Case Discussions – Day #1

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Conflicts of Interest

Ayobami Akenroye: No Conflicts.

Nora Barrett: Funding: NIH, DOD

Consulting: Biohaven, Regeneron,

Uptodate

Grant review: American Lung Association

and NIH





Conflicts of Interest

Elliot Israel:

Asthma Education Prevention Program (NAEPP) Coordinating Committee 2017-

AB Science ConsultantAmgen Consultant

AstraZeneca Consultant & Clinical Research Support
 Avillion Consultant & Clinical Research Support

Circassia Pharmaceuticals Clinical Research Support

Cowen ConsultantGlaxoSmithKline Consultant

Gossamer Bio Clinical Research Support

Merck
 Novartis
 Pneuma Respiratory
 PPS Health
 Regeneron Pharmaceuticals
 Consultant
 Consultant

• Sanofi Consultant

TEVA Consultant & Clinical Research





A 34-year-old woman seeks your help regarding her difficult-to-control asthma.

She had the onset of asthma 8 years ago, following a particularly severe "chest cold." She feels that her chest tightness and shortness of breath never fully resolved thereafter. She is prone to flares of her asthma with respiratory tract infections, strong fumes or odors, and abrupt changes in the weather.

Mass General Brigham



She finds it difficult climbing stairs, particularly if carrying packages from her car, becoming breathless and needing to stop to rest at the top of one flight. She reports a cough with clear sputum production, mostly first thing in the morning, perhaps 1-2 teaspoonfuls in amount. She denies allergic sensitivities, and prior allergy skin testing was uniformly negative. She smoked cigarettes starting in her teenage years, but she quit entirely 10 years ago; and she does not vap mass General Brigham marijuana.



Her work is sedentary as a receptionist in a medical office. She has no pets at home; no unusual hobbies. She has gained weight over the last 2 years – her "Covid weight" – now with a body mass index (BMI) of 45. Her sleep is restless, sometimes disturbed by "heartburn," for which she takes Tums.





She has been taking combination fluticasone/salmeterol dry-powder inhaler for several years, with the dose steadily increased, now at 500/50 one inhalation twice daily, along with montelukast 10 mg/day.





She has received multiple courses of prednisone in the past and last year took prednisone 10 mg daily for approximately 6 months for her asthma; she weaned off prednisone entirely 3 months ago. She uses albuterol by metered-dose inhaler for rescue, typically once or twice a day; and she has albuterol-ipratropium solution for nebulization available if needed.





Her examination in the office is notable for her obesity, clear nasal passages, a narrowed posterior pharyngeal opening, and soft, distant-sounding expiratory wheezes bilaterally on auscultation.





Office spirometry indicates moderate airflow obstruction with a vital capacity at the lower limits of normal. On review, prior pulmonary function tests have documented significant reversibility of airflow obstruction.

Blood studies demonstrate a normal complete blood count (CBC) with normal white blood cell differential and a total serum immunoglobulin E level within the normal range.



Discussion





A 62-year-old man is referred by his primary care physician because of an abnormal chest CT finding. The patient is well known to your practice. He has had asthma since his teenage years. His lung function since you first met him many years ago has been consistently abnormal, with severe airflow obstruction and an FEV1 on the order of 45% of predicted.





Initial attempts to normalize his lung function with a short course of oral steroids and then with highdose inhaled steroids were unsuccessful, and he has maintained treatment with moderate-dose inhaled steroid and long-acting beta-agonist bronchodilator, plus albuterol as needed. He has had rare acute exacerbations of his asthma and other than mild exertional dyspnea, he has few respiratory complaints.



He had recent sinus surgery for recurrent sinusitis and persistent nasal congestion. He describes throat clearing more than productive cough. He works in sales and has no unusual exposures at home. He can walk more than 2 miles at his own pace; he sleeps without respiratory difficulty. He is a lifelong non-smoker without family history of lung disease.





His past history is significant for a benign bony abnormality (polyostotic fibrous dysplasia), hypertension, and anxiety disorder.

