Waldenstrom Macroglobulinemia Presenting as Isolated Persistent Epistaxis: A Very Rare Presentation

Vinish Agarwal · Saurabh Varshney · S. S. Bist · Sanjiv Bhagat ·
Sarita Mishra · Mamta Goyal · Geeta Negi · Namita Kabdiwal

Received: 5 December 2012 / Accepted: 12 December 2012 / Published online: 22 December 2012
© Association of Otolaryngologists of India 2012

Abstract Nose bleed is the most common rhinological emergency. There are multiple risk factors for the development of epistaxis and it can affect any age group, but it is the elderly population with their associated morbidity who often require more intensive treatment and subsequent admission. Most cases of epistaxis occur in the Little's area, a location readily accessible and treatable by cautery or anterior nasal packing. However, posterior epistaxis often requires more aggressive measures including posterior nasal packing and endoscopic cauterization. After posterior nasal packing, the two most common therapies for intractable epistaxis are transantral ligation of the internal maxillary artery and percutaneous embolization of the distal internal maxillary artery. However, optimal management of intractable posterior epistaxis remains controversial. We hereby report fourth case of Waldenstrom Macroglobulinemia in English literature, which presented as isolated persistent epistaxis and was treated by therapeutic plasmapheresis.

Keywords Epistaxis · Little's area · Embolization · Plasmapheresis · Waldenstrom macroglobulinemia

Introduction

Epistaxis, whether spontaneous or otherwise, is experienced by up to 60 % of people in their life time, with 6 % requiring medical attention [1]. There is a bimodal distribution for incidence of epistaxis, with peaks in children and young adults and older adult (45–65 years) [2]. Anterior nose bleeds accounts for 80 % of epistaxis and they occur at Little's area. Posterior nose bleeds occur mainly from the posterior septal nasal artery, which forms part of the Woodruff plexus. The aetiology of epistaxis can be divided into local and general causes, however most are idiopathic [3]. Although uncommon, it is important to exclude neoplasia and systemic disorders as a cause for unexplained recurrent epistaxis. Management of epistaxis should ideally use a systemic protocol by stepwise approach, which starts from nose pinching, anterior and posterior nasal packing, cauterization, arterial ligation and embolization.

Case

Seventy-five years old male came to E.N.T. outpatient department with bilateral merocel anterior nasal packing with complain of bilateral recurrent severe nasal bleeding for the past five months and was treated by repeated anterior and posterior nasal packing. He was transfused eight units of fresh frozen plasma, two units of Packed Red Blood Cells and one unit of platelet in last five months. He had history of hypertension for six years and was on regular medical treatment. He had history of haemorrhoids,

V. Agarwal · S. Varshney (✉) · S. S. Bist · S. Bhagat ·
S. Mishra · N. Kabdiwal
Department of E.N.T., Himalayan Institute of Medical Sciences,
(HIHT University), Jollygrant; Doiwala, Dehradun 248 140,
Uttarakhand, India
e-mail: drsaurabh68@gmail.com

M. Goyal
Department of Radiology, Himalayan Institute of Medical
Sciences, (HIHT University), Jollygrant; Doiwala,
Dehradun 248 140, Uttarakhand, India

G. Negi
Department of Pathology, Himalayan Institute of Medical
Sciences, (HIHT University), Jollygrant; Doiwala,
Dehradun 248 140, Uttarakhand, India

