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Epistaxis : Diverse Causes – Hematologist has a significant role in optimal care

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Abstract - Background: Epistaxis is among the most common otorhinolaryngological emergencies, affecting up to 60% of the population. While most cases are benign and managed with local measures, unusual hematological causes may underlie recurrent or severe presentations.

Objective: To present a case series highlighting diverse hematological etiologies of epistaxis encountered during the initial practice period of a budding hematologist in a remote region of Karnataka, India.

Methods: Six consecutive patients presenting with epistaxis were evaluated comprehensively. Detailed hematological workup was performed, and management was tailored to the underlying diagnosis.

Results: The series included:

- **Drug-induced thrombocytopenia** managed successfully with TPO agonists.
- **Paroxysmal nocturnal hemoglobinuria** diagnosed during pancytopenia evaluation and referred for anti-complement therapy trials.
- **Fanconi anemia** confirmed by cytogenetics and mutation analysis, managed with transfusion support and antifibrinolytics, with transplant planning underway.
- **Immune thrombocytopenic purpura** treated with steroids and hematinics.
- **Eisenmenger syndrome with erythrocytosis** managed by phlebotomy.
- **Erythrocytosis with suspected acquired von Willebrand disease** controlled with local measures, hydration, and lifestyle modification.

Conclusion: This case series underscores the importance of hematologist involvement in epistaxis evaluation, especially in uncovering rare and systemic causes beyond routine ENT practice. Awareness of conditions such as PNH, Fanconi anemia, acquired vWD, and drug-induced thrombocytopenia is crucial for timely diagnosis and appropriate management.

Presentation: This work was presented at the **Association for Haemophilia and Allied Disorders – Asia Pacific (AHAD AP) 2024**, Bengaluru, India.

***Key Words*:** Epistaxis; Thrombocytopenia, Drug-Induced; Paroxysmal Nocturnal Hemoglobinuria; Fanconi Anemia; Purpura, Thrombocytopenic, Idiopathic; Eisenmenger Complex; von Willebrand Diseases; Erythrocytosis

1. INTRODUCTION

Epistaxis is the commonest otorhinolaryngological emergency affecting upto 60% of population. Hypertension, blood thinners and trauma are some of the common risk factors. Here we present a series of six patients who presented to us during the first month of the practice of a budding clinical hematologist.

2. DETAILS OF THE CASES

Interesting Case 1: 65y/M, father of two adult male, mechanic by occupation, had lost elder son to RTA. He had mental health issues following this event was under follow up with psychiatrist. Having recently changed the residence he had taken anti psychotics prescribed by two doctors, hence taking more than twice the dose of multiple medications. He presented to us with epistaxis and altered sensorium. Imaging showed epidural hematoma. BMA / Biopsy showed immature megakaryocytes and he responded well to TPO agonists in three weeks.

Interesting Case 2: 22y/M, younger brother of a medico had repeated epistaxis. He had been managed symptomatically at home for about 3 episodes. Recently he also had multiple episodes of fever. During one such episode, he was admitted and complete blood works were done. At this juncture, the

hematologist opinion was taken for pancytopenia evaluation. Work up showed aplastic anaemia type of Paroxysmal Nocturnal Hemoglobinuria. He was referred to a center undertaking trial for PNH patients comparing two types of Anti–Complement Antibodies.

Interesting Case 3: 21y/M, third child of second degree consanguineous marriage, with a history of transfusion dependent anaemia from the age of five years presented with low platelet count and epistaxis. Consanguinity was present for two generations. On taking further family history, we found that an elder brother had succumbed to ?blood cancer/?bleeding diathesis and that he was also transfusion dependent. Stress cytogenetics was positive and he had mutation in the FANCD. Diagnosis – Fanconi Anaemia. This episode of epistaxis was managed with platelet transfusion and antifibrinolytics. Work up for allogenic transplantation and crowd funding are on going.

Interesting Case 4: 19 y old female presented with epistaxis. She had microcytic hypochromic anaemia with thrombocytopenia. Marrow showed hyperplasia of megakaryocytes. Her platelet count improved with pulse steroids. She also received hematinics.

Interesting Case 5: 25y/M, with known Eisenmenger syndrome secondary to Large outlet/Doubly committed VSD presented with epistaxis. At presentation, he had erythrocytosis. Epistaxis subsided with phlebotomy.

Interesting Case 6: 30y/M, recently married 2.5 years ago presented to OPD for evaluation of erythrocytosis and mild nasal bleeding. He is a resident of western ghat region, with a habit of consuming alcoholic beverages during social occasion. History of primary infertility. Coagulation work up showed : PT-10.8s, APTT-38.0s, FVIII-52.0%, FIX-76.0%, Platelet aggregometry was normal with ADP, Collagen, Epinephrine, Ristocetin. Hb-21.0g%, PCV 60.8%, WBC count was 7600/mm3, Plt count was 2.41 lakh/mm3.

Table -1: Patient details, diagnosis and treatment modality selected.

