

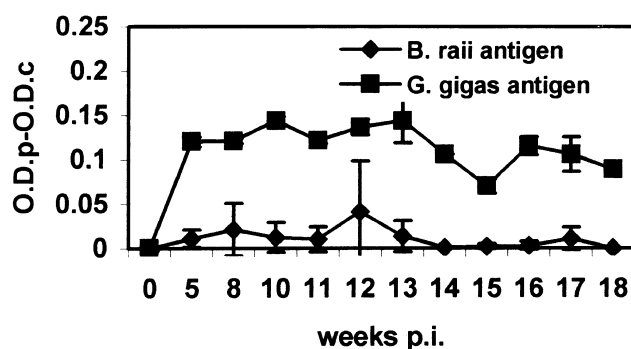


Figure 1. Dynamics of IgE production in BALB/c mice immunized with *G. gigas* extract against *B. raii* and *G. gigas* antigens. Results were expressed as ODp-ODc indexes by subtracting mean OD₄₉₀ of control from mean OD₄₉₀ of test sera once nonspecific reaction with BSA used in postcoating was subtracted. Standard errors are included.

and eight times greater than those observed with the negative control. Cross-reactions between both antigens were not observed. Activity against collagen has been demonstrated (4) in the *G. gigas* plerocercoid stage and is presumably involved in its penetration processes. Moreover, in experimental animals, extracts of cestodes induce symptoms that were mitigated by the administration of antihistaminic drugs (5).

Acknowledgment We thank Dr R. Pelta for his great interest in this topic.

*Departamento de Parasitología
Facultad de Farmacia
Universidad Complutense
28040-Madrid
Spain
Tel. 00 34 1 3941818
Fax: 00 34 1 3941815
E-mail: cuellarh@eucmax.sim.ucm.es

Accepted for publication 17 April 2000
Allergy 2000; 55:784–785
Copyright © Munksgaard 2000
ISSN 0105-4538

References

- MÖLLER H, ANDRES K. Diseases and parasites of marine fishes. Kiel: 1986.
- ENNA. Encuesta de Presupuestos Familiares 1990–91. Estudio Nacional de Nutrición y Alimentación 1991. Madrid: INI, 1995.

- RODERO M, CUÉLLAR C. Humoral immune responses induced by *Gymnorhynchus gigas* extracts in BALB/c mice. J Helminthol 1999;73:239–243.
- VÁZQUEZ C, DE ARMAS C, GIMÉNEZ C, RODRÍGUEZ F. Proteolytic activity of the *Gymnorhynchus gigas* plerocercoid: purification and properties of a collagenase from the crude extract. Parasitol Res 1999;85:64–70.
- MINNITI A, MICALI G, LANUZZA F, PANEBIANCO A. Determination of histamine in common sea fish parasites: *Anisakis simplex* and *Gymnorhynchus gigas*. Ital J Food Sci 1995;3:305–309.

Interleukins in Churg-Strauss syndrome

M. Kurosawa*, R. Nakagami, J. Morioka, H. Inamura, Y. Mizushima, N. Sugawara, T. Yamashita, T. Yokoseki, S. Kitamura, Y. Omura, M. Shibata, J. Chihara

Key words: Churg-Strauss syndrome; ECP; EDN; eosinophil; IgE; IL-4; IL-5; IL-13.

● CYTOKINE production was studied in patients with Churg-Strauss syndrome (CSS). However, as far as we know, no previous study has investigated the levels of IL-4 and IL-13 in CSS. A high level of serum eosinophil cationic protein (ECP) has been reported in a patient with CSS (1). Excretion of urinary eosinophil-derived neurotoxin (EDN) has been shown

to reflect ongoing *in vivo* eosinophil degranulation, and a high level of urinary EDN excretion was found in a patient with CSS (2).

This is the first report describing serial levels of plasma IL-4, IL-5, and IL-13; **IL-13 and EDN, but not IL-4, IL-5, or ECP, paralleled nonspecific inflammatory markers.**

serum ECP; and blood and urine EDN, in a 56-year-old female patient with CSS successfully treated by oral prednisolone, and showing that IL-13 and EDN levels, but not levels of either IL-4, IL-5, or ECP, paralleled nonspecific biologic inflammatory marker levels.

