Severe Esophageal Involvement in Cicatricial Pemphigoid

Dr. Chelsea Harper D.O., Shelby Tipton B.S., Alexandria Goyer B.S./B.A.
PI: Dr. Stephen Weis D.O.

INTRODUCTION

- **Cicatricial Pemphigoid** (CP): is a rare, scarring, vesiculobullos, autoimmune disease[1,2]
- Presenting symptoms: typically present with painful shallow erosions & ulcers from fragile vesicles & bullae of varying size.
- Oral mucosa is often the most involved region (~90%) with the pharynx, larynx and esophagus being the least involved (<10%)
- Esophageal & anogenital involvement ~4% of the cases
- Esophageal involvement: indicator of aggressive course
- Few case reports of CP present as isolated esophageal disease
- Hallmark of the disease:
  - Lesions at any anatomical site to heal with scar formation.
  - Loss of function, most commonly blindness, is a consequence of the disease.
  - This is a major cause of morbidity & mortality.[3-5]
- Minimal evidence on interventions to limit scarring. No trials on prevention of esophageal strictures

PATIENT

- 89-year-old Caucasian male
- Multiple dermatologic issues of 12 months duration
- 60-pound weight loss from painful oral ulcers [Figure 1]
- Referred by wound care for back ulcer that had not responded to standard care
- He had been evaluated by multiple medical specialties

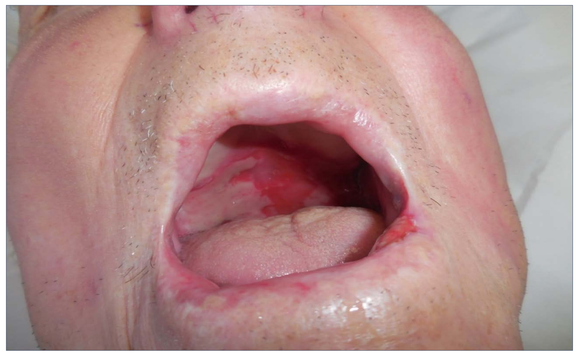

Figure1. Hard & soft palate erosions extending onto buccal mucosa & lower labial mucosa

CASE PRESENTATION

On exam

- A 8cm friable, bleeding, tender ulcerated plaque on his lower back [Figure 2 below], 6cm friable ulcerated plaque on his right forearm, several 1cm oral erosions, 1cm ulcer on scalp; fused penis to scrotum secondary to an active, fibrotic lesion [Figure 3 below] with anal erosions, bleeding from both nares

Initial Treatment

- Liquid prednisone 20mg QD, triamcinolone 0.1% dental paste, betamethasone dipropionate 0.05%.

Pathology

- Multiple biopsies sent for direct immunofluorescence along with indirect immunofluorescence with salt-split skin results
- Pathology report showed CP, IgA variant

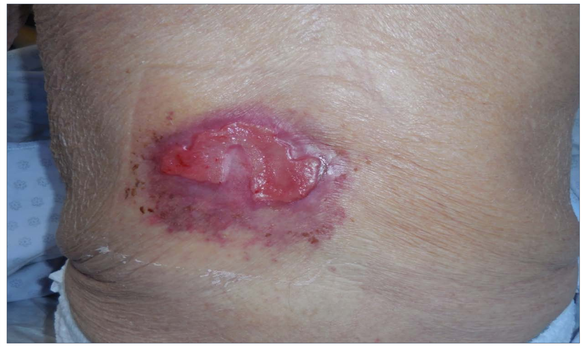

Figure 2. 8cm, friable, ulcerated plaque on left lower back

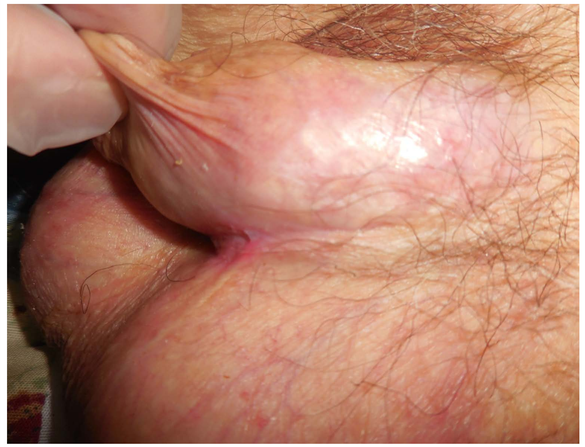

Figure 3. Fused penis to scrotum subsequent to a healed lesion

Course

- Hospitalized because of weakness & falls, received a PEG tube
- Inhaled budesonide 180mcg, dapsone 50mg QD & triamcinolone 1% ointment were added
- **1 month:** resolution of nasal ulcers + Mycophenolate 2500mg added
- **3 months:** oral mucosa & skin ulcerations persisted
- Perianal & anal canal: intralesional injection of 1cc 10mg/cc triamcinolone, Clobetasol 0.05% ointment BID
- Budesonide and dapsone increased to BID.
- Mild improvement with continued dysphagia & globus sensation. EGD: Severe esophageal strictures. GI recommended against dilatation due to risks of perforation. He elected for hospice.
- **6 months**: Passed away due to the complications

