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Hypogammaglobulinemia resembling BOOP

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Key words: bronchiolitis; common variable immunodeficiency; hypogammaglobulinemia.

• A 38-YEAR-OLD woman, a smoker, was referred in January 1995 after a 3-week episode of pain in the left hemithorax, fever, coughing, and hemoptysic expectoration. She had been treated on different antibiotic regimens, with prompt recurrence of the symptoms after withdrawal.

Repeated respiratory infections similar to bronchiolitis with organizing pneumonia (BOOP).

The patient's weight was 70 kg, and her height 161 cm. Pulmonary auscultation showed rales and disperse wheezing. Physical examination was otherwise normal.

Laboratory findings were as follows: erythrocytes 4 680 000/mm^3, hemoglobin 13.9 g/dl, hematocrit 41.9%, white cells 13 900 mm^3 (normal differential count), platelets 256 000/mm^3, and ESR 13 mm.

The tuberculin test and sputum bacilloscopy were negative.

Thorax radiography showed infiltration of the left pulmonary base. Bronchoscopy was normal. Tumoral cytology and mycobacteria culture were negative.

Subsequently, the patient suffered a new episode of coughing and expectoration, with infiltration in the left pulmonary base, which resolved after treatment with erythromycin. Throughout that year, she complained of recurrent, irritative coughing.

From February 1997 to September 1997, she was symptom-free. At that time, there was a recurrence of intensive coughing, expectoration, febricula, and pain at the right scapula. A chest radiograph revealed alveolar infiltration in the upper right lobe that persisted for 12 months, suggesting a diagnosis of bronchiolitis wih organizing pneumonia (BOOP). Bronchoscopy resulted in no pathologic findings, and again bacilloscopy and tumoral cytology were negative; a transbronchial biopsy was not carried out for technical reasons. Given the persistence of the symptoms and the radiographic findings in spite of therapy with different antibiotics, we began treatment with oral steroids, and the coughing and fever disappeared, without change in lung image, but the symptoms reappeared soon after the treatment was stopped.

In February 1998, new complementary examinations were carried out with the following results:

- IgG 30 mg/dl, IgA 0.8 mg/dl, IgM 361 mg/dl, IgE 1 UI/ml; light chains, NBT test, and complement: normal levels
- isohemagglutinins (blood group O, Rh+): anti-A 1/4, anti-B: undetectable
- iymphocyte subpopulations: CD3+ 66%, CD19 30%, CD3+ CD4+ 25%, CD3+ CD8+ 37% (CD4/CD8 0.67), CD4+ CD45RA+ 2%, CD4+ CD45RO+ 19%, CD3+ CD57+ CD56-21%, CD8+ CD57+ 19%, CD8+ CD28-28%
- lymphocyte transformation test with phytohemagglutinin and concanavalin A: normal levels
- expression of CD40L: 27% of CD4 lymphocytes.

Immunoglobulin levels in the patient's family were normal.

In February 1998, therapy with IV nonspecific gamma globulin was begun. Afterward, the patient suffered no new infectious episodes. The coughing, expectoration, and fever disappeared as well, and steroids could be withdrawn. The radiographic image cleared progressively.

We report a patient with immunodeficiency, suffering from repeated respiratory infections. These are typical in her disorder, but, in our patient, two peculiarities were present:

1) At various stages of evolution, the patient had signs and symptoms consistent with BOOP.
2) Hypogammaglobulinemia was present, but IgM levels were high.

Differential diagnosis would include labeling the disease as one of the entities in the WHO humoral immunodeficiencies classification (1). Except for hypogammaglobulinemia with hyper-IgM syndrome, and common variable immunodeficiency (CVI), the other entities are easily excluded given the age of onset, the absence of family history, and the laboratory data. The gamma globulin levels, with a marked decrease of all isotypes except IgM, indicate the former disorder. The marker for this disease – in the X-linked forms – is the absence of the CD40 ligand in the T cells. However, our patient is female; non-X-linked hyper-IgM syndromes have CD40 ligand expressed on activated helper T cells, as was the case in our patient. We believe, however, that our case falls within the CVI syndrome, given the absence of family history, the age at which the symptoms began, and the presence of several of the immunologic irregularities described in these patients: reduction in the CD4/CD8 ratio (2), increase of CD8

suppressr T cells (2), reduction of CD4+ CD45RA+ T cells (1), decreased CD40 ligand expression (1), increase of CD8+ CD57+ lymphocytes (2), and increase of CD8+ CD28– lymphocytes (3).

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Hypersensitivity reaction to ioversol

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Key words: drug-induced anaphylaxis; IgE-mediated hypersensitivity; ioversol; radiographic contrast medium.

• Ioversol is a monomeric, noniodinated radiographic contrast medium. It has three iodine atoms and six hydroxyl groups, but no carboxyl groups. The first monomeric, noniodinated contrast medium known was metrizamide. Second-generation monomeric, noniodinated contrast media (iopamide, ioversol, and iohexol) have intermediate viscosity and osmotoxicity; therefore, the incidence of adverse effects from them is low (1).

Adverse reactions occur in about 5% of contrast media examinations. The incidence of mild reactions (flushing, nausea, and headache) is high. More severe side-effects, such as asthma or anaphylactoid reactions, are rare, but the problems are serious enough to be of concern (2). Side-effects induced by contrast media have a complex etiology, and several pathogenic mechanisms have been suggested. Immunologic mechanisms have been proposed by some authors (3).

A positive skin prick test suggested an IgE-mediated mechanism.

We report the case of a 44-year-old woman who had suffered an adverse reaction to ioversol 4 months before. This patient underwent intravenous urography with ioversol; she immediately developed nausea, vomiting, dizziness, hypotension (80/40 mmHg), widespread pruriginous erythema, lip angioedema, and shortness of breath. She received 6-methyl-prednisolone (60 mg intravenous), dexclorpheniramine (10 mg intramuscular), and epinephrine (0.3 mg subcutaneous). Her symptoms subsided in 4 h.

After the patient gave written consent, an allergy study was carried out. Skin prick tests were performed with sodium and meglumine amidetrizoate (Urografin 76%; 20 ml; Schering AG, Germany), iopromide (Clarograf 300; 100 ml, iopromide DCI 623 mg/ml), and iodinated polyvinylpyrrolidone (Betadine 7.5% and 10% solutions; 100 ml, Asta Médica, Spain). The results of all of them were negative in our patient. We then performed a skin prick test with ioversol (Optiray 320; 100 ml; ioversol DCI 678 mg/ml, Mallinckrodt Medical, Spain), and we obtained a positive result (wheal of 8×8 mm with pruritus and erythema). Skin prick tests with ioversol were also performed in 50 control subjects (25 of whom were atopic subjects), with negative results. Positive (histamine; 10 mg/ml) and negative (saline serum 0.9%) controls were also carried out. Serum total IgE was 231 kU/l. The histamine-release test with ioversol was negative. To develop this test, we used the automated fluorometric method described by Siraganian (4) and Hook, with the Technicon Autoanalyzer II.

We present a patient who developed anaphylactic shock caused by ioversol. The symptoms suffered by the patient, the latency of the reaction, and the positivity of the skin prick test with ioversol strongly suggest an underlying type-I, IgE-mediated hypersensitivity mechanism. *In vitro* tests have a high potential utility in the diagnosis of adverse reactions to drugs. However, their sensitivity is low; the value of the *in vitro* histamine release for the diagnosis of drug-induced anaphylaxis appears to be poor. Therefore, this test is scarcely used for the diagnosis of drug allergy (5).

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