Case of Phrenic Nerve Impairment after COVID-19 Infection

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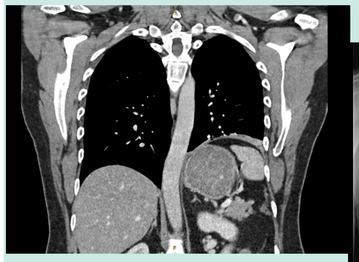
Imaging

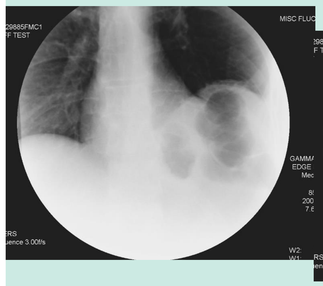
CT Chest



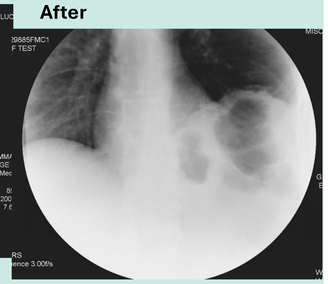
Chest X-ray

SNIFF test

Before



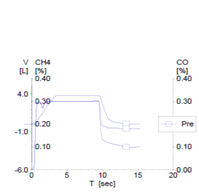
After

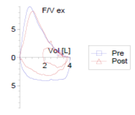


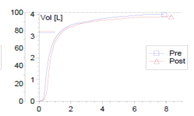
Pulmonary Function Testing

Spirometry

		LLN	ULN	Pred	Pre	Pre%Pred	Post	Post%Pred	%Chg
FVC	L	4.22	6.52	5.37	**4.00**	74 %	**4.00**	74 %	0 %
FEV 1	L	3.33	5.14	4.24	**3.17**	75 %	**3.21**	76 %	1 %
FEV1/FVC	%	69	90	79	**79**		**80**		1 %
FEF 25-75%	L/s	2.17	5.63	3.90	**2.86**	73 %	**3.06**	78 %	7 %
PEF	L/s	7.95	12...	10.37	**10...**	98 %	**9.14**	88 %	-10 %
MVV	L/min	142	142	142	**66**	47 %	**67**	47 %	2 %







Diffusing Capacity

		LLN	ULN	Pred	Pre	Pre%Pred
DLCO_SB	ml/(min*mmHg)	24.09	38.57	31.33	**22.64**	72 %
DLCOcSB	ml/(min*mmHg)	24.09	38.57	31.33	**22.64**	72 %
DL/VA	ml/(min*mmHg*L)	3.49	5.48	4.49	**3.79**	84 %
KCOc_SB	ml/(min*mmHg*L)	3.49	5.48	4.49	**3.79**	84 %
VA_SB	L	5.72	8.34	7.03	**5.97**	85 %
IVC_SB	L	4.22	6.52	5.37	**3.75**	70 %
RV_SB	L	1.09	2.80	1.87	**2.22**	119 %

Lung Volumes

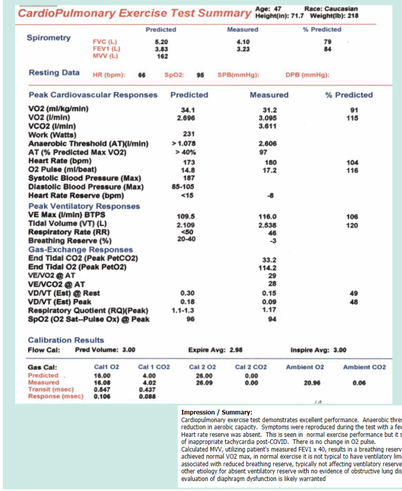
		LLN	ULN	Pred	Pre	Pre%Pred
TLC	L	6.15	9.05	7.60	**5.84**	77 %
VC	L	4.22	6.52	5.37	**4.09**	76 %
IC	L	2.88	5.22	4.05	**2.81**	69 %
FRCpleth	L	2.49	5.09	3.64	**3.03**	83 %
ERV	L	0.69	2.56	1.62	**0.87**	54 %
RV	L	1.09	2.64	1.87	**1.75**	94 %
RV % TLC	%	15	33	24	**30**	
VTG	L				**4.35**	
Raw	cmH2O*s/L		11.42	1.22	**1.74**	142 %
sRaw	cmH2O*s	12...	12.00	12.00	**7.57**	63 %
Gaw	(L/s)/cmH2O	0.33	0.33	0.33	**0.58**	176 %

