PALLIATIVE PEARLS
BY ENCLARA PHARMACIA

Achalasia Management Case
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PATIENT CASE

AR is a 56-year-old male admitted to hospice today with a primary diagnosis of multiple myeloma. Additional diagnoses include gastrointestinal amyloidosis (type AL) and secondary achalasia. He has no drug allergies and lives at home with his wife. A palliative care team followed AR during a recent hospital admission for aspiration pneumonia and continued to follow him as an outpatient just prior to his hospice admission.

Current medications include:

- Famotidine 40mg/5mL suspension; 5mL (40mg) PO twice daily for reflux
- Metoclopramide 5mg/5ml solution; 10mL (10mg) PO TID before meals for nausea
- Methadone 10mg/ml oral concentrate; 2mL (20mg) PO every 8 hours
- Morphine 20mg/mL oral concentrate; 2ml (40mg) PO every 3 hours as needed for pain
- Dexamethasone 4mg/ml oral concentrate; 2mL (8mg) PO twice daily for pain and inflammation
- Lorazepam 2mg/mL oral concentrate; 0.5mL (1mg) SL every 4 hours as needed for anxiety
- Senna; 1 tab PO at bedtime to prevent constipation

AR reports heartburn and frequent regurgitation of bland-tasting liquid. He is currently on a fluid-based diet because of his achalasia and recent aspiration pneumonia. The plan is to discontinue famotidine and begin omeprazole 40mg PO daily. Given AR's medical conditions, are there any other therapies that may relieve his symptoms?

Overview of amyloidosis in AR:

Amyloid is an abnormal protein that is produced in bone marrow and can be deposited in any tissue or organ. Amyloidosis is a rare disease that occurs when amyloid builds up in organs. Type AL (light chain amyloidosis) typically involves the heart, kidney, peripheral nervous system, gastrointestinal tract, respiratory tract, and nearly any other organ.[1] Patients with gastrointestinal amyloidosis and chronic dysmotility will commonly experience diarrhea and present less often with constipation, nausea, vomiting, abdominal pain, bloating, or chronic intestinal pseudo-obstruction. Even more uncommon is achalasia that AR is experiencing.[2]

OVERVIEW OF ACHALASIA

Achalasia is a disorder that results from inflammation and degeneration of neurons in the esophageal wall causing the lower esophageal sphincter to fail to relax and a loss of peristalsis in the distal esophagus.[3,4,5] Achalasia is uncommon with an annual incidence of approximately 1.6 cases per 100,000 individuals and prevalence of 10 cases per 100,000 individuals.[3] Men and women are equally affected and it can occur at any age, however is uncommonly diagnosed in children and those over the age of 60. The cause of primary or idiopathic achalasia is unknown and secondary achalasia is due to diseases that cause esophageal motor abnormalities.[3] In addition to amyloidosis, people with malignancy, especially gastric cancer, and sarcoidosis, among other less common diseases, can develop achalasia.[3]

CLINICAL MANIFESTATIONS[3, 4]

Achalasia has an insidious onset and progression is gradual. Patients may experience symptoms for years prior to seeking treatment and are often treated for other disorders, such as gastroesophageal reflux disease (GERD), before achalasia is diagnosed.

Common symptoms include:

- Dysphagia for solids and liquids
- Regurgitation of bland undigested food or saliva (aspiration risk)
- Difficulty belching
- Substernal chest pain and heart burn
- Hiccups
- Mild weight loss

DIAGNOSIS

Achalasia is typically diagnosed using barium swallow studies and show “a bird-beak appearance of the lower esophagus, dilatation of the esophagus, and stasis of barium in the esophagus”. Esophagogastroduodenoscopy (EGD) studies are often used to rule out cancer.[5]

Suspect achalasia in the following patients: [3, 4]

- Dysphagia to solids and liquids
- Heartburn unresponsive to a trial of proton pump inhibitor therapy
- Retained food in the esophagus on upper endoscopy
- Unusually increased resistance to passage of an endoscope through the esophagogastric junction (EGJ)

Differential diagnosis includes: [3, 4]

- GERD - Regurgitated food is sour-tasting suggesting the presence of stomach acid. With achalasia, regurgitated food is bland-tasting.
- Pseudoachalasia - Rapid progression of dysphagia and profound weight loss, likely due to a GI malignancy. Achalasia progression is gradual and not commonly associated with significant weight loss.

