

# Acquired Factor VIII Deficiency Presenting as Compartment Syndrome

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**Background:** Compartment syndrome of the upper extremity is a surgical emergency that most often presents after an identifiable event, such as a crush injury, a closed fracture, a snake bite, reperfusion after embolectomy, an electrical injury, or a circumferential burn.

**Case Presentation:** We report an unusual case in which an older woman was diagnosed with acquired factor VIII deficiency after presenting with acute nontraumatic compartment syndrome in her right upper extremity. Emergency medicine, plastic surgery,

internal medicine, hematology, and hand therapy specialists worked together to identify the pathology and successfully treat the patient.

**Conclusions:** An isolated elevated partial thromboplastin time level in a patient who is bleeding should raise suspicions for factor VIII deficiency and immediately trigger further evaluation. Once this diagnosis is suspected, multidisciplinary treatment is indicated for immediate and long-term successful outcomes.

Compartment syndrome occurs when the interstitial tissue pressures within a confined space are elevated to a level at which the arterial perfusion is diminished. Multiple etiologies exist and can be extrinsic (a cast that is too tight or prolonged compression on a limb), iatrogenic (aggressive resuscitation, drug infiltration, arterial puncture, or a spontaneous bleed from anticoagulation), and traumatic (fracture, snake envenomation, circumferential burn, or electrocution). If the compartments are not released, irreversible changes happen to the cells, including nerve and muscle death.<sup>1</sup> Definitive management of this emergency requires prompt fasciotomy to decompress the compartment(s).<sup>1-3</sup>

## CASE PRESENTATION

A 76-year-old right-handed woman with a history of chronic obstructive pulmonary disease, hypertension, and hyperlipidemia presented to the emergency department with 2 days of extensive right upper extremity ecchymosis and severe pain that was localized to her forearm (Figure 1). She was taking low-dose aspirin (81 mg/d) for left subclavian stenosis and over-the-counter ginkgo biloba. Leading up to the presentation, the patient was able to perform routine household chores, including yard work, cleaning, and taking care of her cats. Wrist and elbow X-rays were negative for a fracture. An upper extremity ultrasound found no venous occlusion. A computed tomography (CT) angiogram of her arm and chest found diffuse edema around the right elbow and forearm without pulmonary or right

upper extremity emboli, fractures, hematoma, abscess, or air in the tissues.

The plastic surgery service was consulted. The patient was found to have a very tense forearm and pain to passive digital extension. The 2-point discrimination and pulses were intact. The patient was diagnosed with compartment syndrome based on the examination alone and gave consent for an emergent forearm and hand fasciotomy. A carpal tunnel release and a standard S-shaped volar forearm fasciotomy release were performed, which provided immediate decompression (Figure 2). The rest of the hand and extremity were soft. Edematous, healthy flexor muscle belly was identified without a hematoma. Most of the forearm wound was left open because the skin could not be reapproximated. Oxidized regenerated cellulose (Surgicel) was placed around the wound edges and the muscle was covered with a nonadherent dressing. Hemoglobin on admission was 12.9 g/dL (reference range, 12 to 16 g/dL). Kidney function was within normal limits. The rest of the complete blood count was unremarkable. Postoperative hemoglobin was 8.6 g/dL. Over the next several days, the patient's skin edges and muscle bellies continued to slowly bleed, and her hemoglobin fell to 5.6 g/dL by postoperative Day 2. The bleeding was managed with topical oxidized regenerated cellulose, thrombin spray, a hemostatic dressing made with kaolin (QuikClot), and a transfusion of 2 units of packed red blood cells.