anaemia and thrombocytopenia in past. There was no history of nasal obstruction or any nasal mass. There was no history of any trauma to nose or bleeding diathesis in past. There was no significant history of any other medical or surgical illness. At the time of admission he was conscious, well oriented with blood pressure as 150/90 mm of Hg, pulse rate 80/min and respiratory rate 16/min. His neck veins were engorged and he had pallor. Laboratory reports were- haemoglobin 5.56 gm per 100 ml, hematocrit 18 %, white blood cell count 4270 per cu ml (65 % neutrophils, 30 % lymphocytes, 3 % monocytes and 2 % eosinophils), normal platelet count, bleeding time (BT) and clotting time (CT) within normal limit, prothrombin time (PT) 17.3 s (control 13.4 s, International normalized ratio 1.40). Patient's serum was negative for hepatitis B surface antigen and human immunodeficiency virus (HIV). On removal of anterior nasal packs, diagnostic nasal endoscopy (DNE) showed diffuse ooze of blood around posterior ends of inferior and middle turbinate on either side of nasal cavity. The nose bleed could not be controlled completely by bilateral anterior and posterior nasal packing. Contrast enhanced computed tomography (CECT) scan of nose and Paranasal sinuses showed no abnormality on coronal and axial cuts. Digital subtraction angiography (D.S.A.) showed left sphenopalatine artery bleed. Patient underwent angiographic embolization of bilateral sphenopalatine artery using polyvinyl alcohol and bilateral nasal packing was done. (Fig. 1) There was no bleeding from nose for next two days. On third day nasal packs were removed and on performing DNE diffuse oozing of blood was seen at posterior ends of inferior turbinate bilaterally. Patient was further evaluated for haematological and biochemical profile. His total serum protein was 13.8 g per 100 ml {albumin 4.83 g (35 %) and globulin 8.97 g (65 %)}, urine was negative for Bence Jones proteins and serum was negative for anti neutrophilic cytoplasmic antibodies (ANCA). Bone marrow smear findings were suggestive of plasma cell rich lesion with erythroid hyperplasia. (Fig. 2) Based on above findings differential diagnosis of Waldenstrom macroglobulinemia (WM) and multiple myeloma were made. Serum was sent for immunofixation electrophoresis. The patient was started on dexamethasone phosphate and thalidomide and was taken up for therapeutic plasmapheresis next day. The plasmapheresis was uneventful and patient tolerated the procedure well. The patient was cured and was discharged on third day after removing nasal packing. High resolution serum protein electrophoresis revealed the presence of a monoclonal gammopathy ('M' spike) in gamma globulin region (Fig. 3). Immunofixation electrophoresis (IFE) identifies the 'M' spike and its k isomer as IgM, kappa. The patient is on monthly regular follow for the last six months and there has been no episode of nasal bleed since discharge.

Discussion

Adult primary epistaxis challenges otorhinolaryngologists the most. The peak presentation is the sixth decade with male dominance [4]. Adult pattern primary epistaxis is associated with the regular use of nonsteroidal anti-inflammatory drugs, chronic alcohol consumption and hypertension. So, in our case we presumed the diagnosis of hypertension associated epistaxis in our patient. All patients who are actively bleeding need full assessment and resuscitation if necessary. Our patient's laboratory investigations showed very low haemoglobin and hematocrit levels so he was transfused with fresh frozen plasma and packed red blood cells, to make him haematologically stable as he was bleeding from nose continuously. Diagnostic nasal endoscopy showed diffuse oozing of blood around the posterior ends of middle and inferior turbinate bilaterally, hence bilateral anterior and posterior nasal packing was tried which did not stop bleeding. Digital subtraction angiography revealed left sphenopalatine artery bleed. So we were left with options of surgical ligation or angiographic embolization of bleeding vessel. Ligation should be performed as close as possible to the likely bleeding point; thus, the hierarchy of ligation is sphenopalatine artery; internal maxillary artery; external carotid artery and lastly anterior/posterior ethmoidal artery [5]. Sokoloff first undertook angiographic embolization for epistaxis in 1972 [6]. The technique entails cannulation of the external carotid artery and location of bleeding point by water soluble contrast. Steel microcoils, gelfoam and polyvinyl alcohol can be used to embolize the causative artery. The success rate of embolization has been reported to be as high as 87 %, which is similar to arterial ligation [7]. In our case we were not able to control nasal bleeding by percutaneous angiographic embolization. On further evaluation we noted high serum protein with albumin/globulin ratio 0.538 with negative (ANCA) and urine negative for Bence Jones proteins. High total protein levels may be seen with chronic inflammation or infections such as viral hepatitis or HIV. They may be caused by bone marrow disorders such as multiple myeloma. A low A/G ratio may reflect overproduction of globulins, as seen in multiple myeloma or autoimmune diseases, or underproduction of albumin, as occurs with cirrhosis, or selective loss of albumin from the circulation, as occurs with kidney disease (nephrotic syndrome). Bence Jones proteins are present in 2/3 of multiple myeloma cases [8]. Bone marrow smear was suggestive of plasma cell rich lesion in our case. We made differential diagnosis of Waldenstrom macroglobulinemia and multiple myeloma in this patient after investigations. Serum protein electrophoresis revealed the presence of a monoclonal gammopathy ('M' spike) in gamma globulin region. So, diagnosis of Waldenstrom

Fig. 1 Pre & Post embolization of sphenopalatina artery

Fig. 2 Bone marrow aspiration-plasma cell rich lesion with erythroid hyperplasia. (40× magnifications)

