Omalizumab in severe asthma: Evaluation of the clinical impact after its withdrawal

Dear Editor,

Omalizumab is a monoclonal anti-IgE antibody approved for the treatment of uncontrolled severe persistent allergic asthma.[1] Although several studies have shown its benefits,[2–4] the optimal duration of the therapy and the effect after its withdrawal remains unknown.

We performed a study to assess the clinical effect of Omalizumab discontinuation, in patients with severe asthma. A current re-evaluation was conducted through questionnaires of asthma control, respiratory function tests and assessment on exacerbations.

Ten patients were included, all women, with a mean age of 49.5 years. All patients responded to Omalizumab therapy according to the GETE scale (*Global Effectiveness Treatment Evaluation*). The average time of treatment was 43.4 ± 21.7 months (min. 9, max. 73). Omalizumab was stopped in 7 patients for clinical stability, and in the other 3 for complications (1 stroke, 1 breast cancer and another for severe anaemia). The median time from discontinuation of therapy was 28 ± 25.3 months (min. 5, max. 76).

In our re-evaluation, the mean Control Allergic Rhinitis and Asthma test (CARAT) decreased from 21.6 ± 6.6 to 19.9 ± 7.8 and mean fractional exhaled nitric oxide (FeNO) value increased from 28.3 ± 11.1 to 29.03 ± 29.9 ppb. Forced expiratory volume in 1 s (FEV1) increased from 60.5 ± 20.7% to 60.8 ± 18.4%. The number of exacerbations within the last 12 months increased from 0.6 ± 1.1 to 2.1 ± 2.4 (Fig. 1).

Individual analysis showed a decrease in asthma control in 3 cases (30%), an increase in exacerbations was also observed in 4 patients (40%), and none of them had had exacerbations over the past 12 months at the end of treatment. The mean time to the first exacerbation was 6 ± 5.1 months, and three patients had an exacerbation in the first 6 months. Two of these patients had been the most severe patients at the beginning based on ACT scores; they were under treatment for variable lengths of time (25/42/52 months).

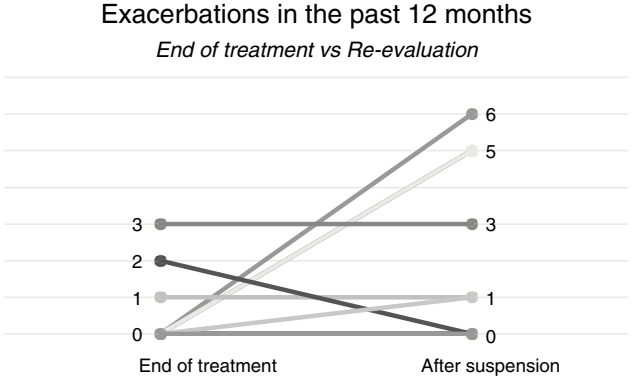

Figure 1 Number of exacerbations/last 12 months at the end of treatment versus re-evaluation.

During the 7 months follow up period, Omalizumab has already been reintroduced in one patient.

In the literature, there are only a few evaluations of patients following suspension of Omalizumab, with different study designs and inconsistent results.

The biggest report is from Nopp et al.[5] who published a 1 long-term study ($n = 18$) with a 3-year period of observation after Omalizumab suspension, where one third of the patients lost their asthma control. Molimard et al.[6] performed a retrospective observational study in severe asthmatic patients ($n = 61$) after discontinuation of Omalizumab therapy and loss of control was observed in 34 patients (55.7%); Omalizumab was reintroduced in 20 out of these 34 patients, but 20% of them became non-responders despite previous sensitivity.

Looking at our patients and at the studies described, it seems reasonable to maintain Omalizumab (beyond the standard period of 5 years[7])/to reintroduce it in patients with frequent exacerbations who achieved control after Omalizumab treatment.

Besides the possibility of losing asthma control, there is a risk of secondary resistance to Omalizumab.[6]

Therefore, decisions on cessation of Omalizumab treatment should always be undertaken individually after weighing all the benefits and risks.

Conflicts of interest

The authors have no conflicts of interest to declare.

References

1. Chung KF, Wenzel SE, Brozek JL, Bush A, Castro M, Sterk PJ, et al. International ERS/ATS guidelines on definition, evaluation and treatment of severe asthma. Eur Respir J. 2014;43:343–73.
2. Abraham I, Alhossan A, Lee CS, Kutbi H, MacDonald K. 'Real-life' effectiveness studies of omalizumab in adult patients with severe allergic asthma: systematic review. Allergy. 2016;71:593–610.
3. Alfarroba S, Videira W, Galvao-Lucas C, Carvalho F, Barbara C. Clinical experience with omalizumab in a Portuguese severe asthma unit. Rev Port Pneumol. 2014;20:78–83.
4. Sousa AS, Pereira AM, Fonseca JA, Azevedo LF, Abreu C, Arrobas A, et al. Asthma control and exacerbations in patients with severe asthma treated with omalizumab in Portugal. Rev Port Pneumol. 2015.
5. Nopp A, Johansson SG, Adedoyin J, Ankerst J, Palmqvist M, Oman H. After 6 years with Xolair; a 3-year withdrawal follow-up. Allergy. 2010;65:56–60.
6. Molimard M, Mala L, Bourdeix I, Le Gros V. Observational study in severe asthmatic patients after discontinuation of omalizumab for good asthma control. Respir Med. 2014;108:571–6.
7. Kuprys-Lipinska I, Kuna P. Loss of asthma control after cessation of omalizumab treatment: real life data. Postepy Dermatol Alergol. 2014;31:1–5.