Blood and urine EDN was measured by an efficient ELISA method for EDN which we have developed very recently (3). Urinary EDN concentrations were expressed as μg per millimole of Cr ($\mu\text{g}/\text{mmolCr}$) to correct for urine volume. ECP in serum was determined by the Pharmacia ECP-RIA kit, and IL-4, IL-5, and IL-13 in plasma were measured by commercially available ELISA kits, respectively.

The laboratory data on 28 June 1999 showed a peripheral blood leukocyte count of 11 000/ μl with 40% eosinophils, an erythrocyte sedimentation rate of 96 mm/h, and a C-reactive protein level of 2.5 mg/dl. The total serum IgE level of 1 July was 929 IU/ml. The plasma IL-4 level was measurable (0.64 pg/ml) only on 28 June; however, the level stayed in the normal range throughout the clinical course. On the other hand, the levels of plasma IL-5 and IL-13, serum ECP, and blood and urine EDN were increased on 28 June (44.5 pg/ml of IL-5; 27.7 pg/ml of IL-13; 234 $\mu\text{g}/\text{ml}$ of ECP; and 725 ng/ml, 185 ng/ml, and 6010.9 $\mu\text{g}/\text{mmolCr}$ of EDN in serum, plasma, and urine, respectively) (Fig. 1). After the start of oral prednisolone therapy, eosinophilia and levels of plasma IL-5 and serum ECP were improved immediately. Total serum IgE and plasma IL-13 levels fell gradually, and the

