A presentation of massive hemoptysis in a patient with Churg-Strauss syndrome

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Churg-Strauss syndrome (CSS) is a systemic small-vessel vasculitis. When involving the lungs, small-vessel vasculitides typically cause capillaritis, leading to diffuse alveolar hemorrhage and submassive hemoptysis. In contrast, massive hemoptysis primarily originates from the bronchial arteries; therefore, small-vessel vasculitis is not considered when a patient presents with massive hemoptysis. The authors describe a patient with CSS who presented with the novel finding of massive hemoptysis. Computed tomography scans lacked alveolar infiltrates and bronchoalveolar lavage lacked hemosiderin-laden macrophages. Bronchoscopy demonstrated a raised mucosal lesion in the right mainstem bronchus and computed tomography angiogram revealed aberrant dilated bronchial arteries underlying the same region, suggesting this as the source of the hemoptysis. To the authors' knowledge, the present report describes the first reported case of CSS to present with massive hemoptysis with likely involvement of the bronchial arterial circulation. CSS should be considered in patients with unexplained massive hemoptysis.

Key Words: Aberrant bronchial arteries; ANCA; Churg-Strauss; Hemoptysis; Inflammation; Vasculitis

Learning objectives

- To recognize that hemoptysis may originate from either of the two circulations supplying the lung, and to recognize how this correlates with the volume of hemoptysis.
- To recognize that aberrant arteries within the bronchial circulation may be the source of hemoptysis, and to understand the bronchoscopic and radiological features.
- To understand Churg-Strauss syndrome (CSS) and to consider it in patients with unexplained massive hemoptysis.

CanMEDS competency: Medical Expert

Pretest

- How would diagnostic modalities implicate the pulmonary circulation as the source of hemorrhage?
- How would computed tomography (CT) angiography implicate a particular artery when hemoptysis originates from the systemic circulation?

The lungs have dual blood supply via the bronchial and the pulmonary circulations. Bleeding may originate from either circulation; however, the volume of bleeding is different in each case. The bronchial arteries are part of the systemic circulation, which conveys blood under high pressure; therefore, bronchial arteries bleed profusely and can cause massive hemoptysis. In contrast, the pulmonary circulation conveys blood at low pressure under normal conditions, and bleeding from its capillaries causes hemoptysis of lower volume or even no apparent hemoptysis whatsoever. Common causes of bronchial

Une hémoptysie massive chez un patient atteint du syndrome de Churg et Strauss

Le syndrome de Churg et Strauss (SCS) est une vascularite systémique des petits vaisseaux. Lorsqu'il touche les poumons, ce type de vascularite provoque généralement une capillarite, qui entraîne une hémorragie alvéolaire diffuse et une hémoptysie submassive. Au contraire, l'hémoptysie massive trouve son origine dans les artères bronchiques, ce qui n'incite pas à envisager la vascularite des petits vaisseaux. Les auteurs décrivent un patient atteint de SCS qui a consulté en raison d'une hémoptysie massive. La tomodensitométrie ne révélait pas d'infiltrats alvéolaires, tandis que le lavage broncho-alvéolaire ne recelait pas de macrophages chargés d'hemosidérine. La bronchoscopie a démontré une lésion muqueuse surélevée dans la bronche souche droite et l'angiogramme, une dilatation aberrante des artères bronchiques dans la même région, ce qui évoquait la source probable de l'hémoptysie. En autant que le sache les auteurs, le présent rapport décrit le premier cas déclaré de SCS se manifestant sous forme d'hémoptysie massive avec atteinte probable de la circulation artérielle des bronches. Le SCS devrait être envisagé chez les patients ayant une hémoptysie massive inexpliquée.

bleeding include bronchiectasis and carcinoma (1). Aberrant bronchial arteries have also been reported to cause massive hemoptysis. Bleeding from the pulmonary circulation is most commonly caused by small-vessel vasculitides, which damage interstitial capillaries and cause what is clinically known as diffuse alveolar hemorrhage. Diffuse alveolar hemorrhage forms an alveolar filling process on roentgenograms and alveolar filling defects on CT scans. Alveolar macrophages take up the released hemoglobin and convert it to hemosiderin in 48 h to 72 h. In turn, these hemosiderin-laden macrophages are detectable in bronchoalveolar lavage fluid and assist in the diagnosis of diffuse alveolar hemorrhage. CSS is a form of small-vessel vasculitis and, as such, may cause diffuse alveolar hemorrhage and submassive hemoptysis; however, here we describe a patient with CSS who presented with the novel finding of massive hemoptysis with likely involvement of the bronchial arterial circulation.

