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June 2023 Pulmonary Case of the Month: An Invisible Disease Lewis J. Wesselius MD

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History of Present Illness

A 78-year-old man presented to the Emergency Department on April 7 for shortness of breath and weakness over the last 2 weeks. He was in good health prior to an outside hospitalization March 29-April 3 for pneumonia and a possible non-STelevation myocardial infarction (elevated troponins). He had a bronchoscopy during his recent outside hospitalization without specific pathogen identified but was treated with antibiotics and discharged on levofloxacin. Since his hospital discharge 4 days previously he feels weaker and increasingly short of breath. He is short of breath even walking around his home. He denies fever or a productive cough.

Past Medical History, Family History and Social History

- Atrial fibrillation, s/p ablation. On Eliquis.
- Prior renal cell carcinoma, s/p resection, no recurrence
- DM Type 2
- GERD
- OSA
- Essential tremor
- Never smoked

Medications

• Apixaban

- Aspirin
- Atorvastatin
- Flecanide
- Insulin
- Levofloxacin
- Lisinopril
- Pantoprazole
- Tamsulosin

Physical Examination

- General: The patient looks comfortable and is in no distress
- Vital Signs: BP 110/62 O2 Sat 94% on room air
- CVS: Heart sounds are regular
- Lungs: Clear to auscultation
- Abdomen: Soft, nontender, bowel sounds present
- Extremities: No edema
- Neuro: Alert and oriented
- Skin: Warm and dry, no rashes

Chest X-ray

A portable chest X-ray was performed (Figure 1).



Figure 1. Portable chest X-ray obtained in the emergency department. To view Figure 1 in a separate, enlarged window click <u>here</u>.

Which of the following should be <u>done next</u>?

- 1. Arterial blood gases
- 2. Bronchoscopy
- 3. Thoracic CT scan
- 4. 1 and 3
- 5. All of the above

Correct! 4. 1 and 3

In most patients with pneumonia not clinically improving a thoracic CT scan should be ordered (1). Arterial blood gases should be obtained in most patients with pneumonia requiring supplemental oxygen admitted to the hospital (2). Arterial blood gases allow detection of hypercapnia and any acid-base abnormalities. A repeat bronchoscopy at this time would seem unlikely to add any clinical important data. A thoracic CT scan was performed (Figure 2).



Figure 2. Representative images from thoracic CT scan in lung windows. To view Figure 2 in a separate, enlarged window click <u>here</u>.

Arterial blood gases (ABGs) were obtained while the patient was receiving oxygen at 2L/min by nasal cannula.

- pH Arterial: 7.419
- pCO2 Arterial: 46.2
- pO2 Arterial: 96.2
- Total Hemoglobin: 10.9

Which of the following is/are <u>true</u>?

- 1. The ABGs show a compensated respiratory acidosis
- 2. The ABGs show an anemia
- 3. The thoracic CT scan shows consolidation in the left lower lobe with bibasilar mucoid impaction
- 4. 1 and 3
- 5. All of the above

Correct! 5. All of the above

The patient's case is relatively strange. He has a radiographic pneumonia with mild respiratory acidosis and shortness of breath with even mild exertion. Bedside spirometry was ordered (Figure 3).

	PREDICTED		CONTROL.		
	Ered	LLN	Actual 2	iffred	4
- SPIROMETRY -					
FVC(L)	3.68	3.08	-1,989	100	11
FEV1 (L)	2.76	2.30	*1.64	199	2
FEV1/FVC (%)	75.24	62.83	86.40	104	a
FEF 25-75% (Losz)	2.00	1.10	1.82	90	1 1/2 3 4
FEF Max (L/sec)	7.03	5.28	5.89	83	
MVV (L/min)	114	95	+24	-	· ·
MEP (cmiH2O)	171	143	*50	*29	
MIP (cmit2D)	-001	-84	6-28	*30	Flow-Volume Loop

Figure 3. Patient's bedside spirometry. To view Figure 3 in a separate, enlarged window click <u>here</u>.

Which of the following is/are <u>true</u>?

- 1. The markedly reduced MIP suggest neuromuscular disease
- 2. The restrictive lung disease seen with the patient's spirometry is highly suggested of COVID-19 pneumonia
- A repeat troponin, a creatinine kinase and an anti-acetylcholine receptor (AChR) antibody (Ab) test should be ordered
- 4. 1 and 3
- 5. All of the above

Correct! 4. 1 and 3

The markedly reduced MIP suggests neuromuscular disease (3). The shape of our patient's flow-volume loop is relatively normal. A "rounded" expiratory peak has been described with neuromuscular disease but this appears to be neither sensitive or specific (3).

