Case Report

Idiopathic acquired haemophilia with inhibitors to factor VIII and IX in an elderly female: a case report

Rupasinghe S[1*], Kularatne WKS[1], Dissanayaka DMDN[1]
[1]National Hospital Kandy, Sri Lanka.

Abstract

Acquired haemophilia is a rare but life-threatening haematological disorder, commonly occurring in postpartum women and elderly age groups. Although 50% of cases are idiopathic, most cases of elderly patients are associated with malignancies and drugs such as penicillin and interferon. Early diagnosis with prompt control of bleeding and treating the underlying condition is important to reduce morbidity and mortality. Here we report a rare case of an elderly female presenting with mucocutaneous bleeding found to have inhibitors against both factors VIII and IX. She was diagnosed to have idiopathic acquired haemophilia after excluding the secondary causes. She was promptly started on immunosuppressive therapy which led to complete remission. We confirm that early diagnosis and aggressive treatment of acquired haemophilia in elderly patients presenting with bleeding disorders will enhance prognosis.

Keywords: Acquired Haemophilia, Inhibitors to clotting factors, Activated prothrombin complex concentrates, Elderly, Idiopathic

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*✉ **Correspondence:** *sawandika33@gmail.com*

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Introduction

Acquired haemophilia is a rare but life-threatening bleeding disorder caused by the development of auto-antibodies against clotting factors which affects 1 to 1.5 per million people yearly (1). Most antibodies are formed against factor VIII, which is known as acquired haemophila A (2). Acquired antibodies against factor IX are very rare and are only reported in association with the postpartum period (3). A majority of patients present with bleeding in the absence of a provocative cause (4). Even though a majority of cases are idiopathic, it's important to rule out malignancies, infections, and autoimmune disorders.

Here we report a case of an 85-year-old female who presented with ecchymotic patches over both arms. She was found to have a high activated partial thromboplastin time (APTT) level with inhibitors to both factor VIII and IX and was diagnosed to have idiopathic acquired haemophilia. Even though there are cases reported with inhibitors against clotting factor VIII and rarely factor IX, cases with inhibitors to both factor VIII and IX are very rare in literature.

Case presentation

An 85-year-old elderly female presented with a history of hypertension presented with purplish-red skin patches in both arms over two weeks duration. She denied any mucosal bleeding or bleeding into joints or muscles. There was no family history of bleeding disorders, autoimmune disorders, or malignancy.

On examination, there were non-tender, large ecchymotic areas on both arms, in the right arm extending from upper arm to elbow region and in the left arm extending just below the elbow region. There was no gum bleeding, epistaxis, petechiae, purpura, or haemarthrosis. She had no cervical, axillary or inguinal lymphadenopathy.

Full blood count revealed a total white cell count of 9 x 10^9/L [neutrophils 62.7%, lymphocytes 25.7% and eosinophils 1.9%], haemoglobin of 8.1 g/dL [normal range: 3.6-17.2 g/dL], mean corpuscular volume of 85 fL [normal range: 80-96fL] and a platelet count of 309 x 10^9/L [normal range: 150-400 x10^9/L]. The blood picture revealed mild anaemia due to anaemia of chronic disease with blood loss and iron deficiency. Clotting profile revealed a prothrombin time of 12.2s [normal: <12s], international normalized ratio of 1.01, and an APTTof 105s [normal: <26s].

Bleeding time was one and a half minutes, and clotting time was more than 10 minutes. Mixing studies were suggestive of acquired inhibitors to factor VIII and IX. Factor VIII level was 0.087% [normal range: 50-150%] and factor IX level was 2.377% [normal range: 65-150%]. Antinuclear antibodies, anti-double-stranded DNA antibodies, and rheumatoid factor were negative. Erythrocyte sedimentation rate (ESR) was 30 mm/hr. Bone marrow biopsy did not reveal any evidence of malignancy. Other investigations, including electrocardiogram, 2D-echocardiogram, posteroanterior chest X-ray, liver function tests, renal function tests, and capillary blood sugar levels, were normal. Ultra-sound scan of abdomen and thyroid profile were normal. Lactate dehydrogenase and reticulocyte count were normal, and the direct antiglobulin test was negative. Contrast-enhanced computed tomography of the abdomen and pelvis did not show any evidence of malignancy.

Bleeding was controlled with tranexamic acid, cryoprecipitate, plasma-derived factor IX concentrate. Since she had symptomatic anaemia, she was transfused with one unit of packed red cells and was started on prednisolone dose of 1 mg/kg/daily.

Despite treatment, she had severe bleeding from the bone marrow aspiration site and was started on intra-venous factor eight inhibitor bypass activity (FEIBA) and cyclophosphamide. She responded to treatment, and her ATPP returned to normal.

She was discharged with oral prednisolone and cyclophosphamide. After three months of treatment mixing studies, factor VIII level, factor IX level, and APTT returned to a normal level.

