Reumatol Clin. 2018;14(2):119–123

Sociedad Española de Reumatología - Colegio Mexicano de Reumatología

Reumatología Clínica

www.reumatologiaclinica.org

Letters to the Editor

Web-like bronchial stenosis secondary to granulomatosis with polyangiitis☆

Estenosis bronquiales web-like *secundarias a granulomatosis con poliangeitis*

To the Editor,

Granulomatosis with polyangiitis (GPA, Wegener's granulomatosis) is a systemic vasculitis that typically affects the otorhinolaryngeal region and the respiratory tract,[1,2] which can be complicated by tracheobronchial stenosis.[3] Subglottic stenoses (SGS) are characteristic, and develop in 10–15% of the patients,[4,5] but bronchial stenoses (BS) can also be observed. We consider it of interest to present a patient with GPA and web-like BS, which to the best of our knowledge, has not been reported to date in Spain.

Case report

The patient was a 16-year-old boy who was admitted with a 1-month history of rhinorrhea, headache, poor general condition, fever, dyspnea and purulent discharge. He had an infraorbital edema and nasal deformity with scabs. A chest radiograph was normal and computed tomography (CT) revealed opacification of the maxillary sinus and ethmoidal cells. He had 22,660 leukocytes/mm^3 (85.7% neutrophils), 1,174,000 platelets/mm^3, C-reactive protein was 18.8 mg/dL (normal value < 0.5) and normal renal function. He did not improve with antibiotic therapy and, thus, the studies were repeated: a second CT scan of the paranasal sinuses showed lysis of the wall of left maxillary sinus and resorption of turbinates, chest radiograph revealed bilateral alveolar infiltrates and chest CT showed multiple cavitated nodules. He was positive for antineutrophil cytoplasmic antibodies (ANCA) with a titer of 1:640, cytoplasmic-ANCA pattern, anti-proteinase 3 (PR3) antibodies >1607 IU and complement levels were normal. A biopsy of a turbinate revealed necrosis, infiltrates with polymorphonuclear cells and lymphocytes, and necrotic vessels. Bronchoscopy revealed friable mucosa and mucopurulent secretions without stenosis and *Staphylococcus aureus* was isolated in the nasal exudate. The diagnosis was GPA-like vasculitis, and immunosuppressive therapy was begun with 250 mg daily of intravenous methylprednisolone for 3 days, followed by oral prednisone in a tapered dose starting at 45 mg/day, 500 mg intravenous pulses of cyclophosphamide every 15 days for 3 months, as well as omeprazole, vitamin D and cotrimoxazole.

Despite treatment, the patient became progressively worse. After 9 months, he had dyspnea on minimal exertion, stridor and hemoptysis. Spirometry revealed a forced expiratory volume in 1 s (FEV_1) of 3.33 and a FEV_1/forced vital capacity (FVC) ratio of 56.85%. A subsequent spirometry disclosed severe airflow limitation, with a FEV_1 of 2.07 and a FEV_1/FVC ratio of 48.46%. Another CT scan showed an improvement in the pulmonary lesions, without BS, and laryngeal endoscopy ruled out SGS. Finally, bronchoscopy was repeated and disclosed several web-like membranous stenoses at the level of the lower and left upper lobes. The patient underwent mechanical dilatations, which achieved clinical improvement. He was treated with a 1 g dose of rituximab, which was discontinued as he had a severe allergic reaction, megadoses of steroids and, again, two 500 mg pulses of cyclophosphamide every 15 days. Nevertheless, the BS recurred, with normalized acute-phase reactants, and he required balloon dilatations and endoscopic treatment (Fig. 1).