A repeat troponin (since he had a previous elevation), creatinine kinase and an AChRAb should be ordered as screening tests for some neuromuscular diseases. The troponin came back elevated at about 600 ng/mL but did not change over time. Creatinine kinase, an enzyme released into the blood stream with myositis, was normal. However, the AChRAb was markedly elevated at 18.0 mmol/L (normal < 0.02). This led to a presumptive diagnosis on myasthenia gravis which was confirmed by a positive AChR modulating flow cytometry and electromyography (EMG).

What <u>medication</u> is the patient taking which likely led to <u>unmasking his myasthenia</u> gravis?

- 1. Atorvastatin
- 2. Flecainide
- 3. Levofloxacin
- 4. Lisinopril
- 5. Tamsulosin

Correct!

3. Levofloxacin

Many medications can unmask or exacerbate known myasthenia gravis (Table 1) although the aminoglycosides and fluoroquinolones are notorious (4). Table 1. Drugs that May Unmask or Worsen Myasthenia Gravis (4) Anesthetic agents •Neuromuscular blocking agents ·Antibiotics ·Aminoglycosides (eg, gentamicin, neomycin, tobramycin) •Fluoroquinolones (eg, ciprofloxacin, levofloxacin, norfloxacin) •Ketolides (eg, telithromycin) ·Macrolides (eg, azithromycin, clarithromycin, erythromycin) ·Beta blockers (eg, atenolol, labetalol, metoprolol, propranolol) ·Procainamide •Quinidine ·Anti-PD-1 monoclonal antibodies (eg, nivolumab and pembrolizumab) ·Botulinum toxin •Chloroquine Hvdroxvchloroquine

- Hydroxychloroquu
- •Magnesium •Penicillamine
- •Ouinine

To open Table 1 in a new, separate window click here.

Reference 4 also has a list of drugs that are usually well tolerated. However, close observation of the patient is advised after starting any new medication.

What treatment(s) for myasthenia gravis

should be started?

- 1. Intravenous immunoglobulin (IVIG)
- 2. Mycophenolate
- 3. Prednisone
- 4. Pyridostigmine
- 5. Treatment should be started when
- the patient is more stabilized

Correct! 1.2.3 and/or 4

Any of the listed treatments has been used (5). We used a combination of all 4 and the patient had a dramatic response to therapy. His troponin remained elevated and was not associated with any other features of cardiac injury. There are reports of elevated troponins without myocardial infarction in patients with myasthenia gravis (6).

References

 Claessens YE, Debray MP, Tubach F, et al. Early Chest Computed Tomography Scan to Assist Diagnosis and Guide Treatment Decision for Suspected Community-acquired Pneumonia. Am J Respir Crit Care Med. 2015 Oct 15;192(8):974-82. [CrossRef] [PubMed]

- O'Driscoll BR, Howard LS, Earis J, Mak V; British Thoracic Society Emergency Oxygen Guideline Group; BTS Emergency Oxygen Guideline Development Group. BTS guideline for oxygen use in adults in healthcare and emergency settings. Thorax. 2017 Jun;72(Suppl 1):ii1-ii90. [CrossRef] [PubMed]
- Schoser B, Fong E, Geberhiwot T, *et al.* Maximum inspiratory pressure as a clinically meaningful trial endpoint for neuromuscular diseases: a comprehensive review of the literature. Orphanet J Rare Dis. 2017 Mar 16;12(1):52. [CrossRef] [PubMed]
- 4. Drugs that may unmask or worsen myasthenia gravis. UpToDate. 2023. Available at: <u>https://www.uptodate.com/contents/imag</u> <u>e?imageKey=NEURO%2F100362</u> (accessed 5/17/23).
- Gilhus NE, Tzartos S, Evoli A, Palace J, Burns TM, Verschuuren JJGM. Myasthenia gravis. Nat Rev Dis Primers. 2019 May 2;5(1):30. [CrossRef] [PubMed]
- Stavroulakis G, Papadopoulou M, Koutroulis G, Zouvelou V, Katsavochristos J, Georgiadis E, Baltogiannis C, Avrampos G. Myasthenia gravis. A potential cause of false positively elevated troponin T? Case report and brief review. Int J Cardiol. 2015 Nov 15;199:40-1. [CrossRef] [PubMed]