Patient ID	Age (in yrs)	Gender	Diagnosis	Treatment
1	65	M	Drug induced thrombocytopenia	TPO Agonist
2	22	M	Paroxysmal Nocturnal Hemoglobinuria	Eculizumab vs Trial Drug
3	21	M	Fanconi Anaemia	Platelet Transfusion + Anti-Fibrinolytics followed by plan for transplant
4	19	F	Immune Thrombocytopenic Purpura	Nasal packing, Steroids and hematinics
5	25	M	Eisenmengers Syndrome	Phlebotomy
6	30	M	Erythrocytosis with ?acquired vWD	Local measures, Abstinence from alcoholic beverages, Hydration; Discontinued native medication for infertility

DISCUSSION: Epistaxis is a common clinical condition encountered by the otorhinolaryngologist. It is prevalent in the 1st to 3rd decade. It is found to be more common in males than females. Most of the epistaxis patients get relieved just by observation. The treatment of epistaxis hasn't change much. Identifying the bleeder, cauterization, endoscopic ligation, application of pressure, packing and decongestant are some of the local measures. Since epistaxis is so common, how extensive would be the workup and treatment of a patient with nasal bleeding can be a difficult decision.

In this series, all cases were thoroughly worked up and each of them got specific treatment for the condition. Drug induced thrombocytopenia could be of various causes and there are no guidelines on the management of same.

Awareness of conditions like Paroxysmal Nocturnal Hemoglobinuria, Fanconi Anemia, Acquired vWD and erythrocytosis as a cause of bleeding tendency is less among otorhinolaryngologists and physicians alike.

Thrombocytopenia after drug administration can be associated with bleeding or thrombosis, depending on the pathophysiology of platelet destruction. Five clinical criteria have been proposed to help physicians to determine the diagnosis of drug-induced immune thrombocytopenia. A systematic evaluation conducted by Arnold et al. determined that there are 153 drugs that are known to have an increased risk of inducing thrombocytopenia. Several review articles and guidelines describe the management of thrombocytopenia due to immune mechanism like VITT, HITT. There is a lack of guidelines for the management of non immune and thrombocytopenia of other mechanism. Also the advent of newer medications like TPO agonists at a reasonable cost has not been considered in preparing these guidelines.

Paroxysmal nocturnal hemoglobinuria (PNH) is a rare disorder caused by an acquired mutation in hematopoietic stem cells (HSCs). It allows for complement system-mediated hemolysis and thrombosis and often occurs in the context of bone marrow failure. The rarity and nonspecific symptoms of PNH can cause a delay in diagnosis, with time spent being referred from one physician to the next, causing psychological stress and resulting in disease progression, including the ongoing risk of thrombosis. Disease awareness among primary physicians and hematologists is necessary to help patients quickly reach the appropriate specialist and receive a timely diagnosis.

Fanconi anemia (FA) is an autosomal recessive disorder, both genetically and phenotypically. It is characterized by chromosomal instability, progressive bone marrow failure, susceptibility to cancer, and various other congenital abnormalities. It involves all the three cell lines of blood. So far, biallelic mutations in 21 genes and one x-linked gene have been detected and found to be associated with FA phenotype. Signs and symptoms start setting in by the age of 4 to 7 years, mainly hematological symptoms. This includes pancytopenia, that is, a

reduction in the number of white blood cells (WBCs), red blood cells (RBCs), and platelets. Well-timed diagnosis is of utmost importance in any genetic disease. Genetic counseling plays an important role in explaining the patients' relatives the course of the disease and also to prevent the occurrence of the same disease in the next child.

Routine venesections (phlebotomy) are not indicated for patients with Eisenmenger syndrome. In addition to the symptoms of the Eisenmenger syndrome, patients may experience symptoms associated with hyperviscosity, attributed to the associated erythrocytosis. Hyper viscosity is, paradoxically enough, associated with increased bleeding diatheses, which is attributed to platelet (low number and dysfunctional) and coagulation-factor abnormalities. The reporting of hyper viscosity-like symptoms in the setting of a hematocrit b65% is more frequently due to iron deficiency and is not an indication for phlebotomy. Fluctuations in the hematocrit and symptoms of hyper viscosity may also be caused by dehydration caused by heat, fever, vomiting, nutritional changes or infection. When phlebotomy is required, it should be done concomitant with isovolumic fluid replacement. Phlebotomy without adequate replacement is potentially hazardous as it may further reduce systemic blood flow, oxygen delivery, cerebral perfusion and cardiac output. Repeated phlebotomy should be avoided as this can lead to rebound response from the bone marrow and iron deficiency anemia, which may worsen symptoms of hyper viscosity, since iron-deficient erythrocytes (microcytic anemia) are less deformable than iron-replete erythrocytes.

STRENGTHS: Each of these case highlights a unique cause of epistaxis.

LIMITATIONS OF THE STUDY: This is a random case series of six consecutive cases of epistaxis, which presented to the clinic of a hematologist who started practising in a remote western ghats region of India. All cases were referred for hematologist opinion. Hence there is a bias of seeing unusual etiology.

FUTURE DIRECTION: A systematic study of all epistaxis cases over longer duration, with complete or comprehensive work up of as many cases as possible will show the true picture.

3. CONCLUSIONS

The Greek philosopher Aristotle famously remarked on discovering the unknown: "The more you know, the more you realize you don't know". The above case series shows how varied the cause of epistaxis maybe. Evaluation
by a trained clinical Hematologist may be required in unfolding unusual causes.

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