

improvement in nasal symptoms (congestion and rhinorrhea, and, to a lesser extent, hyposmia); 2 months later she had also achieved better asthma control (no further need for rescue bronchodilator use and no asthma symptoms, leading to the withdrawal of inhaled corticosteroids and long-acting β_2 agonists, and a significant improvement of FEV₁ up to 90% of predicted). After 16 weeks of treatment with omalizumab, the Asthma Control Test score had risen from 11 to 25 points, and the asthma-related quality of life questionnaire (AQLQ) revealed a score of 6.8. Before starting the anti-IgE therapy, she had a severely impaired quality of life, with an AQLQ of 3.68 (>1.5 points improvement).

In September 2009, a specific bronchial challenge with lysine-acetylsalicylate yielded a negative result, and in October 2009, an oral challenge with aspirin with a cumulative dose of 750 mg was also negative. In the follow-up visit in December 2009, a certain degree of hyposmia persisted, despite continuous therapy with intranasal corticosteroids, and the methacholine test was still positive (PC₂₀, 1.84 mg/mL). The patient, however, had no asthma symptoms under treatment with montelukast and omalizumab only. She had also tolerated ibuprofen 600 mg perfectly on several occasions.

Omalizumab could prove effective in the treatment of AERD, as demonstrated by the experience of our patient, who not only succeeded in controlling the disease and significantly improving her quality of life but is also now capable of tolerating aspirin and other COX-1 inhibitors. Further studies are required in order to confirm the effectiveness of omalizumab in patients with AERD.

References

- Berges-Gimeno M, Simon RA, Stevenson DD. Treatment with aspirin desensitization in patients with aspirin exacerbated respiratory disease. *J Allergy Clin Immunol*. 2003;111:180-6.
- Incorvaia C, Mauro M, Riario-Sforza GG, Frati F, Tarantini F, Caserini M. Current and future applications of the anti-IgE antibody omalizumab. *Biologics* 2008;2:67-73.
- Güzelbey O, Magerl M, Zuberbier T, Maurer M, Metz M. Successful treatment of solar urticaria with anti-immunoglobulin E therapy. *Allergy* 2008;63:1563
- Kanu A, Patel K. Treatment of allergic bronchopulmonary aspergillosis (ABPA) in CF with anti-IgE antibody (omalizumab). *Pediatr Pulmonol*. 2009;44:516.
- Grundmann SA, Hemfort PB, Luger TA, Brehler R. Anti-IgE (omalizumab): A new therapeutic approach for chronic rhinosinusitis. *J Allergy Clin Immunol*. 2008;121:257-8
- M Guglielmo, C Gulotta, F Mancini, M Sacchi, F Tarantini. Recalcitrant Nasal Polyposis: Achievement of Total Remission Following Treatment with Omalizumab. *J Investig Allergol Clin Immunol*. 2009;19(2):158-66.

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Deflazacort: A Possible Alternative in Corticosteroid Allergy

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While cutaneous delayed-type hypersensitivity to topical corticosteroids is common, immediate reactions to systemic corticosteroids (SC) are rare, with little more than 100 cases reported [1-3]. Anaphylaxis and other types of immediate reaction to SCs (including urticaria, angioedema, and bronchospasm) have been described [4-6]. Hydrocortisone, prednisolone, and methylprednisolone are the agents most frequently implicated [1,7,8], although hypersensitivity to dexamethasone is exceedingly rare. Not only should the corticosteroid itself be considered potentially responsible, but its specific ester, and even the excipients (especially carboxymethylcellulose), should be also be taken into account [1,9].

We retrospectively studied all patients attending the drug allergy clinic at Coimbra University Hospitals in the last 10 years with an immediate reaction to SCs and positive skin test results. Clinical records were consulted to obtain information on concomitant medication, timing of administration, the reaction, and treatment. Skin prick tests (SPT) to parenteral dexamethasone, methylprednisolone, hydrocortisone, prednisolone, and latex had been performed using an undiluted formulation.

If the SPT results were negative, intradermal tests (IDT) to the same SC were performed in 10-fold increasing concentrations (0.002 mg/dL, 0.02 mg/dL, 0.2 mg/dL). Ten atopic volunteers (controls) also underwent the same skin tests. Specific immunoglobulin (Ig) E to methylprednisolone (PhadiaTM, Uppsala, Sweden) was determined in the most recent reactions (patients 3 and 6).

All patients gave their informed consent to undergo an oral challenge test with deflazacort (cumulative dose, 60 mg). Dexamethasone was also tested in patients 3 and 5.

Six patients (4 women/2 men, mean [SD] age 48.2 [13.6] y) were evaluated. All had been administered the suspect SC intravenously. All SPTs to latex were negative. The results are summarized in the Table.