A hematology consultation was requested. The patient was noted to have an elevated partial thromboplastin time (PTT) since admission measuring between 39.9 to 61.7 seconds (reference

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**FIGURE 1** Preoperative Compartment Syndrome, Right Upper Extremity



range, 26.2 to 37.2 seconds) and a normal prothrombin time test with an international normalized ratio. A PTT measured 17 months prior to admission was within the normal range. She reported no personal or family history of bleeding disorders. Until recently, she had never had easy bruisability. She reported no history of heavy menses or epistaxis. The patient had no children and had never been pregnant. She had tolerated an exploratory laparotomy 40 years prior to admission without bleeding complications and had never required blood transfusions before. A PTT 1:1 mixing study revealed incomplete correction. Subsequent workup included factor VIII (FVIII) activity, factor IX activity, factor XI activity, von Willebrand factor antigen, ristocetin cofactor assay, and von Willebrand factor multimers. FVIII activity was severely reduced at 7.8% (reference, > 54%) with a positive Bethesda assay of 300 to 400 Bodansky units (BU), indicating a strong FVIII inhibitor was present and establishing a diagnosis of acquired hemophilia A. Further workup for secondary causes of acquired hemophilia A including abdominal and pelvic CT, serum protein electrophoresis, and serum free light chains, were negative. She was started on prednisone 1 mg/kg daily and rituximab 375 mg/m<sup>2</sup>. Her hemoglobin stabilized, and she required no further blood transfusions.

The patient underwent wound closure on postoperative Day 11. At the time of the second surgery, there was still no improvement in her FVIII levels or PTT; therefore, 70 mcg/kg of recombinant coagulation-activated FVII was given just before surgery with no bleeding complications. The skin was closed primarily except for the most distal 3 cm (Figure 3). Due to concerns regarding further bleeding with skin graft, the remaining wound was allowed to close by secondary intention. As a precaution, the wound was covered with oxidized regenerated cellulose and thrombin spray. The patient continued to progress postoperatively without bleeding complications or a need for additional transfusions. She was seen by the hand therapist before and after the second surgery to help with edema management and joint mobility. She completed 4 weekly doses of 375 mg/m<sup>2</sup> rituximab and prednisone was tapered by 10 mg weekly.

Three weeks after starting treatment, her PTT normalized, and her FVIII increased to 33.7%. The Bethesda assay remained high at 198 BU, although it was lower than at admission. She was discharged home with dressing changes and monthly follow-up appointments. The wounds were fully closed at her 3-month appointment when she proudly demonstrated full digital extension and flexion into her palm.

## DISCUSSION

Forearm compartment syndrome is most often caused by fractures—distal radius in adults and supracondylar in children.<sup>2</sup> This case initially presented as a diagnostic puzzle to the emergency department due to the patient's lucid review of several days of nontraumatic injury.

The clinical hallmarks of compartment syndrome are the 5 Ps: pain, pallor, paresthesia, paralysis, and pulselessness. Patients will describe the pain as out of proportion to the nature of the injury; the compartments will be tense and swollen, they will have pain to passive muscle stretch, and sensation will progressively diminish. Distal pulses are the last to go, and permanent tissue damage can still occur when pulses are present.<sup>1</sup>

## Compartment Syndrome

Compartment syndrome is generally a clinical diagnosis; however, in patients who are sedated or uncooperative, or if the clinical findings are equivocal, the examination can be

supplemented with intercompartmental pressures using an arterial line transducer system.<sup>2</sup> In general, a tissue pressure of 30 mm Hg or a 20- to 30-mm Hg difference between the diastolic and compartment pressures are indications for fasciotomy.<sup>1</sup> The hand is treated with an open carpal tunnel release, interosseous muscle release through 2 dorsal hand incisions, and thenar and hypothenar muscle release. The forearm is treated through a curved volar incision that usually decompresses the dorsal compartment, as it did in our patient. If pressures are still high in the forearm, a longitudinal dorsal incision over the mobile wad is necessary. Wounds can be closed primarily days later, left open to close by secondary intention, or reconstructed with skin grafts.<sup>2</sup> In our patient, compartment syndrome was isolated to her forearm and the carpal tunnel release was performed prophylactically since it did not add significant time or morbidity to the surgery.

