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Spontaneous Hematoma of Upper Extremities in a Patient with Antiphospholipid Antibody Syndrome: A Case Report

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Abstract

A 44-year-old woman with underlying systemic lupus erythematosus and antiphospholipid antibody syndrome presented with nausea and vomiting after her 2nd vaccination for coronavirus disease 2019 (COVID-19). Thirteen days after warfarin injection was administered along with steroid therapy, the patient suffered sudden right shoulder pain, paresthesia, and swelling, suggesting acute compartment syndrome. The warfarin regimen was bridged to low molecular weight heparin and fasciotomy was performed. Multiple hematoma evacuation after fasciotomy was done and the patient was referred for skin necrosis. Frequent debridement and negative pressure wound therapy were performed to heal the right upper extremity skin defect. Afterwards, the patient experienced hemorrhage in her left upper extremity and was treated conservatively with simple compression. This report suggests that patients undergoing anticoagulation therapy for antiphospholipid syndrome should be closely monitored for subcutaneous hemorrhage, and that prompt diagnosis and treatment may prevent adverse results. If massive skin necrosis occurs, multiple surgical debridement procedures and application of negative pressure wound therapy may be an option.

Keywords: Compartment syndrome; Antiphospholipid syndrome; Spontaneous hematoma; Case reports

Introduction

Antiphospholipid syndrome (APS) is a systemic autoimmune disease that elevates levels of antiphospholipid antibodies (aPLs), leading to arterial and venous thrombosis throughout the body and may also be associated with repeated miscarriage [1]. Thrombotic tendency is attributed to activated endothelial cells, platelets, and myeloid lineage cells and derangements in coagulation and fibrinolytic systems [2]. Not only does the risk of thrombosis increase, but the risk of bleeding can also increase due to anticoagulation therapy [3]. Cutaneous manifestations, such as necrotizing vasculitis, livedoid vasculitis, thrombophlebitis, cutaneous ulceration and necrosis, erythematous macules, purpura, ecchymoses, painful skin nodules and subungual splint hemorrhages may be observed [1]. Unlike compartment syndrome due to thrombosis of the lower extremities [4], spontaneous hemorrhage leading to acute compartment syndrome of the upper extremities has not been reported to the best of our knowledge.

Here, we present a case of a patient with underlying APS who developed massive spontaneous hemorrhages in the bilateral upper extremities at different time periods. Ethical approval for this study was obtained from the Institutional Review Board of Seoul National University Bundang Hospital (IRB No. B-2111-718-701). Patient informed consent was waived due to the retrospective nature of the study. This research

Case Report

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Case

A 44-year-old woman with underlying systemic lupus erythematosus and APS presented with nausea and vomiting after her 2nd vaccination for coronavirus disease 2019 (COVID-19). Routine laboratory tests showed pancytopenia and an increase in the international normalized ratio (INR) up to 5, suggesting a systemic lupus erythematosus flare. She was admitted to the rheumatology department for steroid therapy. Warfarin injection was administered in the addendum along with steroid therapy. On the 13th day of warfarin injection, the patient complained of sudden right shoulder paresthesia and motor weakness. After the initial impression of brain hemorrhage was ruled out by imaging studies, the patient developed severe pain and swelling accompanied by cutaneous bruising 2 days after the first symptoms. To control the bleeding, the warfarin regimen was stopped and bridged to low molecular weight heparin (LMWH), after which the INR decreased to 0.9–1.5. Computed tomographic angiography suggested active bleeding, most likely from the right lateral thoracic artery, as shown in Fig. 1. Radiologists attempted emergency embolization but failed to find the source of bleeding. With an impression of impending compartment syndrome, emergency fasciotomy was performed by orthopedic surgeons, 9 hours after the diagnosis. At the first operation, active bleeding from a ruptured axillary vein was identified and repaired. No other active bleeding site including the lateral thoracic artery was found. Later, wound exploration was performed several times due to recurrent bleeding and hematoma formation. Intraoperatively, active bleeding from re-rupture of axillary veins and non-specific bleeding from surrounding muscle were repaired and coagulated. The new bleeding sites were assumed to have been initially masked by the high pressure of the compartment syndrome and later exposed after the first fasciotomy. Between each wound exploration, compressive dressings with gauze and elastic band were performed. The patient was then referred to the department of plastic and reconstructive surgery for coverage of the skin defects and necrosis caused by fasciotomy and frequent wound exploration, as shown in Fig. 2. Debridement and reconstruction with a local flap and full-thickness skin graft were performed to cover all defects with drain insertion. Due to repetitive hematoma formation and skin necrosis, the wound bed was not healthy prior to debridement. After 3 days, the drainage spontaneously increased up to 100 mL per hour with a drop of systolic blood pressure to 70 mmHg. In suspicion of active bleeding, hematoma evacuation was performed. Multiple oozing sites were meticulously coagulated, and no definite active source of bleeding was found. The previous skin graft was regrafted after hematoma evacuation. After 4 days, no active bleeding was confirmed, but most of the regrafted skin was not taking well. Negative pressure wound therapy (NPWT) was applied to the remnant shoulder skin defect after removing the grafted skin, in cyclic mode and low oscillating pressures between –25 mmHg and –75 mmHg. After 2 months of NPWT, with significant secondary intention healing, the defect size had decreased, as shown in Fig. 3. With a smaller defect to cover, wound closure with bilateral advancement flaps was not difficult to achieve. The wound healed well, as shown in the postoperative 3 months' photo in Fig. 4. After wound healing, a nerve conduction study revealed grade

