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THE SAFETY OF OMALIZUMAB THERAPY IN A PATIENT WITH SEVERE PERSISTENT ALLERGIC ASTHMA AND HEPATITIS C

Hepatitis C virus (HCV) infection has variable associations with extrahepatic diseases. Although some of these seem obvious and are considered as part of an immune response against HCV, others represent an open question between interdependency and pure co-incidence.

Recently, an increasing number of reports suggest some relationships between HCV infection and lung disease.¹ In particular in asthmatic patients with HCV, the accelerated decline in lung function and certain anomalous effects of antiasthmatic drugs have been described. An increased response to oxitropium bromide and an

impaired response to salbutamol and inhalant corticosteroids have been documented.^{2,3} These abnormalities were reversed in responders to interferon therapy.⁴ To explain these occurrences, the aberrant presence in the bronchi of CD8⁺ T lymphocytes, in response to HCV, has been suggested.⁵

An impaired response to inhalant corticosteroids may represent a significant complication for asthma treatment because increased use of oral steroids may be required, which may exacerbate viral replication through down-regulation of the immune response.⁶

In HCV-positive patients with mild stable asthma, the efficacy of interferon for asthma in a subset of these patients has been demonstrated.⁴ In HCV-positive patients with severe asthma, omalizumab could be of specific importance because its steroid-sparing effect in those with severe asthma is well known.⁷

Unfortunately, the artificial setting of randomized clinical trials usually excludes comorbidities; therefore, no information is available on the effects, in particular on the safety, of omalizumab in patients with hepatitis.

We describe a 46-year-old black male nonsmoker with severe persistent allergic (sensitized to mites) asthma and hepatitis C.

Despite continuous therapy with the association of long-acting β_2 -adrenergic agents (either formoterol or salmeterol) plus high doses of inhalant corticosteroids (fluticasone, 500 mg twice daily, or equivalent), correctly performed in terms of adherence and compliance with therapy, his asthma was not well controlled.

Between February 2, 2000, and May 31, 2007, the mean asthma exacerbation rate, requiring oral steroid treatment, was 3.5 per year. Furthermore, the patient's medical records revealed 7 accident and emergency admissions and 2 hospitalizations.

Because variable levels of reversibility of bronchial obstruction with bronchodilators were constantly present, to improve asthma

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Table 1. Changes in Clinical Characteristics and Laboratory Findings During Omalizumab Therapy^a

Variable	Value at baseline ^b	Value from June to December 2007 ^c	Value from January to June 2008 ^c	Value from July 2008 to February 2009 ^c
FVC, L	3.09	3.22 (0.20)	3.13 (0.29) ^d	3.34 (0.11) ^d
FVC, %	66	70 (5)	69 (4) ^d	72 (3) ^d
FEV ₁ , L	2.23	2.44 (0.18)	2.37 (0.17) ^e	2.55 (0.08) ^e
FEV ₁ , %	63	70 (5)	69 (4) ^d	73 (2) ^d
ACT ^f	9	23 (2)	21 (2)	22 (1)
AST, U/L	37	61 (9)	63 (19) ^d	28 (4) ^d
ALT, U/L	28	84 (15)	76 (29) ^d	25 (2) ^d
GGT, U/L	151	212 (23)	215 (19) ^d	74 (13) ^d
ALP, U/L	185	168 (15)	152 (34) ^d	93 (8) ^d
HCV RNA, UI/mL	2,435,857	2,435,857 (June 2007) and 902,357 (December 2007)	533,421 (April 2008) and 2,606,227 (June 2008)	2,918,679 (October 2008); 23, after 1 mo of interferon/ribavirin therapy (December 2008); and undetectable, after 3 mo of interferon/ribavirin therapy (February 2009)

Abbreviations: ACT, asthma control test; ALT, alanine aminotransferase; ALP, alkaline phosphatase; AST, aspartate aminotransferase; FEV₁, forced expiratory volume in 1 second; FVC, forced vital capacity; GGT, γ -glutamyl transferase; HCV, hepatitis C virus.

^a Data are given as mean (SD). The data were collected twice monthly, except for ACT, which was collected once monthly.

^b These are the features at baseline, before omalizumab treatment.

^c These values are given for the indicated periods.

^d $P < .05$.

^e $P < .01$ (t test for paired data).

^f A score of 19 or greater was considered a marker of good control of asthma, not requiring changes in asthma treatment.

control, in June 2007 omalizumab treatment was added to the maintenance therapy (salmeterol, 50 mg, plus fluticasone, 500 mg, given twice daily).

At the start of treatment, the patient's weight was 60 kg and his IgE level was 542 UI/mL. According to the manufacturer's recommendations, 300 mg of omalizumab was administered every 2 weeks.

In the following 19 months of omalizumab treatment, a stable improvement of asthma control was achieved without modifying the inhalant therapy. Notably, there were no emergency or hospital admissions for asthma and only 1 booster of oral steroid (prednisone, 25 mg/d, for 5 days) was administered in a single respiratory virus asthma exacerbation.

The most important effects of the treatment on the markers of respiratory function and hepatitis activity are summarized in Table 1.

In November 2008, the patient underwent anti-HCV treatment with polyethylene glycol–interferon α -2a, 180 mg/wk, and ribavirin, 1,000 mg/d. After 3 months of this therapy, the HCV RNA completely cleared up, with no unforeseen event or evidence of any abnormality in the laboratory data of liver function.

Although there were no compelling data to suspect potential adverse effects of omalizumab therapy in HCV-positive patients, to the best of our knowledge this is the first report suggesting the safety of 19 months of omalizumab treatment in terms of liver function and noninterference with interferon/ribavirin therapy.

Furthermore, comorbidity with HCV infection does not seem to impair the efficacy of omalizumab, making it suitable to be proposed as therapy for HCV-positive asthmatic patients, whereas interferon/ribavirin therapy is not indicated because of its adverse effects.

Indeed, in our patient, concerns for a reduced tolerance of interferon/ribavirin therapy as a result of poor asthma control, coupled with slightly impaired liver function, delayed the beginning of HCV therapy and suggested the use of omalizumab.

The improvement of asthma in the subset of patients who responded to interferon correlated with a decrease of CD8⁺ T lymphocytes in the bronchial airways.⁵

Because a decrease in CD8⁺ T lymphocytes from a biopsy specimen of lung tissue after omalizumab therapy was found,⁸ we speculate that anti-IgE treatment could be particularly useful for the subset of HCV-positive asthmatic patients who do not respond to interferon therapy.

Further, specifically designed clinical trials will be necessary to confirm whether omalizumab benefits patients with severe allergic asthma and hepatitis C and might also help to provide insight into the specific pathogenetic mechanisms of this comorbidity.

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