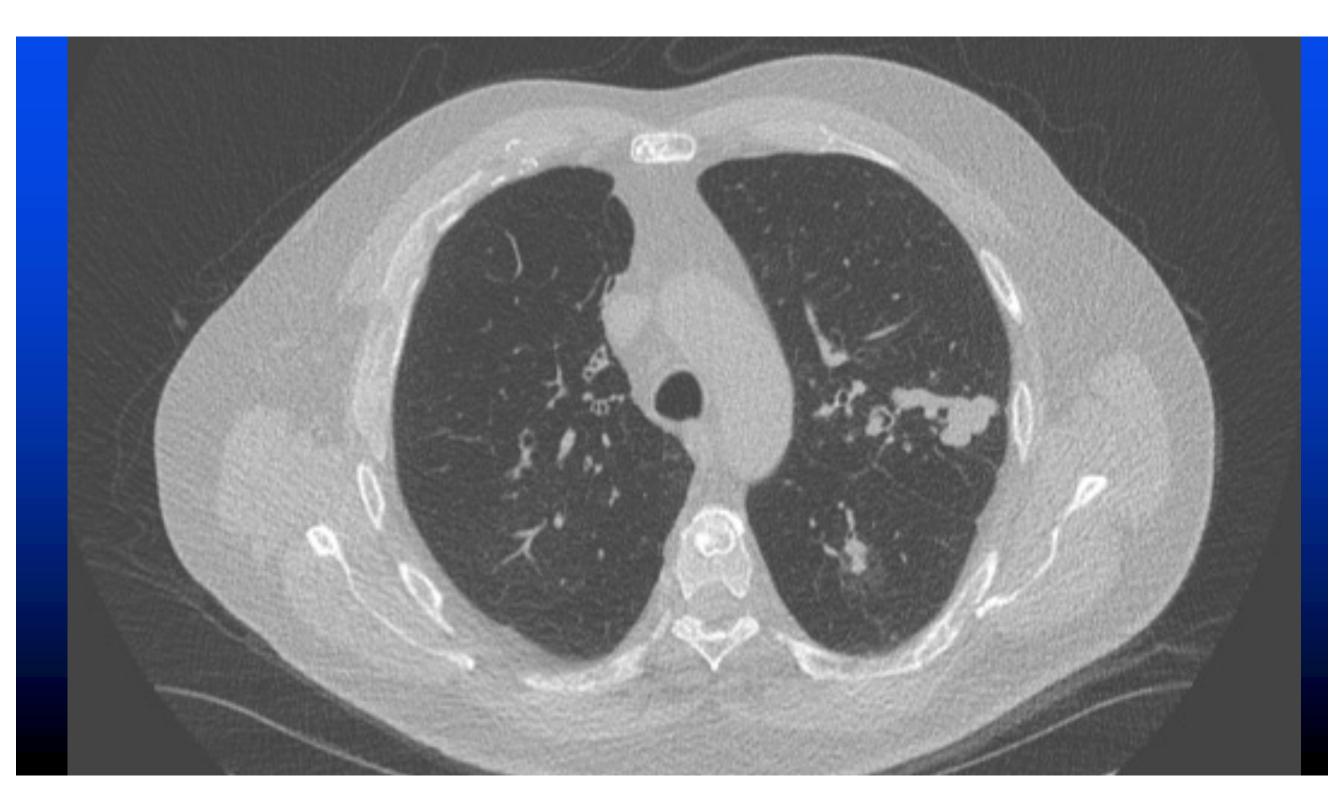




He is referred now, two years after his last visit, because of an abnormality noted on chest CT scan. He had undergone a limited chest CT scan for cardiac calcium scoring, and a 7-mm nodule was noted in the left lower lobe, for which follow-up dedicated chest CT scan was recommended. Other than perhaps somewhat greater exertional dyspnea and mild weight loss, he denies new symptoms.



Chest CT scan and PFT results follow:





Spirometry (BTPS)		Predicted Range		Pre Bronchodilator		Post Bronchodilator		Percent
		Mean	95%	Actual	% Pred	Actual	% Pred	Change
FVC Effort Time	7.1			09:59		10:42		
FEV ₁	L	3.92	2.93	1.47	38	1.74	44	18
FVC	L	5.14	3.90	3.28	64	3.58	70	9
FEV ₁ / FVC	%	77	64	45	58	49	64	9
FEV ₆	L	5.09	4.09	3.02	59	3.39	67	12
FEV ₁ / FEV ₆	%	79	70	49	62	51	65	4
FEF ₂₅₋₇₅	L/s	3.13	1.50	0.57	18	0.78	25	37
PEFR	L/s	9.91	7.35	5.59	56	6.21	63	11
FET	sec			8.20		7.66		-7
MVV	L/m	151.1	94.3					
Lung Volumes (Box)		Predicted Range		Pre Bronchodilator				
		Mean	95%	Actual	% Pred			
VTG Effort Time				10:09				
TLC	L	7.71	6.10	7.73	100			
FRC	L	4.07	2.61	5.72	141			
IC	L	3.64		2.01	55			
ERV	L	1.61		1.35	84			
RV	L	2.46	1.70	4.37	178			
RV/TLC	%	33	22	57	173			
VC	L	5.25	4.13	3.36	64			

Discussion





A 17-year-old boy comes accompanied by his parents for evaluation of asthma that is now interfering with his participation in sports.

Throughout high school he has run cross-country track. On cold days he might use his levalbuterol (Xopenex) inhaler prior to running; on warmer days, he would not need it. Until this year his asthma never seemed to get in the way of his running.



This fall he found that instead of getting better during training season, his "times" were getting worse, and he would experience wheezing and shortness of breath after 10-15 minutes of running, despite pre-medication with his bronchodilator inhaler. He could complete the race, but at much slower speed than his usual.





His primary care provider had him begin twice-daily inhaled beclomethasone (Qvar), first 40 mcg/puff strength, then 80 mcg/puff strength, but he has noted no difference. He expresses frustration, feels "angry with himself," with a sense of "letting down" his teammates and coach.





His parents indicate that he had frequent bronchial infections as a young child, and like his older brother, was diagnosed with asthma around age 3-4 years. He has had mild seasonal rhinitis and conjunctivitis, particularly in the spring, managed with intermittent use of an antihistamine. For symptoms of esophageal reflux, he takes occasional famotidine.





His mother has well-controlled asthma; his older brother has had more troublesome disease, with multiple urgent care visits and courses of oral steroids, now doing well on monoclonal antibody therapy.





On examination, he is breathing comfortably at rest. He is of normal height and weight for his age. His physical examination is entirely normal.





Spirometry performed in the office is normal (FEV1 = 98% of predicted).

His mother asks whether you think that he too would benefit from a biologic agent.





Discussion