MANAGEMENT

The main management goal is to reduce the resting pressure in the lower esophageal sphincter (LES) enough to no longer obstruct the passage of ingested food/liquid from the esophagus to the stomach. It is important to note that available treatments will not normalize swallowing, only improve it, and efficacy of all treatments tend to decrease over time.[4] The most effective therapies for achalasia are surgery to weaken the LES by cutting muscle fibers and pneumatic dilation (PD) using a balloon to dilate the LES. For patients not suited for these procedures, botulinum toxin injection into the LES to lessen muscle tone is a less invasive.[5]

Pharmacologic therapy is the least effective option but should be considered for patients not suited for PD or surgery or who have failed botulinum toxin therapy. Calcium channel blockers and nitrates both decrease LES pressure but do not improve LES relaxation. Administration of the sublingual formulation of nifedipine or isosorbide dinitrate have the most success – unfortunately, these dosage forms are no longer available in the U.S. [5,7]

Nifedipine regular-release capsules 10-30mg taken 30-45 minutes before meals[4,7]

- Oral or retain in mouth for SL absorption: Open capsules and dissolve in water
- Rectal: Administer whole capsules[7]

Isosorbide dinitrate regular-release tablet 5mg taken 30-45 minutes before meals[4,7]

- Oral or retain in mouth for SL absorption: Crush tablet and dissolve in water
- Rectal: No evidence to support administration via this route will provide systemic absorption

Alternative - Nitroglycerin 0.4 mg SL taken 10-15 minutes before meals[4]

Other medications used to treat achalasia, with limited data to support their use: [4]

- 5-phosphodiesterase inhibitors (i.e., sildenafil)
- Anticholinergics (i.e., atropine, dicyclomine)

- Beta adrenergic agonists (i.e., terbutaline)
- Theophylline

ASSESSMENT AND RECOMMENDATIONS:

AR is not a candidate for surgery nor PD. Botulinum toxin injection, although less invasive, is costly and would require a visit to the hospital for an outpatient procedure and is therefore not aligned with his goals of care. AR is assessed for route of administration options for pharmacologic therapy. Although he can swallow small volumes of liquid multiple times per day, his intake of liquid nutrition is not consistent and timing of nifedipine or isosorbide dinitrate before meals would be difficult. In addition to a switch to proton pump inhibitor therapy with omeprazole, nitroglycerin sublingual tablets are recommended for administration prior to meals.

For additional information on this topic, please review these references:

1. Medscape Drugs & Diseases - Rheumatology. Amyloidosis. Published Nov 12, 2018. Available from: https://emedicine.medscape.com/article/335414-overview#a1
2. Camilleri M. Gastrointestinal amyloidosis: Clinical manifestations, diagnosis, and management. Waltham; UpToDate: 2018. Published Oct 3, 2018.
3. Spechler SJ. Achalasia: Pathogenesis, clinical manifestations, and diagnosis. Waltham; UpToDate: 2018. Published Feb 8, 2018.
4. Spechler SJ. Overview of the treatment of achalasia. Waltham; UpToDate: 2018. Published Feb 21, 2017.
5. Medscape Drugs & Diseases – Gastroenterology. Achalasia. Published Dec 28, 2017. Available from: https://reference.medscape.com/article/169974-overview
6. Vaezi MF, et al. ACG Clinical Guideline: Diagnosis and Management of Achalasia. *Am J Gastroenterol.* advance online publication, Jul 23, 2013; doi: 10.1038/ajg.2013.196. Available open access from: http://gi.org/wp-content/uploads/2013/07/ACG_Guideline_Achalasia_July_2013.pdf
7. Clinical Pharmacology [database online]. Tampa, FL: Elsevier/Gold Standard, Inc.; 2018. Access 2018 Sept.