All atopic controls had negative skin test results. Specific IgE to methylprednisolone was positive in patient 3 (1.6 kU_A/L). The challenge test with deflazacort was negative in all patients; the challenge test with dexamethasone was positive in patient 5.

Although the most frequent manifestations were cutaneous, life-threatening anaphylaxis with hypotension

Table. Population and Skin Test Results

Patient	Signs and Symptoms	SC Implicated	Time From Reaction to Skin Tests, y	Skin Tests				Associated Condition
				D	MP	H	P	
1	Bronchospasm	MP	6	SPT (-) IDT (-)	SPT (-) IDT (+) (0.002 mg/dL)	SPT (-) IDT (-)	SPT (-) IDT (ND)	Atopic asthma
2	Bronchospasm	P	13	SPT (-) IDT (ND)	SPT (-) IDT (-)	SPT (-) IDT (ND)	SPT (-) IDT (+) (0.002 mg/dL)	AERD
3	1st episode: U, AE, hypotension	H	2 months	SPT (-) IDT (-)	SPT (+) IDT (ND)	SPT (+)	SPT (+)	
4	1st episode: U 2nd episode: bronchospasm, anaphylactic shock	1st, MP 2nd, P	7	SPT (-) IDT (-)	SPT (-) IDT (+) (0.002 mg/dL)	SPT (-) IDT (+) (0.2 mg/dL)	SPT (-) IDT (ND)	AERD
5	Anaphylactic	MP	13	SPT (-) IDT (-)	SPT (-) IDT (+) (0.02 mg/dL)	SPT (-) IDT (-)	SPT (-) IDT (-)	Atopic asthma
6	Bronchospasm	P	3	SPT (-) IDT (-)	SPT (-) IDT (+) (0.2 mg/dL)	SPT (-) IDT (-)	SPT (-) IDT (-) (0.02 mg/dL)	Atopic asthma

Abbreviations: AE, angioedema; AERD, aspirin-exacerbated respiratory disease; D, dexamethasone; H, hydrocortisone; IDT, intradermal test; SC, systemic corticosteroid; MP, methylprednisolone; P, prednisolone; SPT, skin prick test; U, urticaria.

occur in 2 patients. Latex allergy and concomitant drug hypersensitivity were ruled out in all participants. In contrast to the results of previous reports [1,7], hypersensitivity attributed to hydrocortisone was rare, and both methylprednisolone and prednisolone were the most commonly implicated SCs in 3 out of 6 patients each. This may be related to the generalized use of these SCs in our hospital.

The literature associates intravenous administration with a higher frequency of hypersensitivity reaction [1]. Our results support this association, as the drugs were administered intravenously in all patients.

Consistent with the findings of other studies, the positive skin test results we observed point to an IgE-mediated reaction [1,3,8].

In our population, 3 out of 6 patients were sensitized to 2 or more corticosteroids, suggesting cross-reactivity. This has also been observed by some authors [2,8,10], but not by others [1].

Deflazacort was well tolerated in all cases, thus proving to be a viable alternative. Similar results have been reported elsewhere [8,10]. The results of skin tests to dexamethasone were negative, suggesting that it may be an appropriate parenteral option, although the result of challenge testing was positive in a patient with a negative skin test result.

Asthma and renal transplant have been identified as risk factors for hypersensitivity to SCs [7]. This is supported in our series, as 5 out of 6 patients were asthmatics.

In conclusion, although rare, immediate reactions to SCs

can be life-threatening. Both IgE-mediated and non-IgE-mediated mechanisms have to be considered, and skin tests can be a valuable ally in the workup. Cross-reactivity can occur between different corticosteroids. Finally, deflazacort seems to be a viable alternative in patients who experience hypersensitivity reaction to SCs.

References

- Venturini M, Lobera T, del Pozo MD, González I, Blasco A. Immediate hypersensitivity to corticosteroids. *J Invest Allergol Clin Immunol*. 2006;16:51-6.
- Burgdorff T, Venelmalm L, Vogt T, Landthaler M, Stolz W. IgE-mediated anaphylactic reaction induced by succinate ester of methylprednisolone. *Ann Allergy Asthma Immunol*. 2002;89:425-8.
- Karsh J, Yang WH. An anaphylactic reaction to intra-articular triamcinolone: a case report and review of the literature. *Ann Allergy Asthma Immunol*. 2003;90:254-8.
- Sams WM, Smith JG Jr. Contact dermatitis due to hydrocortisone ointment: report of a case of sensitivity to emulsifying agents in a hydrophilic ointment base. *J Am Med Assoc*. 1957;164:1212-3.
- Sheth A, Reddy S, Jackson R. Worsening of asthma with systemic corticosteroids: a case report and review of literature. *J Gen Intern Med*. 2006;21:C11-3.
- Partridge MR, Gibson GJ. Adverse bronchial reactions to