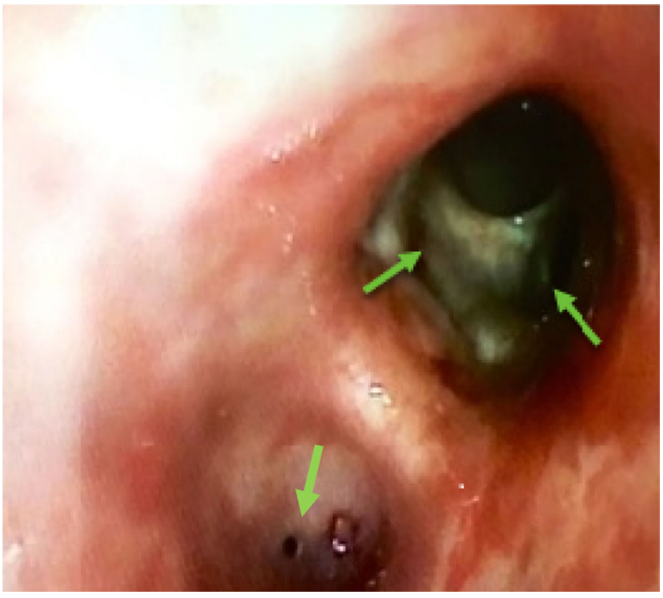

Fig. 1. Bronchoscopic image showing a web-like concentric membranous stenosis that crosses the entrance to the base of right lower lobe, with a minimal central aperture that impedes the passage of the bronchoscope to the distal region. In left bronchus, the same stenosis but with a larger central aperture.

Discussion

There is little information on the management of BS in GPA. Although they are associated with SGS, they can develop in the absence of that lesion. Girard et al.[6] recently reported their experience in 10 French patients with BS. They presented with dyspnea and hemoptysis, but without stridor. In 6 cases, BS was an incidental finding after the performance of a CT scan or fiberoptic bronchoscopy for another reason. In general, the diagnosis was reached within the first 3 months of the disease. In GPA, BS are usually multiple, predominantly involving the left bronchus, generally

☆ Please cite this article as: Ulloa-Clavijo C, Ariza-Prota M, Vaquero-Cacho M, Caminal-Montero L. Estenosis bronquiales *web-like* secundarias a granulomatosis con poliangeitis. Reumatol Clin. 2018;14:119–120.

in the upper lobe, and the tendency for relapses was independent of the treatment. It is unusual that 8 of the 9 patients who had recurrences were in systemic remission as they were receiving immunosuppressive therapy, with a mean of 3 recurrences per patient. One of them had 12 relapses.

Our patient had a web-like stenosis (WLS) or "in diaphragm", that is believed to develop due to an exaggerated inflammatory response and hypertrophy of the mucosa, and formation of fibromembranous tissue that comes to progressively occlude the bronchial lumen.[7–9] Web-like stenoses have been related to infections, traumatic injury and local or systemic inflammatory processes. Three cases of WLS have been reported with GPA and one with microscopic polyangiitis,[8] and isolated cases with vasculitis, sarcoidosis, amyloidosis, Behçet's disease and ulcerative colitis.[9,10] In contrast to non-web-like BS, lung CT is normal. Thus, only pulmonary functions tests and bronchoscopy enable the establishment of the diagnosis. The prognosis is poor, requiring dilatations using a rigid bronchoscope, endobronchial laser, local steroid injections and even the placement of stents in the case of proximal stenoses. Treatment and follow-up should be discussed with bronchoscopists or thoracic surgeons. The purpose is to perform the available endobronchial technique and optimize immunosuppressive therapy.

References

1. Ríos Blanco JJ, Gómez Cerezo J, Vázquez Muñoz E, Suárez García I, López Rodríguez M, Yébenes Gregorio L, et al. Estudio clínico-biológico y radiológico de la granulomatosis de Wegener en un hospital universitario. Rev Clin Esp. 2005:367–73.
2. Martínez-Morillo M, Grados D, Naranjo-Hans D, Mateo L, Holgado S, Olivé A. Granulomatosis con poliangeítis (Wegener). Descripción de 15 casos. Reumatol Clin. 2012;8:15–9.
3. Solans-Laqué R, Lorente J, Canela M. Afección traqueobronquial en la granulomatosis de Wegener. Med Clin (Barc). 2011;137:230–5.
4. Horta-Baasa G, Fernanda Hernández-Cabrera M, Catana R, Pérez-Cristóbal M, Barile-Fabris LA. Estenosis subglótica en granulomatosis con poliangitis (granulomatosis de Wegener): presentación de 4 casos. Reumatol Clin. 2016;12:267–73.
5. Massa M, Emery NC, Bosio M, Finn BC, Bruetman JE, Young P. Subglottic tracheal stenosis in Wegener disease. Report of two cases. Rev Med Chil. 2014;142:382–5.
6. Girard C, Charles P, Terrier B, Bussonne G, Cohen PMD, Pagnoux C, et al. Tracheobronchial stenoses in granulomatosis with polyangitis (Wegener's). A report on 26 cases. Medicine (Baltimore). 2015;94:e1088.
7. Freitag L, Ernst A, Unger M, Kovitz K, Marquette CH. A proposed classification system of central airway stenosis. Eur Respir J. 2007;30:7–12.
8. Amat B, Esselmann A, Reichle G, Rohde HJ, Westhaff M, Freitas L. Tratamiento endoscópico de las estenosis benignas traqueobronquiales tipo web-like con el bisturí endobronquial en combinación con un programa de corte optimizado. Arch Bronconeumol. 2012;48:14–21.
9. Mailloux B, Burguete S, Stupka J, Sonetti D. Web-Like endobronchial membranous stenosis in a patient after H1N1 influenza a infection. Chest. 2011;140:82A.
10. Wilcox P, Miller R, Miller G, Heath J, Nelem Muller N, Ostrow D. Airway involvement in ulcerative colitis. Chest. 1987;92:18–22.