M. D. de Sousa[a,*], C. Ferreira[b], A. Arrobas[b]

[a] *Centro Hospitalar Tondela Viseu, Viseu, Portugal*
[b] *Centro Hospitalar e Universitário de Coimbra, Coimbra, Portugal*

* Corresponding author.
E-mail address: martadias.sousa@gmail.com
(M. D. de Sousa).

http://dx.doi.org/10.1016/j.rppnen.2016.12.004
2173-5115/

Cystic adenomatoid pulmonary malformation in adults: A retrospective study in a tertiary university hospital

Cystic adenomatoid malformation (CAM) of the lung is thought to be a hamartomatous lesion, characterized by bronchiolar maturation disturbance,[1,2] it is very rare in adults[3] and pathogenesis is still unknown.[4] CAM is classified according to Yousem et al.[5] into 4 types which are related with the underdeveloped bronchial-pulmonary segment and histological features. According to the literature the prevalence is as follows: type 1 (50–70%), type 2 (20–40%), type 4 (10–15%), type 3 (10%) and type 0 (1–3%). Clinical presentation varies (perinatal death, repeat infections, hemoptysis to lung carcinomas[6]) and severity relates to the size of the lesion; it is more frequent in the lower lobes and rarely affects more than one lobe. Chest radiograph reveals rounded thin-walled spaces, filled with air or secretions, although CT scan correlates with better morphological characterization. The mainstay treatment is pulmonary resection, usually due to the risk of complications such as infection, cystic expansion or malignant transformation.[6] For asymptomatic patients some authors recommend a conservative approach.

In order to get a better characterization of CAM in adults in our center, all cases between 2008 and 2015 were reviewed. CAM was diagnosed in 17 patients admitted to Coimbra Hospital and University Centre (CHUC). Patient demographics, presenting symptoms, chest radiography, CT scan, type of surgery and histopathology result were analyzed.

Five males and twelve females, aged between 20 and 85 years, with a mean age of 53.4 years were reviewed: the symptoms included recurrent infections in six patients, persistent productive cough in eight patients and hemoptysis in three. Chest radiographs and CT scans showed a pattern of bronchiectasis in seven patients, cystic lesions in six patients and nodular lesions in four patients; eight patients had it in the right lower lobe, four in the left lower lobe, two in the left upper lobe, one in the middle right lobe and two in more than one lobe in the right lung. All patients underwent surgery: lobectomy (9 cases) and pulmonary resection (8 cases). Histopathology reported two patients had CAM type 0, eight patients had CAM type 1, four patients had CAM type 2, one patient had CAM type 3 and CAM type 4 was not observed.

Our retrospective study included 17 adult patients with CAM. Although descriptions regarding gender differentials are not available, the majority of our patients were female. The most frequent complaints were recurrent infections and persistent productive cough, easily explained by the presence of bronchiectasis and fluid-filled cystic lesions depicted imagiologically. In most of these cases the presenting lesion was located in lower lobes, known from the literature to be the most common sites. The definitive diagnosis was only made by histological examination. The differential diagnosis included bronchogenic cysts, pulmonary sequestration, congenital lobar emphysema and mediastinal masses. According to the classification of Yousem et al.[5] the CAM type 0 presents a tracheal/bronchial origin and involve all lobes. CAM type 1 is usually confined

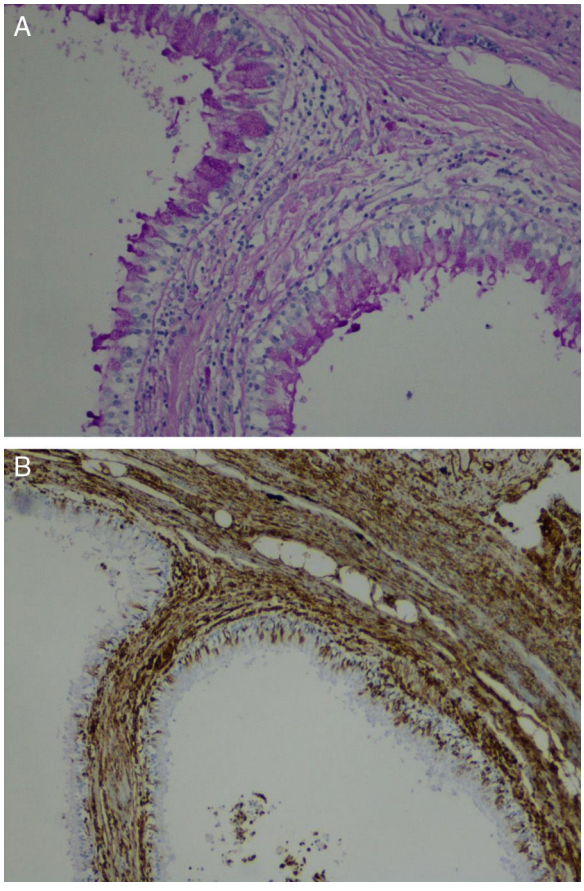

Figure 1 Type 0 CAM. (A) Irregular bronchial-like structures lined by pseudostratified ciliated columnar epithelium (PAS, ×400). (B) Columnar epithelium surrounded by prominent loose mesenchymal tissue (Vim, ×400).