



LETTER TO THE EDITOR

Therapeutic dilemmas in patient with perianal Crohn's disease and corticosteroid dependent difficult-to-control asthma

Dear Sir,

We present a 53 years old woman who suffered from endogenous difficult-to-control asthma from young adult age, with need of chronic use of oral corticosteroid therapy (methylprednisolone 16–24 mg/day >50% year) together with treatment of high doses of inhaled corticosteroids and daily requirement of long acting beta 2 agonist. Despite therapy, asthma was poorly controlled with FEV1<35% of the predicted and daily variability of PEF>20%. In the year 2008 perianal Crohn's disease was diagnosed in this patient.

1. Pulmonary status and findings

She had a history of asthma since young adult age that had been poorly controlled, with need of chronic use of oral corticosteroid therapy. She reported daily symptoms and almost nightly nocturnal awakenings due to shortness of breath, which were temporarily relieved with bronchodilators. She had had several exacerbations of asthma in the past 2 years requiring hospitalization. Her past medical history was negative for perennial allergies. She was a lifelong nonsmoker and denied any illicit drug use. Current pulmonary medication included: methylprednisolone 16–24 mg/day, fluticasone/salmeterol 500 ug/50 ug twice daily, montelukast 10 mg once daily and salbutamol on an as-needed basis which she was currently using three to four times daily. On physical examination vital signs were normal with satO2 on room air of 95%. Her head, neck and skin exams showed Cushingoid changes. Pulmonary exam was significant for diffuse expiratory wheezes with prolonged expiratory phase. Cardiac exam revealed regular rate and rhythm with no murmurs, rubs or gallops. There were no clubbing or cyanosis in her extremities.

1.1. Pulmonary function tests were as followed

Spirometry: FEV1—2.77 L (37%); FVC—3.24 L (76%); FEV1/FVC 42%; post-bronchodilator studies FEV1—2.95 L (increase of 12%); FVC—3.55 L (increase of 10%).

2. Perianal disease

Perianal disease appeared initially in December 2007 presenting with small rectal bleeding, anal pain after defecation with secretion of the perianal region. She was treated by the surgeon who diagnosed perianal abscess and performed incision and drainage followed by antibiotic treatment (ciprofloxacin, metronidazole as an outpatient). In January 2008 the anal pain became severe and she was repeatedly treated surgically. Examination of the anal region detected bilateral intrasphincteric perianal abscess located in the anterior anal wall with thickened edges, very painful at palpation. Anuscopy showed short fistula (at 11 o'clock) which raised suspicion of Crohn's disease. Colonoscopy revealed thickening and ulceration of the rectum (8 cm) with mild proctitis. Histology of the affected region showed abundant mixed inflammatory infiltration with focal fibrosis and reduction of crypts. Despite of nonspecific histological proof (longstanding corticosteroid therapy of asthma) Crohn's disease could not be ruled-out. Radiology exams including pelvic MRI showed bilateral transsphincteric fistulas without abscess collections or signs of active luminal disease, except rectal inflammation.

A population-based study from the University of Manitoba, Canada, made in 2006, showed that patients with inflammatory bowel diseases (IBD) had a significantly higher prevalence for the following disorders: asthma, bronchitis, arthritis, multiple sclerosis, chronic renal disease, psoriasis and pericarditis ¹. The study included 8072 patients diagnosed with IBD over a 19-year period. Each of these patient was matched randomly with 10 members of the general population by age, gender and geographic location. Ulcerative colitis patients were 50 to 70%, and patients with Crohn's disease 30 to 40% more likely to have asthma than the general population. A potential genetic link between Crohn's disease and asthma has been searched. A gene called ORMDL3 on chromosome 17, known to be a risk factor for childhood asthma, could also be associated with Crohn's disease ².

Difficult-to-control asthma, severe asthma or resistant asthma is an illness that causes severe life threatening attacks, provokes frequent hospitalizations and requires corticosteroids prescriptions. Such patients have an increased risk of death, experience greater morbidity, have a reduced quality of life and often have adverse side effects from drug therapy. The following types of difficult-to-control asthma have been identified: fatal or near-fatal

asthma, brittle asthma types I and II, airway narrowing, aspirin-induced asthma, premenstrual asthma, adult-onset asthma.

In order to maintain asthma controlled, some patients need high doses of oral corticosteroids causing undesirable side effects. The following recommendations of anti-inflammatory or immune-suppressing treatment of asthma have been proposed:

1. *Azathioprine*: up to now there is little evidence to support its administration in chronic asthma treatment as a steroid-sparing agent (*evidence level B*).
2. *Cyclosporine*: the use of cyclosporine in chronic asthma has questionable clinical importance, and available evidence does not support its routine prescription for oral corticosteroids-dependent asthma treatment (*evidence level B*).
3. *Methotrexate*: the conclusions that were obtained from clinical trials were far too modest, a reduction of only 20% in steroid consumption can be obtained after three to six months of consumption, and only 60% of all cases show a significant response. This improvement is not enough to reduce significantly side effects and justify toxicity risk (*evidence level B*).
- 4 *anti TNF*: preliminary tests showed improvement in quality of life, but however, there is a marked heterogeneity in response to the treatment, which indicates that its advantages may be reserved for a small subgroup of patients [3](#).

There are few serious dilemmas with introducing immunosuppressive therapy in our patient with perianal Crohn's disease and difficult-to-control asthma. Currently there is a lack of clear evidence to support the use of azathioprine in the treatment of chronic asthma. The trial reviews of

methotrexate as a potential steroid-sparing agent in asthma, also useful for perianal disease, do not provide relief for asthma with adding its own adverse effects. The use of anti-TNF is also doubtful suggesting not to use these agents in patients with bronchial hypereactivity or asthma. Cyclosporine A in both diseases is of questionable clinical importance and available evidence does not support its prescription.

In conclusion, we have complex comorbidity in patient with difficult-to-control asthma and perianal Crohn's disease, significantly reducing therapeutic immunosuppressive options, which requires multidisciplinary team approach.

References

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