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CASE REPORT
Arrhythmias/Electrophysiology

Percutaneous left atrial appendage closure in a patient with haemophilia and atrial fibrillation: a case report

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Background Atrial fibrillation (AF) is the most common cardiac arrhythmia and is a major cause of embolic stroke. In patients with hereditary bleeding disorders such as haemophilia, management of AF particularly anticoagulation can be quite challenging. Left atrial appendage (LAA) closure is an emerging option in AF patients who are not eligible for oral anticoagulation therapy because of contraindications or high bleeding risk.

Case summary A 67-year-old man with permanent AF and haemophilia was referred for further evaluation of our cardiology clinic by his primary haematologist. The CHA_2DS_2-VASc score was estimated to be 3 and the HAS-BLED score was 3. Due to high risk of bleeding, we decided to perform percutaneous LAA closure instead of oral anticoagulation. Pre-procedural cardiac computerized tomography angiography and transoesophageal echocardiography were performed for measurements of LAA dimensions and exclude LAA thrombus. Percutaneous LAA occlusion was performed using a 28-mm Amplatzer™ Amulet™ device. The final result was excellent without significant residual leak, pericardial effusion, and embolic complication. Clopidogrel 75 mg/day and aspirin 81 mg/day for 1 month with adequate FVIII prophylaxis and then only aspirin 81 mg/day for 2 months were recommended. No antiplatelet was given after 3 months. The patient did not report any thrombotic or haemorrhagic adverse events and there were no complications related to implanted device after 1 year of follow-up.

Discussion In patients with hereditary bleeding disorders such as haemophilia, management of AF particularly anticoagulation can be quite challenging. In this report, we present a case of percutaneous LAA occlusion using Amplatzer™ Amulet™ device in a patient who has haemophilia and permanent AF. LAA closure has the potential to be more cost effective as compared to oral anticoagulation therapy due to lesser necessity of clotting factor infusion.

Keywords Atrial fibrillation • Haemophilia • Left atrial appendage closure • Case report

Learning points

- Anticoagulation therapy for atrial fibrillation can be challenging in patients with hereditary bleeding disorders such as haemophilia due to the increased risk of bleeding. Also, the requirement of clotting factor infusions increases cost.
- Instead of long-term oral anticoagulation therapy, left atrial appendage closure with a percutaneous device can decrease thromboembolic risk and has the potential to be more cost effective due to the lower requirement of clotting factor infusion.

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Introduction

Management of atrial fibrillation (AF) is particularly challenging in patients with hereditary bleeding disorders such as haemophilia. Due to prolonged survival rates of haemophilia patients, age-related chronic cardiovascular disorders such as AF are seen more frequently. Atrial fibrillation is the most common cardiac arrhythmia and is a major cause of embolic stroke.[1] Transoesophageal echocardiography (TOE) data and surgical reports reveal that >90% of AF-related thrombi originate from the left atrial appendage (LAA).[2] Left atrial appendage closure is an emerging option in AF patients who are not eligible for oral anticoagulation therapy because of contraindications or high bleeding risk.[3] In this case report, we present a haemophilia patient in whom LAA closure was performed by using an Amplatzer™ Amulet™.

Timeline

Day 1	A 67-year-old man with permanent atrial fibrillation and haemophilia. Patient's CHA_2DS_2-VASc score was 3 and HAS-BLED score was 3. Percutaneous closure of left atrial appendage (LAA) instead of oral anticoagulation to prevent thromboembolic complications was decided.
Day 3	Pre-procedural cardiac computerized tomography angiography and transoesophageal echocardiography (TOE) for measurements of LAA dimensions and excluding LAA thrombus.
Day 4	Successful percutaneous LAA closure procedure
Day 5	The patient was discharged in stable condition with dual antiplatelet therapy and adequate FVIII prophylaxis
Week 6	Repeat TOE: stable device position and LAA occlusion without significant residual leak and device associated thrombus
Year 1	No thromboembolic and bleeding complications and adverse events related to LAA closure device after 1 year of follow-up