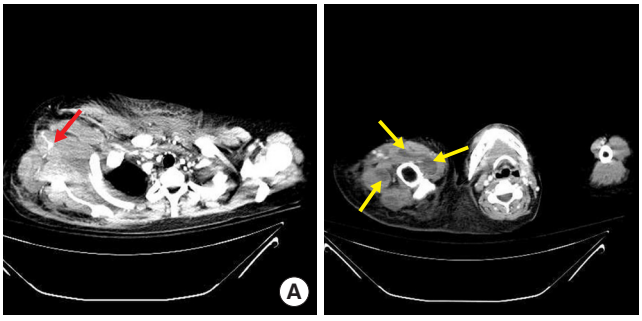

Fig. 1. Computed tomography angiography of upper extremity and chest wall. (A) Active bleeding with large amount of hematoma from the suspicious right lateral thoracic artery (red arrow). (B) Diffuse intramuscular and intermuscular hematoma (yellow arrows) in the right upper extremity which indicated compartment syndrome with muscle necrosis.

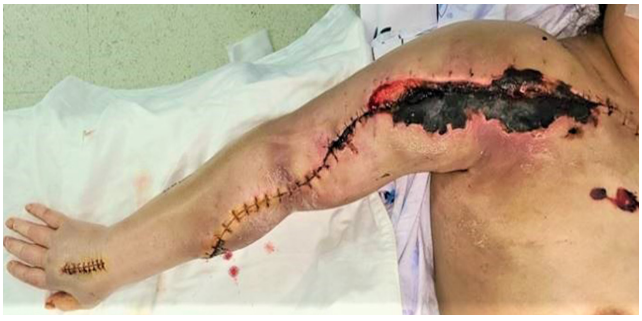

Fig. 2. Skin necrosis caused by fasciotomy and frequent wound exploration. Preoperative photography of right upper extremity before debridement and reconstruction with local flap and full thickness skin graft.

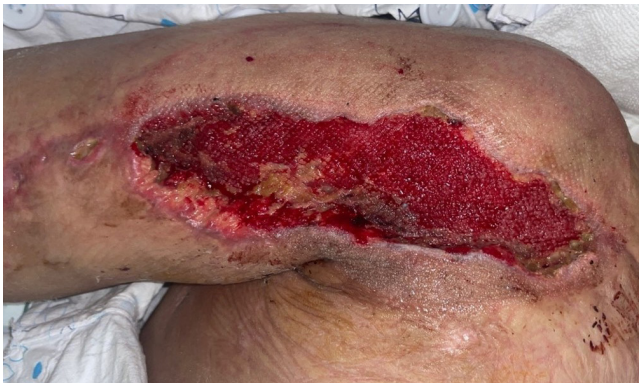

Fig. 3. Medical photo after negative pressure wound therapy treatment. Defect size of right upper extremity decreased with 2 months of negative pressure wound therapy application, followed by wound closure in the operating room.

