American Journal of Case Reports

e-ISSN 1941-5923
© Am J Case Rep, 2019; 20: 1046-1048
DOI: 10.12659/AJCR.916783

Received: 2019.04.05
Accepted: 2019.05.22
Published: 2019.07.18

Emicizumab Use in Treatment of Acquired Hemophilia A: A Case Report

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

E 1 Kadhim Al-Banaa
E 2 Alsadiq Alhillan
E 3 Fadi Hawa
E 1 Raai Mahmood
E 1 Ahmed Zaki
E 1 Mohamad El Abdallah
E 1 Ammar ELJack
E 1 Jonathan Zimmerman
E 1 Faisal Musa

1 Department of Internal Medicine, Beaumont Hospital, Dearborn, MI, U.S.A.
2 Department of Internal Medicine, Jersey Shore University Medical Center, Neptune, NJ, U.S.A.
3 Department of Internal Medicine, St. Joseph Mercy Hospital, Ann Arbor, MI, U.S.A.

Corresponding Author: Kadhim Al-Banaa, e-mail: Kadhim.al-banaa@beaumont.org
Conflict of interest: None declared

Patient: Female, 87
Final Diagnosis: Acquired hemophilia A
Symptoms: Chest discomfort • shortness of breath
Medication: —
Clinical Procedure: —
Specialty: Hematology

Objective: Unusual setting of medical care

Background: Acquired hemophilia A (AHA) is a rare hemorrhagic disorder that is caused by producing autoantibodies against factor VIII. It is usually characterized by severe, spontaneous bleeding, which can be life-threatening. The current standard treatments for bleeding prophylaxis are highly effective but accompanied with some disadvantages such as frequent intravenous infusions, high cost, and risk of thromboembolic complications. Emicizumab is a bispecific antibody with a therapeutic FVIII-mimetic nature. Emicizumab has shown a reduction in annualized bleeding rate in congenital hemophilia patients with and without inhibitors. The pathophysiological concepts and preclinical data suggest that Emicizumab can be effectively used for treating AHA.

Case Report: We present the case of an 87-year-old woman admitted for symptomatic anemia and large chest wall and pelvic hematomas confirmed by imaging, without history of trauma. Her coagulation studies showed isolated prolonged activated partial thromboplastin time (aPTT), low factor VIII activity level, and high levels of factor VIII inhibitor. She was successfully treated with activated prothrombin complex concentrate (aPCC), which was transitioned to Emicizumab on discharge. No recurrent bleeding episodes or adverse events related to Emicizumab were reported during the 2-month follow-up period.

Conclusions: A subcutaneous weekly or biweekly injection of Emicizumab, a recombinant monoclonal antibody, offers several advantages: less frequent infusions, good hemostatic efficacy, possible outpatient therapy, and even more cost-effective than bypassing agents. More clinical studies should be conducted to compare Emicizumab with the current standards of care.

MeSH Keywords: Antibodies, Bispecific • Factor VIII • Hemophilia A

Full-text PDF: https://www.amjcaserep.com/abstract/index/idArt/916783

Indexed in: [PMC] [PubMed] [Emerging Sources Citation Index (ESCI)] [Web of Science by Clarivate]

Background

Acquired hemophilia A (AHA) is an uncommon hemorrhagic disorder that is caused by producing autoantibodies against factor VIII [1]. It is usually characterized by severe, spontaneous bleeding, which can be life-threatening [1]. AHA is predominantly seen in the elderly. Among elderly patients, 80% of the affected population are age 65 years or older. AHA may also occur in the younger population [2]. Among all reported cases, 50% are idiopathic, and the remaining cases are related to various medical conditions such as pregnancy, malignancy (including solid tumors and hematological malignancies), autoimmune disorders or collagen vascular disorder, respiratory disorder, infections, and drugs [1]. A patient can be suspected to have AHA if they bleed easily but have no prior or family history of bleeding, an unexplained prolongation of activated partial thromboplastin time (APTT), and other etiologies of prolonged APTT are ruled out [1]. One of the primary objectives of AHA treatment is to treat bleeding and/or prevent future complications. AHA patients with inhibitors need to be followed up for a longer period, as they have a high risk of severe and life-threatening hemorrhage [3]. The current standard treatments for hemorrhage are bypassing agents such as recombinant activated human factor VII (rhFVIIa) and activated prothrombin complex concentrates (aPCC), and FVIII concentrates (human-based or porcine-based). These standard treatments are highly effective but have some disadvantages such as frequent intravenous infusions, expense, and risk of thromboembolic complications [4]. Emicizumab is a bispecific antibody with a therapeutic FVIII-mimetic nature. Emicizumab has shown a reduction in annualized bleeding rate in congenital hemophilia patients with and without inhibitors. Hence, Emicizumab use in patients with congenital hemophilia has been approved [5]. The pathophysiological concepts and preclinical data suggest that Emicizumab can be effectively used for treating AHA. Outside the clinical studies, few patients with AHA have been treated with Emicizumab, showed interesting clinical responses [6].