Case presentation

A 67-year-old man with permanent AF and haemophilia was referred for further evaluation to our cardiology clinic by his primary haematologist. His past medical history included hypertension and heart failure. Recombinant factor VIII infusion was prescribed regularly and his baseline factor VIII activity level was kept around 10% by his primary haematologist. The CHA_2DS_2-VASc score was estimated to be 3 and the HAS-BLED score was 3. Due to the high risk of bleeding, we decided to perform percutaneous LAA closure. Pre-procedural cardiac computerized tomography angiography and TOE were performed for measurements of LAA dimensions and exclude LAA thrombus (*Figure 1*). The procedure was performed under mild anaesthesia, with the aid of TOE and fluoroscopy guidance. Additional recombinant factor VIII was administered according to the recommendations of haematologist before catheterization. Based on measurements, a 28-mm Amplatzer™ Amulet™ device was chosen for occlusion. Initially, trans-septal puncture was performed at the posteroinferior interatrial septum using the right femoral vein as the access site, and then 5000 IU of intravenous heparin was administered. The transseptal sheath was exchanged for the 12-Fr delivery catheter which was subsequently loaded with the 28-mm Amplatzer™ Amulet™ device. The delivery catheter was advanced up to the LAA ostium and under TOE guidance the lobe of the device was carefully pushed to the landing zone and deployed at that level. The deployment of the proximal disc was then achieved by advancing the delivery cable while unsheathing the disc (*Figure 2*). The final result was excellent without significant residual leak, pericardial effusion, and embolic complication (*Figure 3*).The remaining hospital stay was uneventful and he was discharged on the following day. Clopidogrel 75 mg/day and aspirin 81 mg/day for 1 month with adequate FVIII prophylaxis and then only aspirin 81 mg/day for 2 months were recommended. No antithrombotic was given after 3 months. The patient did not report any thrombotic or haemorrhagic adverse events and there were no complications related to implanted device after 1 year of follow-up.

Discussion

Warfarin and the novel oral anticoagulants are current options for systemic anticoagulation in AF. However, there is still a significant number of patients who are poor candidates for oral anticoagulation.

Haemophilia is a rare genetic disorder mostly inherited in an X-linked recessive manner and males are affected more frequently. There are two main types: haemophilia A (factor VIII deficiency) and haemophilia B (factor IX deficiency).[4] Use of recombinant clotting factors has prolonged the expected life of patients with haemophilia beyond 60–70 years of age; therefore, this aged population are at risk for developing AF and other chronic cardiovascular conditions.[5,6] Management of AF in patients with haemophilia can be quite complex particularly for long-term stroke risk reduction and procedural considerations.

No robust published data exist to guide the management of patients with haemophilia and AF. Rather, expert consensus based on case reports and observational data serve as the primary references for clinicians.[7–9] Recently, it has been demonstrated that in patients at high risk for stroke (CHA_2DS_2VASc score ≥2), with associated high bleeding risk (HAS-BLED ≥3) prolonged anticoagulation resulted in more serious bleeding.[7] Oral anticoagulation (warfarin or direct oral anticoagulants) should only be prescribed to patients with very mild haemophilia (native factor activity level ≥20–30%). In those with more severe forms of haemophilia, coagulation factor infusion to obtain an activity level goal of 20–30%, in addition to oral anticoagulation, should be considered.[6,7,9,10] However, none of these suggestions were extensively studied. Besides, the cost of recombinant factor infusion must always be kept in mind. Another current alternative is the LAA occlusion by surgery or devices.[11,12] We present a

