Case 2

A 68-year-old Thai woman from Bangkok

Chief complaint: large hematoma on right buccal mucosa with extensive clear & hemorrhagic tense bullae on trunk and extremities for 3 days

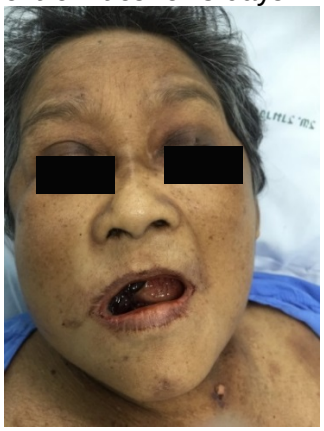

Fig 2.1

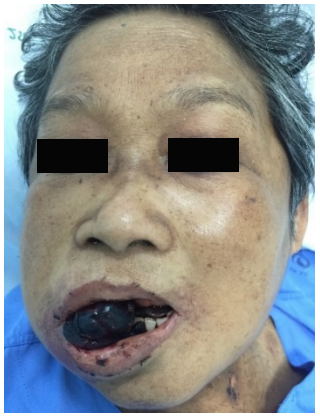

Fig 2.2

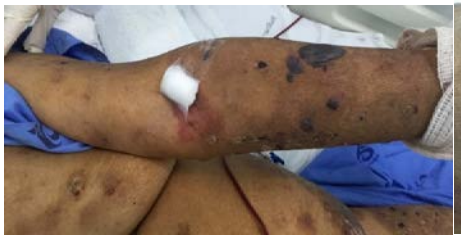

Fig 2.3

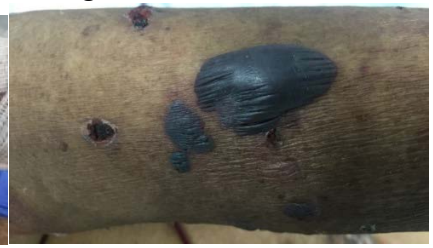

Fig 2.4

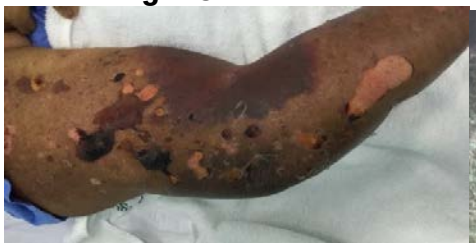

Fig 2.5

Fig 2.6

Present illness:

Known case bullous pemphigoid who presented with tense clear fluid bullae. The disease was stable for 11 months with maintenance dose of oral prednisolone 5 mg/day and nicotinic acid 200 mg/day

1 month history of new clear fluid & hemorrhagic tense bullae on trunk and extremities. She received oral prednisolone 15 mg/day with no clinical improvement

3 days ago, she developed large hematoma on right buccal mucosa with extensive new clear & hemorrhagic tense bullae on trunk and extremities.

Past history

Her underlying disease was type2 DM, DLP, HT

No previous bleeding tendency

Dermatologic examination

(Figure 2.1) Large hematoma on right buccal mucosa and floor of mouth.

(Figure 2.2) Progression of hematoma within 1 day after admission.

(Figure 2.3) Multiple tense hemorrhagic bullae with erosion on left forearm.

(Figure 2.4) Large tense hemorrhagic bullae on left forearm.

(Figure 2.5) Ecchymosis and multiple tense hemorrhagic bullae with erosions on right forearm and arm.

(Figure 2.6) Clear fluid tense bullae on right arm.

Physical examination

General appearance: A Thai female, good conscious and general well-being

HEENT: moderately pale conjunctivae, anicteric sclerae,

large hematoma on right buccal mucosa

Heart: Normal S1S2, no murmur

Lung: Normal breath sound, no adventitious sound

Abdomen: Soft, not tender, no hepatosplenomegaly

Lab investigations:

- CBC:
  - **WBC 14,610 /cumm** (N 72%, L 9%, **Eo 10%,** M 5%, B 1%, Band 3%)
  - **Hct 23.4 %**, Plt 341,000 /cumm
- **Coagulogram**: PT/INR: 10.4/0.9, **aPTT: 75.1**
  Thrombin time: 10.2
- **Mixing test:**
  aPTT (before mixing): 108
  aPTT (pool normal plasma): 23.9
  aPTT (after mixing): 33.6
  aPTT (after mixing and incubated 2 hr): 68
- **Factor VIII: 0%**
- **Factor VIII inhibitor: 27.84 Bu**
- **Anti-BPAG 180: > 200 Ru/mL**
- **Anti-BPAG 230: > 200 Ru/mL**
- ANA 12 profile: negative
- Skin swab:
  Gram stain: no organism seen, few PMN
  Culture: no growth

