Case Report

Glucocorticoid-resistant Bronchial Asthma

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Introduction

Glucocorticoids have potent anti-inflammatory actions and are most effective agents in the treatment of bronchial asthma. However, a subset of asthmatic patients do not benefit from glucocorticoid therapy. Management of these patients with glucocorticoid resistant bronchial asthma presents unique challenges because of lack of effective and well-tolerated alternatives to steroids. Treatment should employ non-steroidal agents as required to control symptoms. Recent experience with other immunomodulatory agents such as cyclosporin, methotrexate and intravenous immunoglobulin has highlighted their potential as steroid-sparing agents. This paper presents one such difficult case. Relevant literature is briefly reviewed.

Case Report

A 45 year old male, known case of bronchial asthma for past 10 years, on regular bronchodilator therapy since then, presented with complaint of increased difficulty in breathing for past 2 years. Patient had been put on systemic steroids, along with other inhaled and oral bronchodilators since then and was on maintenance dose of Tab prednisolone 10mg/day for past 12 months without relief.

Clinical evaluation revealed middle-aged male with truncal obesity, blood pressure-140/100mm Hg, pulse-92/min, regular; respiratory rate-32/min with accessory muscles of respiration active. Patient was unable to complete sentences and his single breath count was 06. Chest examination revealed bilateral scattered rhonchi. His routine hematological and biochemical parameters were within normal limits.

Patient was initially managed with oxygen at 4L/min, systemic corticosteroids (Inj hydrocortisone 200mg IV stat and 100 mg IV 6 hourly), frequent (4 hourly) salbutamol nebulization, IV aminophylline infusion and ipratropium bromide 0.5 mg 6 hourly nebulization. Later, patient was switched over to asthalin and beclate inhalers, oral sustained-action theophylline and oral prednisolone. The patient failed to respond to a 14 day course of daily prednisolone (1 mg/kg/day) as measured by less than a 15% improvement in morning prebronchodilator FEV1 following the glucocorticoid course and was diagnosed as a case of glucocorticoid-resistant bronchial asthma. Patient was started on Tab methotrexate 10 mg weekly. During follow-up, over the next 16 weeks,

patient started showing improvement and his oral prednisolone was gradually tapered off. Presently patient is off steroids. He is on aerocort inhaler, sustained-action theophylline and methotrexate 10 mg weekly. For the first time in past 2 years, the patient, during review after 20 weeks, was without any wheeze and denied any symptoms. Single breath count was 14. Chest examination revealed occasional rhonchi in both lung fields. He is off steroids for past 1 month now. Patient is tolerating methotrexate therapy quite well without any adverse effects and is on regular monthly follow-up.

Discussion

The term “steroid resistant (SR) asthma” refers to a group of asthmatics that have persistent airway obstruction and immune activation despite treatment with high doses of systemic glucocorticoids. To make the diagnosis of SR asthma, the patient must fail to respond to a 7 to 14 day course of daily prednisolone as measured by less than a 15% improvement in morning prebronchodilator FEV1 following the glucocorticoid course [1]. There are at least two forms of SR asthma, i.e. primary and acquired types. Type I SR asthma is acquired and is associated with abnormally reduced glucocorticoid receptor (GCR) ligand and DNA binding affinity. Type II SR asthma appears to be due to a constitutive defect and is associated with low numbers of GCRs [2].

Before the diagnosis of a glucocorticoid resistant asthma is made, a number of other entities that may confound patient response to steroids must be excluded:

Medication noncompliance

Occult occupational asthma with ongoing antigenic exposure

Aspirin and NSAID sensitivity and exposure

ABPA

Unrecognized food allergy

Unsuspected gastroesophageal reflux

Irreversible airflow obstruction

Underlying systemic vasculitis

Paradoxical vocal cord motion

The management of the SR asthmatic is challenging, and every attempt should be made to maximize conventional therapy in these patients prior to embarking on alternative therapies as all of the alternative anti-inflammatory/immunomodulatory modalities are associated with significant toxicity or cost [3]. Second-generation inhaled glucocorticoid therapy, methotrexate, cyclosporine, IVIG, and leukotriene antagonists are potential alternative therapies. Some success has been achieved with conventional immunosuppressants such as methotrexate, gold, and cyclosporin A. Leukotriene receptor antagonists have proved a useful addition to asthma therapy and have been shown to have a modest steroid-sparing effect. Several new therapeutic agents have been developed to target specific components of the inflammatory process in asthma. These include IgE antibodies, cytokines, chemokines, and vascular adhesion molecules [4]. Similarly, preliminary studies of selective phosphodiesterase inhibitors in asthmatic individuals have been encouraging. Other potential therapies include platelet-activating factor receptor antagonists, tryptase inhibitors and prostaglandin E analogs [5]. The continued development of such targeted treatments should ensure a greater diversity of therapeutic options for the management of glucocorticoid resistant asthma in the new millennium.

The patient with SR asthma presents several challenges. These individuals often display many of the sequelae of long-term systemic glucocorticoid use while achieving little therapeutic benefit. Prior to making the diagnosis of SR asthma, diseases that can contribute to poor control of asthma must be ruled out, and

noncompliance issues addressed. Alternative asthma therapies are often used; however, they also carry the potential for adverse effects, and have not been thoroughly studied in this population of asthmatic patients. Over the years, number of systemic steroid-dependent asthma patients has come down significantly as more effective inhalational delivery methods (like dry powder inhalers) and effective inhaled steroids have been introduced. Cytotoxic agents and immune-modulators do play a significant role in reducing the need for steroids and symptom relief. Methotrexate 10 mg weekly has a modest steroid-sparing effect [6,7] and is usually well tolerated in this subset of patients.

References

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