Fig. 3 Serum immunofixation electrophoresis (IFE), high resolution serum protein electrophoresis showing the presence of a monoclonal gammopathy ('M' spike) in gamma globulin region

macroglobulinemia was concluded. This condition was originally described in 1944 by Waldenström, who reported two patients with oronasal bleeding, severe anaemia, lymphadenopathy, hypofibrinogenemia, elevated erythrocyte sedimentation rates, and presence of large amounts of

a high-molecular-weight gamma globulin in the serum [9]. Presentation with epistaxis as the dominant clinical feature is very unusual. We could only find two other cases, one of them reported by Wright [10] and other by Karim Bakri et al. [11]. Hence, this is the fourth case reported. We planned therapeutic plasmapheresis for this patient and he tolerated it well, and there was no nasal bleed after removal of nasal packs. In several patients with WM, the predominant symptoms are caused by the elevated serum viscosity. Because 80 % of IgM is intravascular, plasmapheresis, conducted with an automatic blood separator that uses albumin and saline replacement, is an effective means of rapidly reducing the amount of circulating IgM [12]. Nevertheless, plasma exchange has been used as the sole treatment in the occasional elderly patient with resistant WM and predominant symptoms of hyperviscosity [13]. The median survival of patients with WM averages 5 years, but at least 20 % of patients survive for more than 10 years and up to one-fifth of patients die of unrelated causes [14].

Conclusion

It is not surprising that epistaxis, such a common hemorrhagic condition of elderly patients is associated with significant morbidity and mortality. After head and neck cancer, epistaxis stands out as a prominent cause of mortality in ear, nose and throat patients. Over the last twenty years, there has been a significant expansion in the options available for the management of epistaxis. Effective management of adult epistaxis follows a systematic incremental sequence of interventions. Unusually severe or persistent bleeding should initiate a search for secondary factors with use of haematological investigation and angiography to exclude neoplasia and systemic disorders. Therapeutic plasmapheresis represents an effective way of managing hyperviscosity

syndrome secondary to immunoglobulin M paraproteins in patients with Waldenstrom macroglobulinemia.

References

1. Petruson B, Rudin R (1975) The frequency of epistaxis in a male population sample. *Rhinology* 13:129–133
2. Watkinson JC (1997) Epistaxis. In: Mackay IS, Bull TR (eds.) *Scott Brown's otolaryngology*, vol 18. Butterworths, London, pp 5–7
3. Varshney S, Saxena R (2005) Epistaxis: a retrospective clinical study. *Indian J Otolaryngol HNS* 57:125–129
4. Padgham N (1990) Epistaxis: anatomical and clinical correlates. *J Laryngol Otol* 104:308–311
5. Michael Gleeson (ed) (2008) *Scott-Brown's otorhinolaryngology: head and neck surgery*, 7th edn. vol 2, London, Hodder Arnold, p 1603
6. Sokoloff J, Wickbom I, McDonald D, et al. (1974) Therapeutic percutaneous embolization in intractable epistaxis. *Radiology* 111:285–287
7. Vitek J (1991) Idiopathic intractable epistaxis: endovascular therapy. *Radiology* 181:113–116
8. Hoffbrand V, Moss P, Pettit J (2006) *Essential haematology (Essential)* (5th edn). Blackwell Publishing Professional, Massachusetts, p. 218
9. Waldenstrom J (1944) Incipient myelomatosis or “essential” hyperglobulinemia with fibrinogenopenia: a new syndrome? *Acta Med Scand* 117:216–222
10. Wright I (1966) Waldenstrom macroglobulinemia: a cause of epistaxis in the elderly. *J Laryngol Otol* 80(2):194–198
11. Karim Bakri et al (2004) Waldenstrom macroglobulinemia presenting as isolated epistaxis: a common complaint but rare cause. *Int J Clin Pract* 58:(1) 81–82
12. Schwab PJ, Fahey JL (1960) Treatment of Waldenstrom's macroglobulinemia by plasmapheresis. *N Engl J Med* 263:574–579
13. Buskard NA, Galton DAG, Goldman JM, et al (1977) Plasma exchange in the long-term treatment of Waldenstrom's macroglobulinemia. *Can Med Assoc J* 117:135–137
14. Facon T, Brouillard M, Duhamel A, et al (1993) Prognostic factors in Waldenstrom's macroglobulinemia: a report of 167 cases. *J Clin Oncol* 11:1553–1558