CASE PRESENTATION

A 50-year-old man presented with sudden onset of massive (>500 mL) hemoptysis. He denied recent fevers, chest pain or melena.

He had asthma for three years, which was complicated by chronic sinusitis and nasal polyposis, unilateral sensorineural hearing loss and a thalamic ischemic stroke within the previous month. He had no history of smoking. His medications included acetylsalicylic acid, inhaled tiotropium, fluticasone and salmeterol.

Physical examination demonstrated stable vital signs and an oxygen saturation of 99% on room air. Lung examination revealed scattered rhonchi without crackles.

Laboratory investigation data are shown in Table 1. A chest radiograph was unremarkable, and a chest CT scan was notable for the

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TABLE 1
Laboratory results

	At presentation	Day 5 and 6
Hemoglobin, g/L	146	108
White blood cells, $\times 10^9/L$	12.3	11.7
Eosinophils, proportion	0.17	0.024
Eosinophils, $\times 10^9/L$	2.1	0.3
Erythrocyte sedimentation rate, mm/h	54	34
C-reactive protein, nmol/L	923.83	200.00
p-ANCA	Positive	Positive
c-ANCA	Negative	Negative
International normalized ratio	1.1	
Prothrombin time, s	33.9	
Sputum Gram stain	Negative	
Urine analysis	Normal	
Immunoglobulin E, KIU/L*		1115
Anti-myeloperoxidase		Positive
Anti-proteinase 3		Negative
Antiglomerular basement membrane		Negative

*Reference range 0–87 KIU/L. c-ANCA Cytoplasmic antineutrophilic cytoplasmic antibody; p-ANCA Perinuclear antineutrophilic cytoplasmic antibody

Figure 1) Representative slice from chest computed tomography scan at the time of presentation is notably significant for absence of alveolar filling defects

absence of alveolar filling defects (Figure 1). Bronchoalveolar lavage was free of abnormal bacterial growth, malignant cells and hemosiderin-laden macrophages. The patient developed left foot drop and allodynia, for which an electrophysiology study showed absent/low amplitudes in several nerves of the limbs and confirmed mononeuritis multiplex. Given this constellation of findings, a diagnosis of CSS was made.

DISCUSSION

CSS is a systemic antineutrophil cytoplasmic antibody (ANCA)-associated small-vessel vasculitis that is clinically characterized by three overlapping phases: allergic airways disease (rhinitis, nasal polyps and asthma); eosinophilia with eosinophilic tissue infiltrates; and systemic vasculitis (2). The American College of Rheumatology requires any four of the following six criteria to secure the diagnosis of CSS with 99.7% specificity: asthma, eosinophilia $>10\%$, neuropathy, nonfixed pulmonary infiltrates, paranasal sinus abnormality and biopsy containing a blood vessel with extravascular eosinophils (3). Moreover, with the presence of ANCA and mononeuritis multiplex, a biopsy is not required to diagnose CSS (4). The present case – with sinusitis, nasal polyps, asthma, eosinophilia, and mononeuritis

Figure 2) Image taken during fiberoptic bronchoscopy demonstrating a raised mucosal lesion within the right main-stem bronchus (arrowhead)

Figure 3) Arterial-phase chest computed tomography scan revealing numerous dilated arteries abutting the right main-stem bronchus (arrowhead)

multiplex – meets both the description of phases and the requirements for diagnosis of CSS.

His clinical presentation of massive hemoptysis was not typical of CSS. Small-vessel vasculitides typically cause capillaritis leading to diffuse alveolar hemorrhage and submassive hemoptysis. Such a scenario is prominent with other types of ANCA-associated small-vessel vasculitides (ie, granulomatosis with polyangiitis and microscopic polyangiitis), but is uncommon with CSS (5). The volume of hemoptysis and the lack of hemosiderin in bronchoalveolar lavage and of alveolar filling defects on CT scan suggested a proximal source of hemoptysis from the systemic circulation.