Recent case reports suggest that phrenic nerve injury and diaphragmatic dysfunction are rare but notable complications of COVID-19. FitzMaurice et al. and Lowenkamp et al. describe unilateral diaphragm paralysis with elevated hemidiaphragms on imaging, positive Sniff tests, and abnormal PFTs, although both patients were hospitalized for their infection. Law et al. described testing phrenic nerve function through EMGs or phenic nerve conduction studies to investigate COVID-19 associated phrenic nerve mononeuritis versus neuropathy/myopathy. Our case report describes an outpatient case of phrenic nerve impairment, but not paralysis after recurrent COVID-19 infections that did not require hospitalization.

Case Report

A 47-year-old man with a past medical history of restless leg syndrome and recurrent COVID-19 infections for the past three years presented to the outpatient pulmonary office with complaints of progressive dyspnea on exertion and orthopnea that began after his first COVID-19 infection. He is a never smoker. He had no prior pulmonary or neuromuscular conditions and was never hospitalized or intubated for COVID-19. After his first COVID-19 infection, patient developed profound exercise intolerance, shortness of breath at rest, persistent cough associated with post-tussive emesis, and feeling like his left side "does not expand all the way." In addition, he was diagnosed with postural orthostatic tachycardia syndrome due to increased heart rate with minimal exertion. Prior to his illness, he was in good health and able to run 4 to 5 miles multiple times a week compared to less than half a mile currently. Symptoms have improved while on beta-blocker therapy. However, he continued to report dyspnea and the sensation of not being able to take a full breath.

Diagnostic Work-up	Results
Initial chest x-ray	Elevated left hemidiaphragm (new finding)
Initial CT chest	Elevated left hemidiaphragm (new finding)
Pulmonary Function Testing	Normal
SNIFF test	Negative
Cardiopulmonary Exercise Testing (obtained after 3rd infection)	Ventilatory defect
Electromyography	Left phrenic nerve impairment



CardioPulmonary Exercise Test Summary — Age: 47 Height(in): 71.7 Race: Caucasian Weight(lb): 218

		Predicted	Measured	% Predicted
Spirometry	FVC (L)	5.20	4.10	79
	FEV1 (L)	3.83	3.23	84
	MVV (L)	162		

Resting Data — HR (bpm): 66 SpO2: 98 SPB(mmHg): DPB (mmHg):

Peak Cardiovascular Responses	Predicted	Measured	% Predicted
VO2 (ml/kg/min)	34.1	31.2	91
VO2 (l/min)	2.696	3.095	115
VCO2 (l/min)		3.611	
Work (Watts)	231		
Anaerobic Threshold (AT)(l/min)	> 1.078	2.606	
AT (% Predicted Max VO2)	> 40%	97	
Heart Rate (bpm)	173	180	104
O2 Pulse (ml/beat)	14.8	17.2	116
Systolic Blood Pressure (Max)	187		
Diastolic Blood Pressure (Max)	85-105		
Heart Rate Reserve (bpm)	<15	-6	
Peak Ventilatory Responses			
VE Max (l/min) BTPS	109.5	116.0	106
Tidal Volume (VT) (L)	2.109	2.538	120
Respiratory Rate (RR)	<50	46	
Breathing Reserve (%)	20-40	-3	
Gas-Exchange Responses			
End Tidal CO2 (Peak PetCO2)		33.2	
End Tidal O2 (Peak PetO2)		114.2	
VE/VO2 @ AT		29	
VE/VCO2 @ AT		28	
VD/VT (Est) @ Rest	0.30	0.15	49
VD/VT (Est) Peak	0.18	0.09	48
Respiratory Quotient (RQ)(Peak)	1.1-1.3	1.17	
SpO2 (O2 Sat–Pulse Ox) @ Peak	96	94	

Calibration Results — Flow Cal: Pred Volume: 3.00 Expire Avg: 2.98 Inspire Avg: 3.00