Histopathology (59-3502, Left forearm) (Fig 2.7, 2.8)

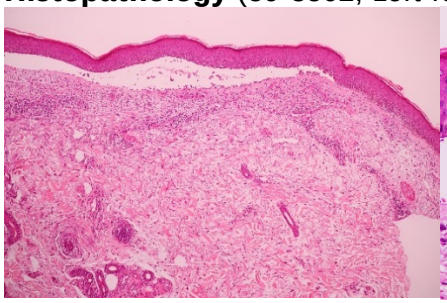

Fig 2.7

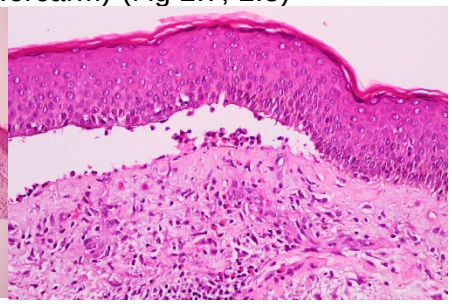

Fig 2.8

Subepidermal vesicles, well preserved dermal papillae, dense inflammatory cells infiltrate predominantly eosinophils

DIF: Linear IgG, C3 deposition along dermoepidermal junction compatible with bullous pemphigoid

Diagnosis: Bullous pemphigoid associated with acquired hemophilia A

Treatment:

- Dexamethasone 15 mg IV daily for 1 week then prednisolone 30 mg daily
- Cyclophosphamide 50 mg daily
- Activated prothrombin complex concentrate (aPCC)
- Dressing, blood transfusion, parenteral nutrition

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Consultant: Penpun Wattanakrai, MD

Discussion

Acquired hemophilia (AHA) is a rare autoimmune bleeding disorder, occurring in about one per million per year.[1,2]
The mortality rate resulting from bleeding complications range between 7.9% and 22.2%.[3] AHA occurs due to spontaneous development of autoantibodies against factor VIII.[4,5]

AHA is commonly observed in elderly population. The most common presentation of AHA is subcutaneous bleeding (ecchymosis) followed by hematoma, gastrointestinal, genitourinary (hematuria) and retroperitoneal bleeding. On the other hand, hemarthrosis which is a common symptom in congenital hemophilia, rarely occurs.[6]

Approximately 50% of the patients, no underlying disease is identified. The remaining coexisting conditions are autoimmune disease, malignancy, pregnancy (post-partum period) and drug.[7]

There are few case report of AHA associated with BP. The etiology remains unknown. However there are some hypothesis to explain the relation between BP and AHA such as cross-reactivity of antibodies due to sequence homology between epitopes on factor VIII and the BP 180 collagen XVII domain.[8]

Based on literature review of AHA associated with BP by Binet Q et al[9] in 25 documented cases, the age distribution varied from 24 to 88 years old and there was no gender predisposition. All of the patients developed AHA after the onset of BP, like our patient.

The prognosis of bullous pemphigoid associated with acquired hemophilia A depends on the severity of hemorrhage and response to immunosuppressive drug. Poor prognosis of AHA is old age, comorbidity and high factor VIII inhibitor titers (>20 Bu).[3]

Treatment of AHA focus on the eradication of autoantibodies by immunosuppressive drug and bleeding control by bypassing agents.[10,11]

In eradication of autoantibodies, corticosteroid alone or combination with cyclophosphamide are the first line therapy. Other immunosuppressives used in the literature include; cyclosporine, azathioprine, vincristine, high dose immunoglobulins (IVIG) and mycophenolate mofetil.[2] Rituximab has been shown to be successful in some case reports of acquired hemophilia A.[12] Relapsing disease is common after discontinuing immunosuppressive drug.

First-line therapy for bleeding events in patients who develop autoantibodies against factor VIII (FVIII) must often rely on FVIII-bypassing agents such as activated prothrombin complex concentrate (e.g., factor eight inhibitor bypassing activity [FEIBA VH, Baxter BioScience, Westlake Village, CA]) or recombinant factor VIIa (rFVIIa [NovoSeven, NovoNordisk, Bagsvaerd, Denmark]) due to their high effectiveness and rapid action.

FEIBA (factor eight inhibitor bypassing activity) contains various activated clotting factors which bypass certain steps in blood clot formation.[13]

In conclusion acquired hemophilia associated with bullous pemphigoid is rare and should be suspected in BP patients presenting with hemorrhagic bullae, hematoma, ecchymosis and systemic bleeding. Life threatening conditions such as massive bleeding, upper airway obstruction can occur, so early diagnosis and effective treatments are important. The treatment composes of suppression of antibody by immunosuppressive drug and bleeding control with FVIII-bypassing agents. Long term follow up is essential, even after complete remission due to relapsing disease.

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