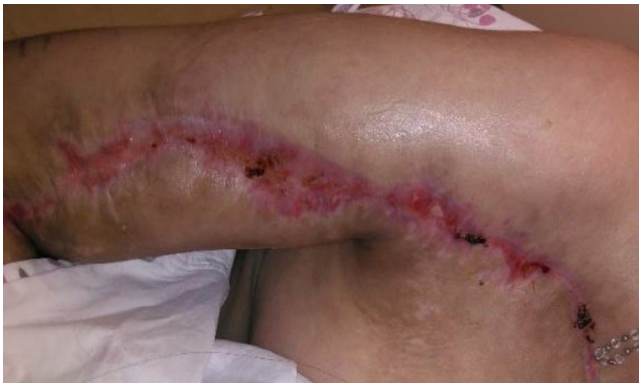

Fig. 4. Photograph of right upper extremity 3 months after wound closure.

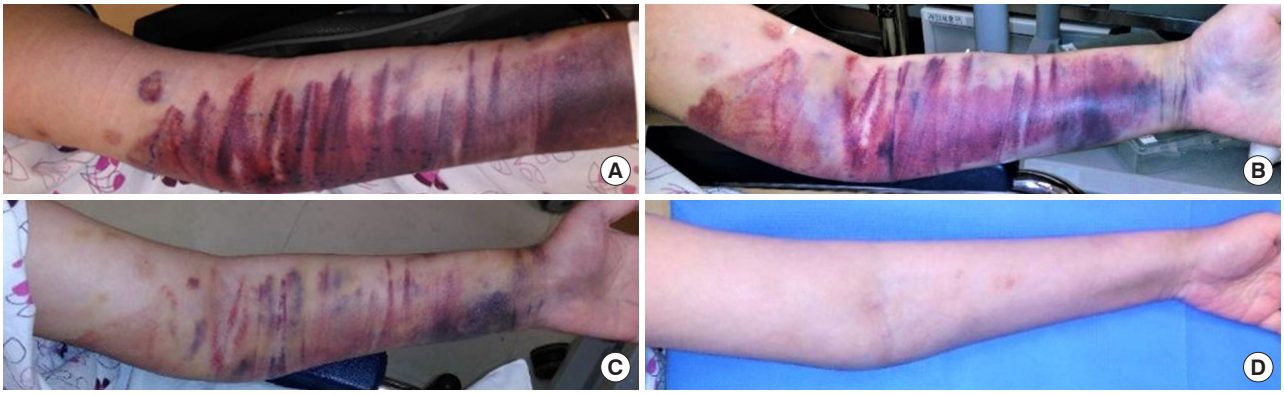

Fig. 5. Photographs of left upper extremity spontaneous hemorrhage and progress. (A) First appearance of the spontaneous hemorrhage when it was identified and (B) a week later. Mild elastic band compression was applied and anticoagulation treatment was replaced from warfarin to low molecular weight heparin to aspirin. (C) Two weeks later. (D) Finally, it subsided without operative management and without any neurologic sequelae.

3 motor brachial plexopathy in the proximal portion and grade 1 in the distal portion. As acute compartment syndrome was the only incident the patient presented with, it was assumed to be the main culprit for brachial plexopathy. Despite transferal to the rehabilitation medicine department, the patient showed no improvement in symptoms including wrist drop and poor grasp/pinching function at 4 months' follow-up.

After the wound in the right extremity healed completely, spontaneous hemorrhage developed in the left upper extremity, as shown in Fig. 5, 5 months after the right-side initial hemorrhagic event. Magnetic resonance imaging angiography showed a subfascial hematoma around the biceps and triceps brachii muscles; however, no active bleeding from any specific artery was identified. Mild elastic band compression was performed, and the warfarin regimen that had been re-started 2 months after the last surgical procedure was stopped immediately and bridged to LMWH, and then replaced with aspirin. Fortunately, the hemorrhage did not progress, nor did the patient develop compartment syndrome. As shown in Fig. 5, the left arm hemorrhage subsided without surgical management or any neurologic sequelae.

Discussion

Patients with underlying APS are at risk of both thrombosis and bleeding [1]. To the best of our knowledge, hematoma leading to acute compartment syndrome of the upper extremity in patients with underlying APS has not been reported in the literature. There have been case reports of acute compartment syndrome in patients under anticoagulation regimen, al-

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though the prevalence is unknown. In those cases, minor trauma was the predisposing factor [5].