Nontraumatic upper extremity compartment syndrome is rare. A 2021 review of acute nontraumatic upper extremity compartment syndrome found a bleeding disorder as the etiology in 3 cases published in the literature between 1993 and 2016.<sup>4</sup> One of these cases was secondary to a known diagnosis of hemophilia A in a teenager.<sup>5</sup> Ogrodnik and colleagues described a spontaneous hand hematoma secondary to previously undiagnosed acquired hemophilia A and Waldenström macroglobulinemia.<sup>4</sup> Ilyas and colleagues described a spontaneous hematoma in the forearm dorsal compartment in a 67-year-old woman, which presented as compartment syndrome and elevated PTT and led to a diagnosis of acquired FVIII inhibitor. The authors recommended prompt hematology consultation to coordinate treatment once this diagnosis is suspected.<sup>6</sup> Compartment syndrome also has been found to develop slowly over weeks in patients with acquired FVIII deficiency, suggesting a high index of suspicion and frequent examinations are needed when patients with known acquired hemophilia A present with a painful extremity.<sup>7</sup>

Nontraumatic compartment syndrome in the lower extremity in patients with previously undiagnosed acquired hemophilia A has also been described in the literature.<sup>8-11</sup> Case reports describe the delay in diagnosis as the patients were originally seen by clinicians for lower extremity pain and swelling within days of presenting to the emer-

## FIGURE 2 Intraoperative Fasciotomy, Right Upper Extremity



Carpal tunnel release and standard S-shaped volar forearm fasciotomy release were performed.

## FIGURE 3 Closure of Fasciotomy, Right Upper Extremity



On Day 11, the skin was closed primarily except for the most distal 3 cm, which was allowed to close by secondary intention.

gency room with compartment syndrome. Persistent bleeding and abnormal laboratory results prompted further tests and examinations.<sup>8,9,11</sup> This underscores the need to be suspicious of this unusual pathology without a history of trauma.

### Acquired Hemophilia A

Acquired hemophilia A is an autoimmune disease most often found in older individuals, with a mean age of approximately 70 years.<sup>12</sup> It is caused by the spontaneous production of neutralizing immunoglobulin autoantibodies that target endogenous FVIII. Many cases are idiopathic; however, up to 50% of cases are associated with underlying autoimmunity, malignancy (especially lymphoproliferative disorders), or pregnancy. It often presents as bleeding that is subcutaneous or in the gastrointestinal system, muscle, retroperitoneal space, or genitourinary system. Unlike congenital hemophilia A, joint bleeding is rare.<sup>13</sup>

The diagnosis is suspected with an isolated elevated PTT in the absence of other coagulation abnormalities. A 1:1 mixing study will typically show incomplete correction, which suggests the presence of

an inhibitor. FVIII activity is reduced, and the FVIII inhibitor is confirmed with the Bethesda assay. Clinically active bleeding is treated with bypassing agents such as recombinant coagulation-activated FVII, activated prothrombin complex concentrates such as anti-inhibitor coagulant complex (FEIBA), or recombinant porcine FVIII.<sup>12,14</sup> Not all patients require hemostatic treatment, but close monitoring, education, recognition, and immediate treatment, if needed, are indicated.<sup>13</sup> Immunosuppressive therapy (corticosteroids, rituximab, and/or cyclophosphamide) is prescribed to eradicate the antibodies and induce remission.<sup>12</sup>

## CONCLUSIONS

An older woman without a preceding trauma was diagnosed with an unusual case of acute compartment syndrome in the forearm. No hematoma was found, but muscle and skin bleeding plus an elevated PTT prompted a hematology workup, and, ultimately, the diagnosis of FVIII inhibitor secondary to acquired hemophilia A.

While a nontraumatic cause of compartment syndrome is rare, it should be considered in differential diagnosis for clinicians who see hand and upper extremity emergencies. An isolated elevated PTT in a patient with a bleed should raise suspicions and trigger immediate further evaluation. Once suspected, multidisciplinary treatment is indicated for immediate and long-term successful outcomes.

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indications, contraindications, warnings, and adverse effects—before administering pharmacologic therapy to patients.

## Ethics and consent

The patient consented to the presentation of her case report for publication.

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