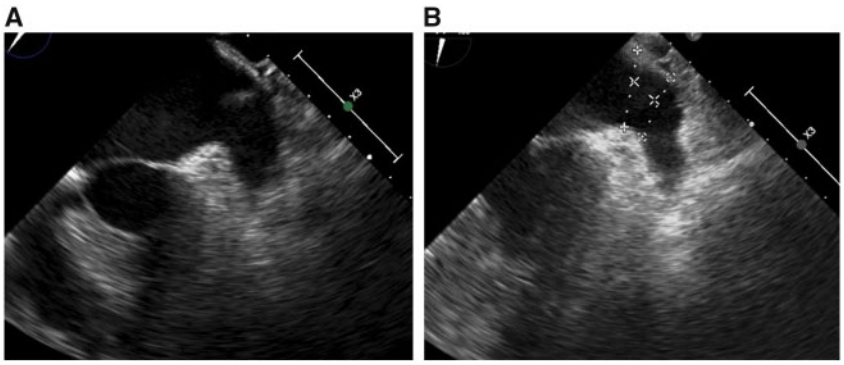

Figure 1 Two-dimensional transoesophageal echocardiography image of left atrial appendage (*A*), diameters of left atrial appendage ostium and 10 mm distal to ostium (*B*). LAA, left atrial appendage; TOE, transoesophageal echocardiography.

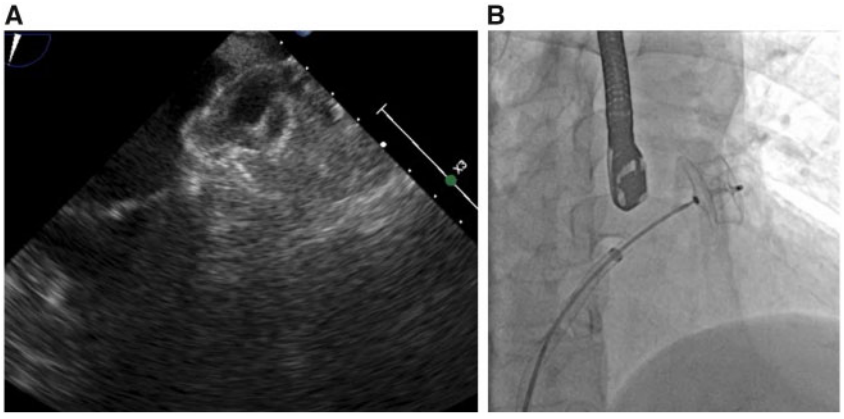

Figure 2 The deployed left atrial appendage closure device (24-mm Amplatzer™ Amulet™) was confirmed with transoesophageal echocardiographic imaging (*A*) and fluoroscopic imaging (*B*).

patient with haemophilia A who successfully underwent percutaneous LAA closure by using a standard factor replacement protocol. To our knowledge, this is the first reported case of percutaneous LAA closure with Amplatzer™ Amulet™ device in a patient with haemophilia. Only one report has been published in a similar patient with haemophilia and AF using a previous version of the device.[11] Transcatheter closure of the LAA is becoming more common as an interventional therapy to prevent thromboembolic complications in patients with AF and contraindications or resistance to chronic oral anticoagulation.[1,11,12] Percutaneous occlusion of LAA may also decrease cost and improve patient's compliance as compared to oral anticoagulation which necessitates frequent clotting factor replacement. In general, short duration of anticoagulant therapy is suggested after percutaneous LAA occlusion. However, recent data suggested that LAA occlusion device implantation followed by dual antiplatelet treatment (DAPT) for several weeks to months and a single antiplatelet drug or nothing thereafter can also be performed safely in patients at high bleeding risk.[11–13] Although the coagulation cascade is impaired in patients with haemophilia, both platelet count and functions are normal. However, adding dual or single antiplatelet therapy further increase the overall bleeding risk.[12] Thus, the period of DAPT should be kept as short as possible and prophylactic factor replacement is indicated depending on haemophilia severity.[13] Some reviews suggested that in mild or moderate haemophilia, factor trough levels of 25–30% should be obtained with once daily infusion or residual clotting factor level should be 25% or higher during DAPT and minimum trough levels should be kept at 5–15%.[7,9,13] Also on long-term treatment with ASA alone, trough factor levels of ≥1% are thought to be acceptable.[7,9,13] We chose not to use any post-procedure anticoagulation in our patient, given his high bleeding risk, instead DAPT with 81 mg aspirin and 75 mg clopidogrel for 1 month with adequate factor VIII replacement was used. ASA 81 mg/day for 2 months were recommended subsequently.