Bronchoscopy demonstrated a mucosa-covered, nonpulsatile, raised lesion within the right mainstem bronchus (Figure 2). A CT angiogram demonstrated aberrant dilated bronchial arteries traceable to the right hilum and reaching the same location as the lesion noted on bronchoscopy (Figure 3), suggesting a source for the massive hemoptysis. Three-dimensional mapping demonstrated clearly these aberrant arteries as well as their origin from the aortic arch and their traceability to the right hilum (Figure 4).

Bronchial mucosal lesions in CSS have been described in the past and consist of either granulomas or of necrotizing inflammation with eosinophils, and appear as whitish-coloured lesions on bronchoscopy

(6,7). In contrast, we observed a lesion consistent with the surrounding mucosa, suggesting a submucosal process – abutting dilated arteries. Similar raised mucosal lesions were previously described in patients with hemoptysis but without CSS, and were found on pathological examination to be caused by submucosal arteries of abnormally large size and superficial course (8,9).

Although we do not know the etiology of the dilated aberrant bronchial arteries in our patient, the development of such arteries in CSS and their implication in massive hemoptysis is consistent with accumulating knowledge. First, chronic inflammation can trigger angiogenesis and remodelling, and ANCA-associated vasculitides are associated with elevated levels of angiogenesis markers (10,11). Second, markers of angiogenesis are associated with massive hemoptysis (12), and aberrant bronchial arteries are known to spontaneously bleed and cause massive hemoptysis, both when their existence is primary and when secondary to inflammation (9,13). Third, such aberrant arteries may be found on bronchoscopy to form raised mucosal lesions, which may or may not be pulsatile (8,9,14). Fourth, arteries found on CT angiography to be both dilated and traceable to the hilum are often responsible for hemoptysis (15). In our patient, there was no other mechanism to better explain the existence of these arteries; the patient had neither history of smoking, deep venous thrombosis, nor did he have bronchiectasis or pulmonary hypertension, as estimated by Doppler echocardiography.

To our knowledge, the present report describes the first case of CSS to present with massive hemoptysis. The present report should alert physicians investigating a case of massive hemoptysis that its cause may be a disease that is classically believed to affect the interstitium rather than airways.

To recapitulate, this patient presented with massive hemoptysis due to CSS, and was treated with transfusion of two units of packed red blood cells and corticosteroids, which normalized the eosinophil count and reduced inflammatory marker levels (Table 1). After the development of mononeuritis multiplex, cyclophosphamide was added. He was subsequently referred to our centre for further evaluation (approximately 13 weeks after initial presentation). Our investigations identified the aberrant dilated bronchial arteries (Figures 2 to 4) as a potential cause for his massive hemoptysis. It was believed that the vasculitic process of CSS led to the formation of these aberrant arteries and, therefore, that the treatment targeting the vasculitic process (with corticosteroids and cyclophosphamide) would cause them to regress. Embolization of the aberrant bronchial arteries was reserved for recurrent hemoptysis, which the patient did not experience up to three years of follow-up.

CONCLUSION

We described a patient with CSS who presented with the novel finding of massive hemoptysis. Bronchoscopy and imaging implicated hypertrophied, aberrant bronchial arteries as the source of bleeding. CSS should be considered in patients with unexplained massive hemoptysis.

Post-test

- How would diagnostic modalities implicate the pulmonary circulation as the source of hemorrhage?

Diffuse alveolar hemorrhage forms an alveolar filling process on roentgenograms and alveolar filling defects on CT scans. Bronchoscopy demonstrates progressively bloody bronchoalveolar lavage in sequential aliquots, which establishes the diagnosis of diffuse alveolar hemorrhage. Alveolar macrophages take up the released hemoglobin and convert it to hemosiderin in 48 h to 72 h. In turn, these hemosiderin-laden macrophages are detectable in bronchoalveolar lavage fluid and assist in the diagnosis of diffuse alveolar hemorrhage.

- How would computed tomography (CT) angiography implicate a particular artery when hemoptysis originates from the systemic circulation?

A vessel diameter >2 mm and traceability to the hilum. Extravasation of contrast medium is a specific but not sensitive sign.

Figure 4) Three-dimensional mapping of computed tomography angiography demonstrating an aberrant dilated artery originating from the aortic arch, having a diameter of 7 mm, supplying multiple prominent arteries and traceable to the right hilum

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