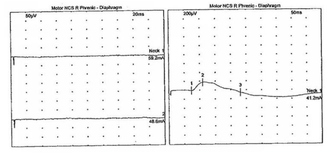
Gas Cal:	Cal1 O2	Cal 1 CO2	Cal 2 O2	Cal 2 CO2	Ambient O2	Ambient CO2
Predicted	16.00	4.00	26.00	0.00		
Measured	16.08	4.02	26.09	0.00	20.96	0.06
Transit (msec)	0.847	0.437				
Response (msec)	0.106	0.088				

Impression / Summary:
Cardiopulmonary exercise test demonstrates excellent performance. Anaerobic threshold was met. Overall normal exercise test with no reduction in aerobic capacity. Symptoms were reproduced during the test with a few patterns noted within interpretation.
Heart rate reserve was absent. This is seen in normal exercise performance but it should be noted the patient has been having episodes of inappropriate tachycardia post-COVID. There is no change in O2 pulse.
Calculated MVV, utilizing patient's measured FEV1 x 40, results in a breathing reserve of 95%, outside range of normal. Although he achieved normal VO2 max, in normal exercise it is not typical to have ventilatory limitation. Unilateral diaphragm paralysis in obesity was associated with reduced breathing reserve, typically not affecting ventilatory reserve in normal BMI patients. The patient has no other etiology for absent ventilatory reserve with no evidence of obstructive lung disease or gas exchange abnormalities. Therefore further evaluation of diaphragm dysfunction is likely warranted

Clinical Course

Patient was diagnosed with a left phrenic nerve impairment. He had no history of trauma or cervical/abdominal injury to explain this finding. Prior imaging from pre-COVID-19 era showed no diaphragmatic elevation, supporting a post-viral etiology. He was referred to a tertiary care center, where pulmonary rehabilitation, a sleep study, and evaluation for diaphragmatic pacing were recommended.

EMG



Motor NCS

Nerve / Sites	Rec. Site	Lat. ms	Amp mV	Dist cm	Vel m/s
R Ulnar - ADM					
Wrist	ADM	2.90	13.1	7	
B.Elbow	ADM	6.86	12.4	24.5	61.6
A.Elbow	ADM	8.50	11.8	10	61.5
R Phrenic - Diaphragm					
Neck	Diaphragm	7.35	0.2		
L Phrenic - Diaphragm					
Neck	Diaphragm	NR	NR		

Highlights

This case highlights an unusual presentation of phrenic nerve dysfunction as a complication of post-COVID-19 syndrome. While the referenced literature described diaphragm paralysis most in patients who were hospitalized for COVID-19, this patient was never hospitalized. He did not have diaphragm paralysis but was rather diagnosed with phrenic nerve impairment leading to ventilatory defect. Notably, the Sniff test and PFTs were inconclusive, whereas EMG and CPET were critical for diagnosis.

Clinicians should consider phrenic nerve injury/impairment in the differential diagnosis of persistent dyspnea post-COVID infection. Structure and function of the phrenic nerve and diaphragm are reciprocally interrelated as demonstrated in this case. Thus, a thorough evaluation of phrenic nerve and diaphragm function in patients who present with persistent dyspnea with a history of COVID-19 or other respiratory viral infections is critical.

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2. Francois Maurier, Benoit Godbert, & Julie Perrin. (2020). Respiratory distress in SARS-COV-2 without lung damage: Phrenic paralysis should be considered in COVID-19 infection. European Journal of Case Reports in Internal Medicine, (Vol 7 No 6). https://doi.org/10.12890/2020_001728

3. Law, S. M., Scott, K., Alkarn, A., Mahjoub, A., Mallik, A. K., Roditi, G., & Choo-Kang, B. (2022). Covid-19 associated phrenic nerve mononeuritis: A case series. Thorax, 77(8), 834–838. https://doi.org/10.1136/thoraxjnl-2021-218257

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5. Medina-Pérez, J. J., Balderas-Juárez, J. A., Vega-Rosas, A., Ballesteros-Penedo, P. G., & Coubert-Pelayo, S. G. (2023). Acute phrenic neuropathy and diaphragmatic dysfunction as a complication of COVID-19: A report of four cases. Cureus. https://doi.org/10.7759/cureus.34419

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