Case Report

We present the case of an 87-year-old female patient with a known diagnosis of chronic atrial fibrillation, who had a recent history of GI bleeding during warfarin use, which lead to discontinuation of anticoagulation therapy. The patient was admitted to the hospital for symptomatic anemia, as well as a significant left upper-extremity, axillary, and breast hematoma, without a history of trauma. The patient had no family history of hemophilia, bleeding, or any blood clots. The patient's initial laboratory findings showed hemoglobin 7.0 g/dl, white cell count 12 000/µl, and platelet count 171 000/µl. The patient's prothrombin time (PT) and the international normalized ratio

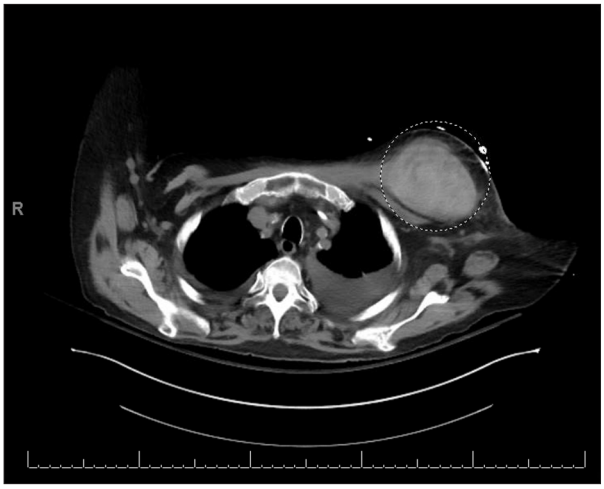

Figure 1. CT scan of the chest with contrast, showing left chest wall and left breast hematoma, measuring approximately 7.9×5.5 cm.

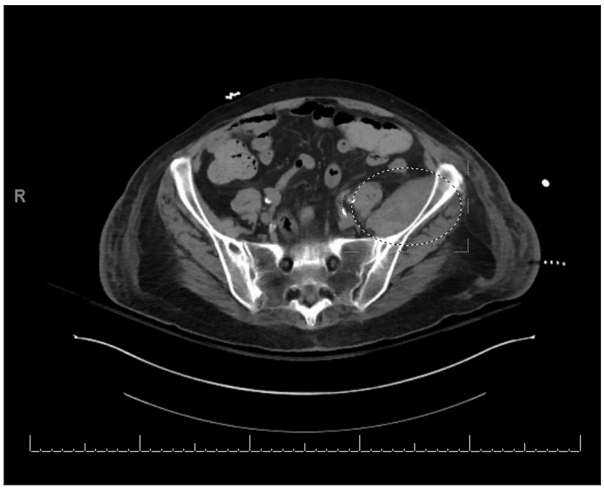

Figure 2. CT scan of the abdomen and pelvis showing a left iliacus muscle hematoma, measuring 6.6×2.3 cm.

(INR) were found to be normal (12.2 seconds and 1.1 seconds, respectively). However, activated partial thromboplastin time (aPTT) was found to be prolonged (110 seconds). Hepatic function test results were normal. CT scan of the chest revealed hematoma in the left chest wall and left breast, with a measurement of approximately 7.9×5.5 cm (Figure 1). CT scan of the abdomen and pelvis revealed a left iliacus muscle hematoma measuring 6.6×2.3 cm (Figure 2). Later, a mixing study revealed the presence of inhibitors. Factor VIII activity level was <1%, and the inhibitor level was >100 Bethesda units. Lupus anticoagulant testing showed a negative result. Factor IX, XI, XII, XIII, and von Willebrand factor activities were found to be normal. Infectious work-up for hepatitis B and C, in addition to rheumatologic serologic testing to look for a secondary cause for AHA, showed a negative result. Based on symptoms and laboratory work, the patient was diagnosed

Indexed in: [PMC] [PubMed] [Emerging Sources Citation Index (ESCI)] [Web of Science by Clarivate]

with AHA. The patient was started on activated prothrombin complex concentrate (aPCC) 50 units/kg every 12 hours for 2 weeks. Hemostatic efficacy was achieved (hematoma size reduced, stabilized hemoglobin level, no more blood transfusions needed). The patient was discharged and bypass treatment was stopped for 1 day. The patient's treatment was transitioned to Emicizumab 3 mg/kg/week for 1 month, then to 1.5 mg/kg/week. The patient was followed up for 2 months after hospitalization while continuing Emicizumab treatment. There were no reported adverse events or any complaint of major bleeding related to Emicizumab treatment.