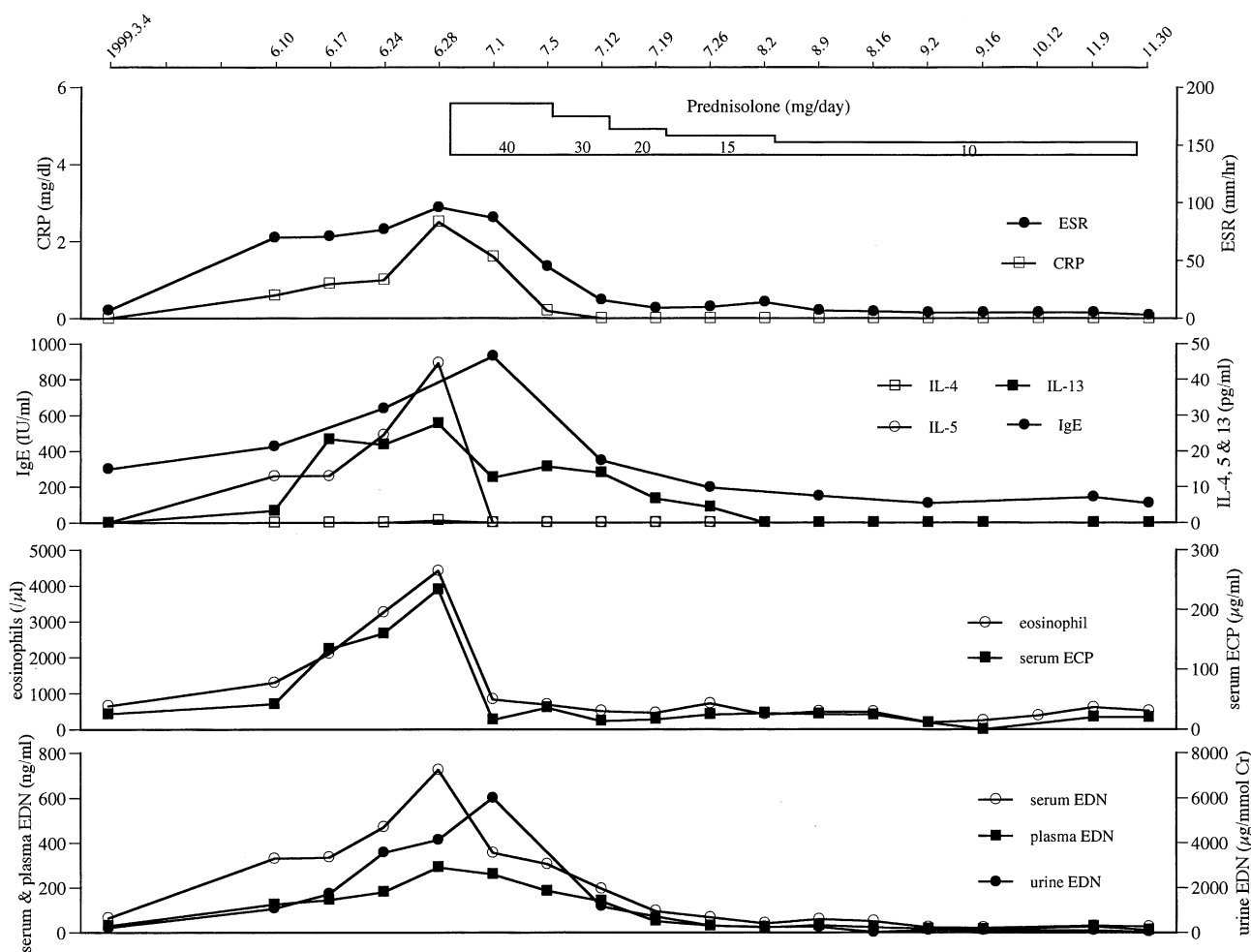


Figure 1. Changes of levels of plasma IL-4, IL-5, and IL-13; serum ECP; blood and urine EDN; and nonspecific inflammatory markers in patient with Churg-Strauss syndrome.

nonspecific inflammatory markers fell to normal ranges on 12 July. It took almost 2 months before EDN levels in serum, plasma, and urine fell to normal ranges. Afterward, the laboratory data were stable with 10 mg/day prednisolone therapy.

One of the new findings in this study is that the kinetics of decrease in EDN levels, especially urine EDN, was markedly delayed as compared with the dramatic drop in ECP. Different kinetics was also observed between the delayed decrease in the level of EDN and the peripheral blood eosinophil count, which rapidly dropped to a normal value after the beginning of corticosteroid treatment. Although Cottin et al. (2) reported this distinct kinetics for urine EDN and blood

eosinophil count in CSS, they did not measure the levels of serum ECP and plasma cytokines. The distinct kinetics between EDN levels, especially urine EDN, and peripheral blood eosinophils was interesting, and the explanation for a sustained release of EDN in the patient when she no longer had eosinophilia is not clear. The delayed decrease in EDN levels may simply reflect continued release of EDN by eosinophils that no longer circulated but may still have been present in tissues. Little is known about the kinetics and process of elimination of EDN after it has been released from eosinophils.

*Department of Clinical and Laboratory Medicine

Akita University School of Medicine
1-1-1 Hondo
Akita 010-8543
Japan
Tel. and Fax: +81-18-884-6181
E-mail: motohiro@hos.akita-u.ac.jp

Accepted for publication 14 April 2000
Allergy 2000; 55:785-787
Copyright © Munksgaard 2000
ISSN 0105-4538

References

- MORITA H, KIHARA T, TATSUMI Y, KITANO Y, SAGAMI S. Allergic granulomatosis and angiitis of Churg-Strauss. A case of high serum level of eosinophil cationic protein. *Acta Derm Venereol* 1992;72:201-202.

2. COTTIN V, TARDY F, GINDRE D, VERNET G, DEVILLER P, CORDIER JF. Urinary eosinophil-derived neurotoxin in Churg-Strauss syndrome. *J Allergy Clin Immunol* 1995;**96**:261–264.
3. MORIOKA J, KUROSAWA M, INAMURA H, et al. Development of a novel enzyme-linked immunosorbent assay for blood and urinary eosinophil-derived neurotoxin: a preliminary study in bronchial asthmatic patients. *Int Arch Allergy Immunol* 2000 (in press).

Selective hypersensitivity to piperacillin

A. Romano*, M. Di Fonso, M. Viola,
F. B. Adesi, A. Venuti

Key words: piperacillin; selective immediate hypersensitivity; skin tests.

● PIPERACILLIN is a highly effective bactericidal ureidopenicillin with a wide spectrum of activity. There have been very few reports of type-I allergies to this β -lactam antibiotic diagnosed mainly on the basis of skin-test positivity (1–3).