DISCUSSION

- CP is a rare, chronic, debilitating sub-epidermal blistering disease that affects the ocular, oral mucosa & rarely involves the esophagus
- CP is one of a collection of sub-epidermal, blistering diseases
- Diagnosis requires a high index of suspicion
  - Differentiate by clinical presentation, histology, direct & indirect immunofluorescence
  - Direct immunofluorescence: most sensitive & specific
- Several different antigens have been implicated in CP
  - Often autoantibodies against autoantigens of the basement membrane (BM) are detected through direct or indirect immunofluorescence
  - Linear IgG, IgA or C3 against protein components of the BM lead to sub-epidermal blisters
  - This causes inflammation & fibroblasts are activated secondary to certain cytokines
  - Transforming growth factor beta (TGF-b) induces fibrosis
  - In the esophagus, fibrosis can lead to extensive & debilitating strictures
- Diagnosis of CP can be a diagnostic dilemma
- A patient may seek various medical specialties dependent upon their symptomatology[5,6]
- No recommendations to limit scarring sequelae. Clinical remission is required prior to intervention as trauma can exacerbate disease

DISCUSSION

- Case reports indicate that esophageal involvement is typically symptomatic, however there are cases with asymptomatic, yet severe, involvement. This could potentially lead to under-diagnosis and inadequate treatment.

Current Recommendations

based on disease severity,
determined by rate of progression, & areas of involvement

Low risk:	High risk:
Lesions restricted to oral mucosa & skin	Ocular, anogenital, laryngeal, nasopharyngeal or esophageal involvement • Numerous treatments with varying results have been used
Mild:	**Severe:**
Topical treatments (corticosteroids or tacrolimus)	Systemic treatments (corticosteroids, dapsone, cyclophosphamide, mycophenolate mofetil or intravenous immunoglobulin) [6-11]

- Our gentleman presented with a several months history of undiagnosed CP with severe & extensive oral, nasopharyngeal, anogenital & skin involvement with subsequent fibrosis.
- Involvement of his esophagus wasn't diagnosed until late in his course.
- His course was fatal secondary to complications of malnutrition & severe esophageal strictures
- This case is useful to raise awareness of this condition & of the need for early, aggressive treatment & monitoring for debilitating sequelae of CP

REFERENCES

1. Trimarchi, T., Bellini, C., Fabiano, B., Gerevini, S., Bussi, M. Multiple mucosal involvement in cicatricial pemphigoid. *Acta Otorhinolaryngologica Italica.* 2009; 29:222-225
2. Furusawa, K., Hasegawa, T., Hirasawa, Y., Ikeda, S. Mucous membrane pemphigoid with esophageal stricture treated with balloon dilatation. *The Journal of Dermatology.* 2015
3. Prudencio, S., Senra, D., Rodriguez, D., Mateu, B., Jimenez-Zarza, C., Lopez, F., Reyes, J., Santos, M., de Cuenca Moron, B. Esophageal Cicatricial Pemphigoid as an Isolated Involvement Treated with Mycophenolate Mofetil. *Case Reports in Gastrointestinal Medicine.* 2015
4. Barbosa, L., Verardino, G., Alves, M., da Silva, R., Gripp, A. Mucous membrane pemphigoid with severe esophageal stricture. *Anais Brasileiros de Dermatologia.* 2011; 86(3):565-8
5. Xu, H., Werth, V., Parisi, E., Sollecito, T. Mucous Membrane Pemphigoid. *Dental Clinics of North America.* 2013; 57(4):610-630
6. Benoit, S., Scheurlen, M., Goebeler, M., Stoevesandt, J. Structured Diagnostic Approach & Risk Assessment in Mucous Membrane Pemphigoid with Oesophageal Involvement.*Acta Dermato-Venereologica.* 2018;98;660-666
7. Yuan, H., Pan, M. Endoscopic characteristics of oesophagus involvement in mucous membrane pemphigoid. *British Journal of Dermatology.* 2017; 177(4):902-903
8. Labowsky, M., Stinnett, S., Liss, J., Daluvoy, M., Hall III, R., Shieh, C. Clinical Implications of Direct Immunofluorescence findings in Patients with Ocular Mucous Membrane Pemphigoid. *American Journal of Ophthalmology.* 2017; 183:48-55
9. Sallout, H., Anhalt, G., Al-kawas, F. Mucous membrane pemphigoid presenting with isolated esophageal involvement: a case report. *Gastrointestinal Endoscopy.* 2000;429-432
10. Tavakolpour, S. The role of intravenous immunoglobulin in treatment of mucous membrane pemphigoid: A review of literature. *Journal of Research in Medical Sciences.* 2016;21
11. Chan, L., Ahmed, A., Anhalt, G., Bernauer, W., Cooper, K., Elder, M., Fine, J-D., Foster, S., Ghohestani, R., Hashimoto, T., Hoang-Xuan, T., Kirtschig, G., Korman, N., Lightman, S., Lozada-Nur, F., Marinkovich P., Mondino, B., Prost-Squarcioni, C., Rogers III, R., Setterfield, J., West, D., Wojnarowska, F., Woodley, D., Yancey, K., Zillikens, D., Zone, J. The First International Consensus on Mucous Membrane Pemphigoid: definition, diagnostic criteria, pathogenic factors, medical treatment, & prognostic indicators. *Arch Dermatology.* 2002; 138:370-379