Discussion

A major challenge in AHA patients is attaining hemostasis stability. Patients with high inhibitor titer (>5BU) are treated with recombinant FVII (rFVIIa) or activated prothrombin complex concentrate (aPCC) to control acute bleeding [7]. Patients with low inhibitor titer (<5BU) are treated with desmopressin (DDAVP) or concentrates of FVIII. Treatment with aPCC shown a good hemostatic response in 93% of the bleeding episodes, and treatment with rFVIIa showed a good response in 92% of episodes [8]. Duration of use of bypassing agents as hemostatic therapy in AHA patients has not been established yet because there are no optimum markers to assess the risk of hemorrhage [9]. Many cases have been judged subjectively by each physician, deciding that few patients need long-term prophylactic treatment. It is difficult to perform in an outpatient setting because the bypassing agents have a shorter half-life (rFVIIa is 2 h and aPCC is 8–12 h) and intravenous access is needed. Thrombosis is considered a major complication during treatment with bypassing agents [7]. Thrombotic events were reported in 3.6% of patients treated with bypassing agents, and the incidence rate with rFVIIa is 2.9% and 4.8% with aPCC. Old age was also considered a risk factor for thrombosis [8].

Emicizumab is a bispecific recombinant monoclonal antibody containing 2 different antigen-binding fragments – one fragment recognizes FIX/FIXa and the other recognizes FX/FXa. Emicizumab bridges both factors FIX and FX, and activates factor VIII, which is necessary for effective hemostasis [10]. This unique structure of Emicizumab is not affected by existing factor VIII inhibitors [5]. Patients with hemophilia A with inhibitors treated with Emicizumab show a significantly lower rate of bleeding events [5]. Since there is a pathophysiology similarity between congenital hemophilia with inhibitors and AHA, we believe Emicizumab can be effectively used as a bleeding prophylactic modality for AHA patients, and it can be started after treating any acute bleeding episode with the current standard of care treatment (bypassing agents), as Emicizumab has been only studied for bleeding prophylaxis [5]. Emicizumab has a longer half-life than other modalities; it therefore requires less frequent subcutaneous infusions (every week or every 2 weeks), allowing for long-term outpatient treatment, which could be more cost-effective than treatment with other modalities [6]. There were no reported thrombotic events with Emicizumab prophylaxis alone [5]. However, thrombotic microangiopathy was reported in patients concurrently treated with bypassing agents (aPCC) [4].

Conclusions

Emicizumab was recently approved and can effectively treat AHA patients, with advantages of good hemostatic efficacy, weekly subcutaneous infusions, a good adverse events profile, and the possibility of outpatient therapy. Treatment with Emicizumab is more cost-effective than treatment with bypassing agents. More clinical studies should be conducted to compare the safety and efficacy of Emicizumab with the current standard treatment.

Conflicts of interest

None.

References:

1. Webert KE: Acquired hemophilia A. Semin Thromb Hemost, 2012; 38(7): 735–41
2. Rivera Cora NI, Irizarry Delgado F, Merle Ramirez SM, Vera Quinones J: Acquired hemophilia A in an advanced age patient of Hispanic origin: A case report. BMC Res Notes, 2017; 10(1): 438
3. Shetty SD, Ghosh K: Challenges and open issues in the management of acquired hemophilia A(AHA). Blood Cells Mol Dis, 2015; 54: 275–80
4. Knobl P: Prevention and management of bleeding episodes in patients with acquired hemophilia A. Drugs, 2018; 78(18): 1861–72
5. Oldenburg J, Mahlangu JN, Kim B et al: Emicizumab prophylaxis in hemophilia A with inhibitors. N Engl J Med, 2017; 377(9): 809–18
6. Knoebl P, Sperr W, Schellongowski P, Staudinger T: Emicizumab for the treatment of acquired hemophilia A: Lessons learned from 4 very different cases. Hamostaseologie, 2019; 39
7. Kruse-Jarres R, Kempton CL, Baudo F et al: Acquired hemophilia A: Updated review of evidence and treatment guidance. Am J Hematol, 2017; 92(7): 695–705
8. Baudo F, Collins P, Huth-Kuhne A et al: Management of bleeding in acquired hemophilia A: Results from the European Acquired Haemophilia (EACH2) Registry. Blood, 2012; 120(1): 39–46
9. Zdziarska J, Musial J: Acquired hemophilia A: An underdiagnosed, severe bleeding disorder. Pol Arch Med Wewn, 2014; 124(4): 200–6
10. Lenting PJ, Denis CV, Christophe OD: Emicizumab, a bispecific antibody recognizing coagulation factors IX and X: How does it actually compare to factor VIII? Blood, 2017; 130(23): 2463–68

Indexed in: [PMC] [PubMed] [Emerging Sources Citation Index (ESCI)] [Web of Science by Clarivate]