We studied a 54-year-old woman who had suffered acute bronchitis and had developed urticaria, angioedema, dyspnea, hoarseness, and syncope within 5 min of a 2-g intravenous injection of piperacillin. The symptoms resolved completely after treatment with epinephrine, betamethasone, and chlorphenamine.

Eight months later, we gave the patient skin tests with penicilloylpolylysine (Allergopen, Reinbek, Germany); minor determinant mixture (Allergopen); benzylpenicillin up to 10 000 IU/ml; and ampicillin, amoxicillin, and piperacillin at 1 and 20 mg/ml, as well as ceftriaxone, cefuroxime, cephalothin, ceftazidime, and cefamandole at 2 mg/ml (all diluted in normal saline), as previously described (4).

Intradermal piperacillin at 1 mg/ml produced a maximum wheal diameter of 13 mm. Prick and intradermal histamine tests produced wheals with maximum diameters of 7 and 12 mm, respectively. No other reactions were observed.

Intradermal tests with the above cephalosporins and piperacillin were negative in 40 healthy control subjects, eight of whom had previously tolerated piperacillin. Assays (UniCAP[®] specific IgE; Pharmacia & Upjohn, Uppsala, Sweden) for specific IgE to penicilloyl G, penicilloyl V, ampicilloyl, amoxicilloyl, cefaclor, and piperacillin were negative (<0.35 kU/l). The piperacillin assay was an experimental prototype.

Single-blind, placebo-controlled oral challenges with penicillin V (1 000 000 IU), ampicillin (1 g), and cefaclor (500 mg) were also performed (each on a different day). Increasing amounts (0.01, 0.1, and 1.0) of the therapeutic doses, indicated in parentheses, were administered at 1-h intervals with negative results.

Our clinical findings and intradermal-test positivity to piperacillin lead us to believe that the patient may have developed a type-I hypersensitivity reaction. RAST negativity may be explained by the fact that we used an experimental prototype and performed our assays 8 months after the anaphylactic shock. Meanwhile, the IgE titer may have fallen below the cutoff value, as observed with penicilloyl IgE antibodies (5).

To our knowledge, there have been only two reported cases, published as an abstract, of selective immediate hypersensitivity to piperacillin diagnosed on the basis of skin-test positivity (2). These subjects were assessed with piperacillin and penicillin determinants and challenged only with penicillin V. The present subject displayed skin-test and RAST negativity to penicillin as well as to other β -lactams, including ampicillin, that were subsequently tolerated. The patient's sensitization could therefore have been to piperacillin side-chain

determinants. Since the latter determinants distinguish the different penicillins, cross-reactions among these antibiotics do not generally occur when antibodies recognize mainly side-chain groups (6).

Suspect penicillins should be used in diagnosis, because allergic reactions to them may not be detected by tests performed only with penicillin determinants in cases where side-chains are important in sensitization.

*Unità di Allergologia
Complesso Integrato Columbus
Via G. Moscati, 31
00168 Rome
Italy
Tel. +39 06 3503782
Fax: +39 06 3503653
E-mail: columbus.allerg@linet.it

Accepted for publication 3 April 2000
Allergy 2000; 55:787
Copyright © Munksgaard 2000
ISSN 0105-4538

References

1. MOSS RB, BABIN S, HSU YP, et al. Allergy to semisynthetic penicillins in cystic fibrosis. *J Pediatr* 1984;**104**:460–466.
2. ANTONICELLI L, GARRITANI MS, BILÒ MB, et al. Allergy to piperacillin [Abstract]. *Schweiz Med Wochenschr* 1991;**121** Suppl 40/II:86.
3. MOSCATO G, GALDI E, SCIBILIA J, et al. Occupational asthma, rhinitis and urticaria due to piperacillin sodium in a pharmaceutical worker. *Eur Respir J* 1995;**8**:467–469.
4. ROMANO A, QUARATINO D, VENEMALM L, et al. A case of IgE-mediated hypersensitivity to ceftriaxone. *J Allergy Clin Immunol* 1999;**104**:1113–1114.
5. ADKINSON NF Jr. Risk factors for drug allergy. *J Allergy Clin Immunol* 1984;**74**:567–572.
6. BALDO BA. Penicillins and cephalosporins as allergens – structural aspects of recognition and cross-reactions. *Clin Exp Allergy* 1999;**29**:744–749.