- intravenous hydrocortisone in two aspirin-sensitive asthmatic patients *Br Med J* 1978;1:1521-2.
7. Kamm GL, Hagemeyer KO. Allergic-type reactions to corticosteroids *Ann Pharmacother*. 1999;33:451-60.
 8. Rodrigues-Alves R, Spinola-Santos A, Pedro E, Branco-Ferreira M, Pereira-Barbosa M. Immediate hypersensitivity to corticosteroids: finding an alternative. *J Investig Allergol Clin Immunol*. 2007;17:277-85.
 9. Beaudouin E, Kanny G, Gueant JL, Moneret-Vautrin DA. Anaphylaxis caused by carboxymethylcellulose: report of 2 cases of shock from injectable corticoids *Allerg Immunol*. 1992;24:333-5.
 10. Ventura MT, Calogiuri GF, Matino MG, Dagnello M, Buquicchio R, Foti C, Di Corato R. Alternative glucocorticoids for use in cases of adverse reaction to systemic glucocorticoids: a study on 10 patients *Br J Dermatol*. 2003;148:139-41.

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Omalizumab in Severe Allergic Asthma: Efficacy Assessment by Comparison of Symptom Score and Peak Expiratory Flow Values Before and After Therapy

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The anti-immunoglobulin (Ig) E monoclonal antibody omalizumab (Xolair) has been proposed as an innovative pharmacological tool in the treatment of poorly controlled moderate to severe allergic asthma, which is characterized by frequent exacerbations, functional instability, and the need for high-dose inhaled corticosteroids, systemic corticosteroids, or both [1-3].

Management of severe asthma can benefit from both prospective and retrospective monitoring in order to control the disease and prevent exacerbations [4,5].

We developed a retrospective monitoring procedure

based on daily recording of the symptom score and of peak expiratory flow (PEF), which we routinely apply for as long as 10 months (or more, when necessary) in new patients with poorly controlled severe asthma. The valuable information we collect enables us to confirm our diagnosis and fine-tune therapy. The data recorded by patients at follow-up visits on monitoring cards are processed in real time by the graphic software Sigmaplot 1.0-11.0 (Systat, London, UK), which produces high-quality self-explanatory charts that can aid management-related rapid decision making through visual pattern recognition [5].

We describe our application of these monitoring techniques in patients with severe asthma treated with omalizumab (at the recommended individually tailored dose). The procedure has enabled us to assess the clinical and functional effects of omalizumab on asthma before and after treatment in a measurable and detailed manner (as in 4 of the 35 cases we are currently managing).

As an example of this concept, the Figure depicts the results for a 52-year-old male farmer sensitized to *Parietaria judaica* (a perennial allergen in Southern Italy), grass pollen, cypress pollen, and cat, and who had been receiving omalizumab from March 2007. Comparison of monitoring data collected from March 18 to April 16, 2005 (*P judaica* peak pollen season) with those from the same period in 2008 revealed a clear-cut decline in symptom scores: a constant score of 3 (maximum, 12) in 2005 compared with absence of symptoms in 2008. Moreover, PEF values stabilized and increased, with a mean (SD) morning value of 437 (16) L/min in 2005 vs 498 (12) L/min in 2008, and mean evening values of 428 (6) L/min and 493 (6) L/min, in 2005 and 2008, respectively. Both differences, which were analyzed using the *t* test for unpaired data, were statistically significant ($P < .0001$). The concomitant pharmacological treatment (inhaled budesonide 1200 µg tid, nedocromil sodium 4 mg tid, formoterol 12 µg bid, and montelukast 10 mg daily) remained unchanged over the 2 monitoring periods.

Similar results were obtained in the other cases we analyzed. A 65-year-old housewife had a mean morning PEF of 259 (9) L/min in 2005 compared with 308 (11) L/min in 2008 (monitoring period, April 1-30; $P < .0001$). A 49-year-old male police officer had an average morning PEF of 536 (18) L/min in 2005 compared with 591 (15) L/min in 2008 (monitoring period, April 15-May 14; $P < .0001$).

Analysis of monitoring data for a 67-year-old housewife during December 13-January 11 in 2004/2005 and 2008/2009 revealed a sharp reduction in PEF variability, from 26% to 8%, as assessed using the method of minimum morning prebronchodilator PEF over 1 week and expressed as a percentage of the recent best (Min%Max) [6].

We conclude that retrospective card-based monitoring of the symptom score and PEF followed by appropriate graphic rendering of the data collected is essential in the management of patients with poorly controlled severe asthma. This is particularly true when assessing the efficacy of novel therapeutic agents such as omalizumab. The effects of this treatment in individual patients can be appraised using visual pattern recognition after generation of high-quality charts and quantitative determination of changes in PEF values and PEF variability.