Discussion

Acquired haemophilia is a haematological disorder caused by the formation of antibodies commonly against factor VIII and rarely against factor IX and other clotting factors. It is a rare bleeding disorder common in the elderly, where the commonest presentation is spontaneous bleeding (5). In most cases, autoantibodies are formed against factor VIII, which is known as acquired haemophilia A (2). But in our case, inhibitors were present against both factor VIII and IX, which has the incidence as 1 per million per year, with many cases being undiagnosed (5).

The most common presenting symptom is mucocutaneous and soft tissue bleeding. Hemarthrosis is

less common, unlike inherited haemophilia. 50% of cases are thought to be idiopathic, while others are associated with autoimmune conditions, haematological malignancies, and solid tumours. Some cases are reported in association to drugs, including interferon and penicillin, as well as during pregnancy and the postpartum period (6). Unlike inherited haemophilia, acquired haemophilia has equal sex distribution with a median age of presentation of 60-67 years (6).

Patients with acquired haemophilia have prolonged activated partial thromboplastin time with a normal prothrombin time as in our case. Mixing test or inhibitor screen is the initial diagnostic test for acquired haemophilia. But the mixing test will not detect the specificity of inhibitors. Thus, the Bethesda Assay should be performed as it will confirm the presence of inhibitors for clotting factors as well as quantifies the titre (7). Our patient's factor VIII level was 0.087% and factor IX level was 2.377%. Mixing study was suggestive of acquired inhibitors to both factor VIII and IX. Bethesda assay was not performed due to the unavailability of reagents.

The main goals of treatment include controlling and preventing bleeding, inhibitor eradication, and treating the underlying disease (8). Prompt haemostatic control is mandatory to reduce morbidity and mortality (8). In patients with confirmed acquired haemophilia with severe bleeding, anti-haemorrhagic drugs should be started irrespective of inhibitor titre. Options include factor bypassing agents and increasing factor VIII/IX levels. Available bypassing agents include recombinant activated factor VII and activated prothrombin complex concentrates [aPCC or factor eight inhibitor bypass activity (FEIBA)]. Treatment modalities that increase factor VIII level are only used in cases of mild bleeding or cases with low inhibitor titres. These include infusion of factor VIII concentrate or desmopressin (DDAVP) that increases the release of factor VIII by endothelial cells (6).

Inhibitor eradication is recommended in all cases of confirmed acquired haemophilia unless there are contraindications (9). The recommended regimens are corticosteroids alone or corticosteroids in combination with cyclophosphamide and rituximab (10). Our patient was started on prednisolone 1mg/kg along with cyclophosphamide, after which complete remission was achieved.

Conclusion

When considering our case and available literature, acquired haemophilia should be considered a differential diagnosis in an elderly patient presenting with bleeding manifestations. Even though 50% are idiopathic, its important to rule out associated underlying causes such as autoimmune diseases and malignancies. Bleeding should be controlled and prevented promptly. Early diagnosis of acquired haemophilia, as well as the underlying cause, is mandatory in order to reduce morbidity and mortality.

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References

1. Stephen SE, Loong JLX, Hoong CK, Lim SM, Botross NP. Acquired hemophilia of unknown etiology in an elderly man: Case report. Am J Case Rep. 2018 23;19:858–63.
2. Franchini M, Gandini G, Di Paolantonio T, Mariani G. Acquired hemophilia A: a concise review. Am J Hematol. 2005;80(1):55-63. doi: 10.1002/ajh.20390. .
3. Miller K, Neely JE, Krivit W, Edson JR. Spontaneously acquired factor IX inhibitor in a nonhemophiliac child. J Pediatr. 1978;93(2):232–4.
4. Knoebl P, Marco P, Baudo F, Collins P, Huth-Kühne A, Nemes L, et al. Demographic and clinical data in acquired hemophilia A: Results from the European Acquired Haemophilia Registry (EACH2). J Thromb Haemost. 2012;10(4):622–31.
5. Yousphi AS, Bakhtiar A, Cheema MA, Nasim S, Ullah W. Acquired hemophilia A: A rare but potentially fatal bleeding disorder. Cureus. 2019;11(8):e5442.
6. Baudo F, Collins P, Huth-Kühne A, Lévesque H, Marco P, Nemes L, et al. Management of bleeding in

acquired hemophilia A: Results from the European Acquired Haemophilia (EACH2) registry. Blood. 2012;120(1):39–46.

7. Kasper CK, Aledort L, Aronson D, Counts R, Edson JR, van Eys J, et al. Proceedings: A more uniform measurement of factor VIII inhibitors. Thromb Diath Haemorrh. 1975;34(2):612.

8. Baudo F, Caimi T, de cataldo F. Diagnosis and treatment of acquired haemophilia. Haemophilia. 2010;16(102):102–6.

9. Hay CRM. Acquired haemophilia. Baillieres Clin Haematol. 1998;11(2):287–303.

10. Delgado J, Jimenez-Yuste V, Hernandez-Navarro F, Villar A. Acquired haemophilia: review and meta-analysis focused on therapy and prognostic factors. Br J Haematol. 2003;121(1):21-35. doi: 10.1046/j.1365-2141.2003.04162.x. .