Catalina Ulloa-Clavijo,[a,*] Miguel Ariza-Prota,[b] Manuel Vaquero-Cacho,[b] Luis Caminal-Montero[c]

[a] *Área de Gestión Clínica de Nefrología, Hospital Universitario Central de Asturias, Oviedo, Asturias, Spain*
[b] *Área de Gestión Clínica del Pulmón, Hospital Universitario Central de Asturias, Oviedo, Asturias, Spain*
[c] *Consulta de Enfermedades Autoinmunes Sistémicas, Unidad de Gestión Clínica de Medicina Interna, Hospital Universitario Central de Asturias, Oviedo, Asturias, Spain*

* Corresponding author.
E-mail address: catalinaulloac@hotmail.com (C. Ulloa-Clavijo).

2173-5743/

A Reflection on How We Define, Determine and Interpret the Finding of Lupus Anticoagulant☆

Una reflexión sobre el anticoagulante lúpico: cómo lo definimos, determinamos e interpretamos

To the Editor,

International criteria for the diagnosis of antiphospholipid syndrome (APS) include the detection of antiphospholipid antibodies: anticardiolipin and anti-β2-glycoprotein I (anti-β2GPI) of immunoglobulin (Ig) G and IgM isotopes and lupus anticoagulant (LA), and its detection in patients with a history of thrombosis or pregnancy complications is considered to be essential in the management of APS.[1–3]

During the 1950s, it became evident that patients with systemic lupus erythematosus (SLE) had a circulating anticoagulant factor, and the concept of LA was coined to designate a heterogenic group of coagulation inhibitors that affect prothrombin activation by the prothrombinase enzyme complex.[4] Lupus anticoagulant is currently described as an Ig like IgG/IgM that inhibits phospholipid (PL)-dependent coagulation reactions *in vitro*. However, is LA always associated with SLE? Does it inhibit coagulation? Is it an antibody? First, the majority of the patients who are positive for LA do not have SLE. In the absence of concomitant thrombocytopenia or a deficiency of coagulation factors or inhibitors of coagulation factors, with certain exceptions, LA is related to processes of hypercoagulability and arterial and venous thrombosis, but is not, *per se*, a risk factor for bleeding or hemorrhage. With the currently available scientific evidence, it can be said the LA is constituted by a group of antibodies that have yet to be characterized.[5,6]

Lupus anticoagulant is detected using functional assays that demonstrate a PL-dependent prolongation of the clotting time, due to the *in vitro* interference of antibodies with PL-dependent function, as with certain essential cofactors in the coagulation cascade (Fig. 1) that result in the prolongation of the activated partial thromboplastin time. The International Society on Thrombosis and Haemostasis (ISTH),[7] a society that has unsuccessfully attempted to change the name, established the following criteria to confirm the presence of LA:

1. Phospholipid-dependent prolonged coagulation tests.
2. Demonstration of the coagulation inhibitor utilizing mixed plasma.
3. Demonstration of the PL dependence of the inhibitor.
4. Ruling out other coagulation disorders, particularly due to deficiency of coagulation factors.

Lupus anticoagulant can be detected in patients with SLE, and with other autoimmune diseases, infections like human immunodeficiency virus, hepatitis and malaria, neoplastic disease or those taking certain drugs (procainamide and chlorpromazine).[6,8] A prevalence of 5% has been reported in the general adult population and up to 9.5% in women of reproductive age. Although the

☆ Please cite this article as: Valor L, Hernández-Flórez D, Martínez-Barrio J, López Longo FJ. Una reflexión sobre el anticoagulante lúpico: cómo lo definimos, determinamos e interpretamos. Reumatol Clin. 2018;14:120–122.