In our patient, hemorrhage developed in the bilateral upper extremities sequentially. In the left upper extremity, which presented after the right side, the subcutaneous hemorrhage disappeared after early mild compression and discontinuation of warfarin. Surgical treatment was not required. In the right upper extremity, active arterial bleeding was observed on computed tomography angiography. Compartment syndrome was diagnosed with symptoms of pain, paresthesia, swelling and hemorrhage, and emergency fasciotomy was performed after a failed embolization. After fasciotomy, the patient underwent serial hematoma evacuation and debridement due to both repetitive bleeding and tissue necrosis. Although immediate flap coverage or skin grafts are the treatment of choice for covering skin defects, the first coverage procedure failed because of repetitive hematoma formation under the skin graft. Instead of re-attempting a single-stage procedure, we chose to minimize the skin defects using NPWT and planned to cover the remnant defect later. Between each debridement, NPWT was applied in cyclic mode with low oscillating pressures between –25 mmHg and –75 mmHg.

A previous study has described the use of NPWT in an APS patient who healed well by secondary intention. The authors pointed out three important considerations when treating patients at a high risk of bleeding. First, perform conservative debridement several times to minimize bleeding. Second, even when debriding conservatively, spend sufficient time and effort to ensure successful coagulation. Third, when applying NPWT, initiate with lower pressures and educate the patient or the nursing staff to consider a sudden increase in discharge or bleeding with NPWT as a red alert sign [6]. We agreed with the recommendations and have applied them to our patient.

The patient in our case presented with spontaneous bleeding in bilateral upper extremities sequentially with underlying APS. It took several conservative debridement and bleeding control procedures in the operating room and NPWT application in between procedures for complete healing of the skin necrosis of the right upper extremity. As we were closely monitoring the patient's bleeding events, the subcutaneous hemorrhage of the left extremity was identified at an early stage, and conservative treatment was sufficient.

In this case, the patient first presented with nausea and vomiting after the 2nd COVID-19 vaccination. Several studies have shown the presence of aPLs in the serum of COVID-19 patients, yet the association with thrombotic events remains debatable. COVID-19 infection and APS are similar in that both cause a systemic inflammatory response. The possibility that a newly formed aPL in COVID-19 patients may lead to an increased risk of clotting is supported by conflicting research. In a Belgian investigation of critically ill COVID-19 patients, aPLs were present but did not seem to increase clotting problems [7]. On the other hand, a different US-based study contends test results indicating the presence of new aPL are linked to an increase in clots [8].

While close monitoring is recommended in any patient under anticoagulant therapy, patients with underlying APS require even closer vascular attention because they usually maintain anticoagulation even when undergoing operations with risks of major bleeding [9]. Procedures associated with a low risk of bleeding can usually be performed without stopping anticoagulation. In high-risk bleeding surgery, the perioperative INR is recommended to be maintained under 1.5. However, for patients with previous thrombotic events, higher INR values, sometimes even over 3.0, are recommended and close monitoring is more important in these cases [10,11]. As such, patients with underlying APS require even more attention.

Our case showed strikingly different courses between the right and left upper extremities depending on the severity of hemorrhage. APS itself can cause bleeding tendency and if active bleeding is suspected, imaging studies are necessary to find the source of bleeding. Moreover, they can help diagnose acute compartment syndrome in the early course of the disease. Warfarin, frequently used for patients at a risk for thrombosis, should be bridged to LMWH immediately when active bleeding is expected. As in the left extremity of our patient, conservative treatment such as mild compression may prevent further development of hematoma and preclude the need for additional operative treatment. If hemorrhage becomes severe enough to develop compartment syndrome as in the right extremity of our case, fasciotomy should be performed. Generally, irreversible muscle and nerve injuries occur after 8 hours of ischemia. A thorough decompressive fasciotomy of all affected muscle compartments, nerves, and vessels is essential to obtain good clinical outcomes and to prevent catastrophic results [12,13]. While skin defects caused by fasciotomy are normally reconstructed using flaps or skin grafts, these options may not be available for patients with high bleeding tendency. In such circumstances, serial conservative debridement with meticulous hemostasis and NPWT are alternative options of treatment.

Conflict of interest

No potential conflict of interest relevant to this article was reported.

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