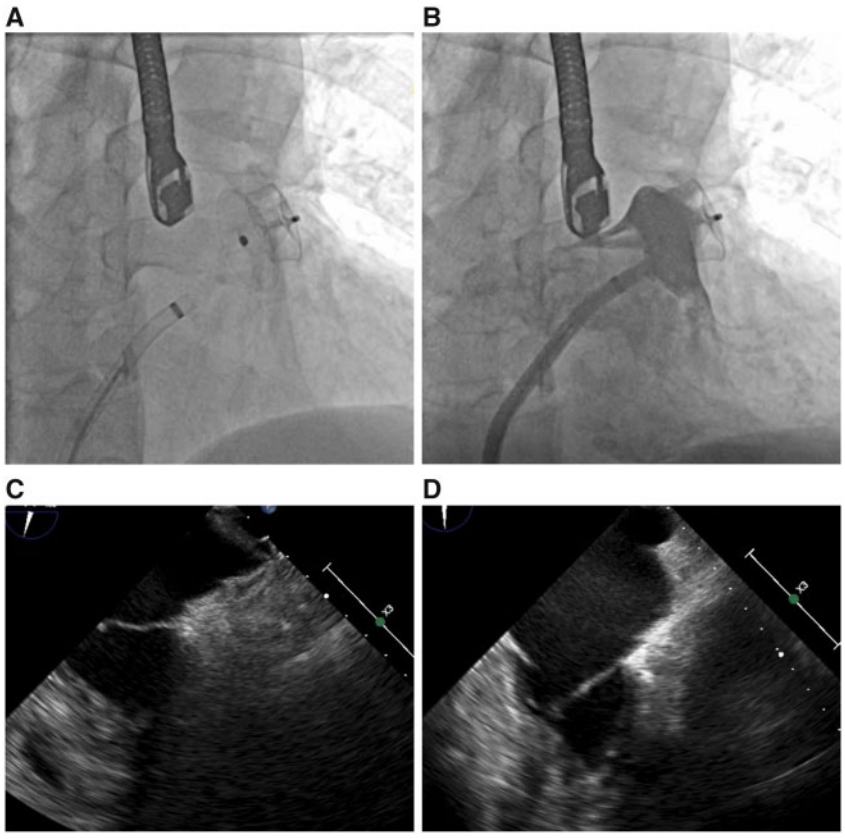

Figure 3 A final fluoroscopy and angiographic image after device release (*A* and *B*), final device position on transoesophageal echocardiographic (*C*), and repeat transoesophageal echocardiographic images 6 weeks later (*D*). TOE, transoesophageal echocardiography.

Conclusion

To the best of our knowledge, this is the first reported case of LAA closure with the Amplatzer™ Amulet™ device in a patient who has permanent AF and haemophilia A.

Percutaneous LAA closure seems a viable alternative to oral anticoagulation in patients with AF and haemophilia who are at high risk for embolic and bleeding complications and in long term it has a potential to be more cost effective as compared to oral anticoagulation therapy due to lesser necessity of clotting factor infusion.

Lead author biography

Ümit Güray is an Associate Professor of Cardiology. Currently, he works for Department of Cardiology in Ankara City Hospital. His main interests are electrophysiology and interventional cardiology.

Supplementary material

Supplementary material is available at *European Heart Journal - Case Reports* online.

Slide sets: A fully edited slide set detailing this case and suitable for local presentation is available online as Supplementary data.

Consent: The author/s confirm that written consent for submission and publication of this case report including image(s) and associated text has been obtained from the patient in line with COPE guidance.

Conflict of interest: none declared.

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