include glucose intolerance, constipation, pallor, flushing, palpitations, anxiety, and certain others. Catecholamines like epinephrine and norepinephrine are produced and released in excess and their degradation products are detected in the body fluids viz, serum or urine. This forms the basis of investigative testing of pheochromocytoma.[9]

Out of a constellation of investigations for polycythemia, the following investigations are important in terms of greater specificity and sensitivity (see Table 2): (1) Plasma metanephrine testing (2) 24-hour urinary collection for catecholamines and metanephrines (3) CT scan, MRI, M-iodobenzylguanidine (MIBG) imaging, PET scan.

Table 2: Specificity and Sensitivity of Different Markers of Pheochromocytomas[10]

Test		*Sensitivity (%)*	*Specificity (%)*
Plasma	Free metanephrines	97-99	82-96
	Catecholamines	69-92	72-89
Urine	Fractionated metanephrine	96-97	45-82
	Catecholamines	79-91	75-96
	Total metanephrines	60-88	89-97
	Vanillylmandelic acid	46-77	86-99
Imaging	USG abdomen	83-89	30-60
	CT abdomen	85-94	29-50
	MRI abdomen	93-100	50-100
	1231-MIBG	83-100	95-100
	18F-DOPA PET	100	100

24-hour urinary tests are considered superior because tumors often secrete catecholamines intermittently, and the short half-life of catecholamines can result in normal plasma catecholamines levels. 24-hour urinary levels plus an imaging test like MIBG and CT scan can give a fair assessment of the tumor.[11]

Primary treatment is surgery (laparoscopic surgery common). The mechanism of action of catecholamines is by their agonist action on alpha and beta receptors. These mediators act on alpha 1 receptors of blood vessels to cause vasoconstriction and beta 1 receptor on the heart to cause tachycardia. That's why the

preoperative therapy includes Alpha Blockers like phenoxybenzamine, doxazosin; Beta-blockers like atenolol, propranolol, metoprolol, and a high salt diet for around 7-10 days. Calcium channel blockers may also be used in place of alpha or beta-blockers with an added benefit of no interference with plasma metanephrine assays along with optimum blood pressure control.[12] Complete surgical resection, if possible, is the treatment of choice with adjunct-targeted radiation therapy using[13] I MIBG in case of a malignant tumor.

The paraneoplastic syndromes are caused by the chemical mediators produced by the tumor cells in some neoplasias. The removal of the underlying tumor generally resolves the condition.[13]

Conclusion

The presence of polycythemia secondary to pheochromocytoma is an uncommon presentation but can present with features of vasomotor instability and hypertension. We recommend that physicians take this differential into account while managing a patient with these symptoms. 24-hours urine metanephrines and VML levels are important investigations for pheochromocytoma. Prompt diagnosis with the available investigations and intervention could have been beneficial in saving the patient's life.

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