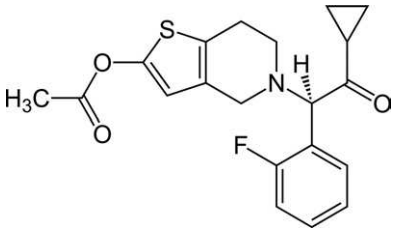

Figure 1. Structure of clopidogrel and prasugrel. Both structures share the thiophene and pyridine ring.

thought it was in our patient's best interest given his previous reaction and the possibility of cross-reactivity.

Clopidogrel is a medication used by many patients for conditions ranging from cardiac to neurologic disease, and given the incidence of hypersensitivity to clopidogrel, more investigation is necessary.

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MACROGOL HYPERSENSITIVITY IN MULTIPLE DRUG ALLERGY

Polyethylene glycols (macrogols) are condensation products of glycols with ethylene oxide and are widely used as excipients in food, cosmetics, and topical and systemic drugs because of their stabilizing properties. Although macrogols are used frequently and extensively, only a few immediate hypersensitivity reactions have been reported, probably because they are poorly absorbed by the gastrointestinal tract. Immediate hypersensitivity reactions have been reported after parenteral and oral administration of products containing macrogols, such as corticosteroids,[1,2] laxative oral solutions,[3] and tablets.[4,5] We report the first case, to our knowledge, of a positive basophil activation test result after exposure to macrogol in a patient who reported systemic reactions after the oral intake of 2 different drugs in 2 different pharmaceutical preparations (granules and syrup) containing macrogols 4,000 and 6,000.

A 46-year-old man, without a previous history of allergy, was referred to our outpatient clinic for suspected drug reactions. He reported mild urticaria and mouth itching a few minutes after the intake of nimesulide granules (Nimesulide DOC, containing macrogol 4,000; DOC Generici, Milan, Italy). A few months later, after 1 dose of paracetamol syrup (Tachipirina, containing macrogol 6,000; Angelini Farmaceutica, S.A., Barcelona, Spain), he rapidly developed generalized urticaria, face and neck angioedema, and dyspnea, requiring medical assistance in an emergency department, where he recovered after antihistamine and intravenous methylprednisolone. Metamizole, ibuprofen, and acetylsalicylic acid (without macrogol) were well tolerated after these episodes. He also reported skin erythema using some types of bath soap and shaving cream. Standard patch test series (ALK-Abelló, Madrid, Spain), a shaving cream series (cetyl alcohol, stearyl alcohol, cinnamic alcohol, camphor, menthol, sorbitan monolaurate, triethanolamine), and polyethylene glycol patch (F.I.R.M.A., Muggiò, Italy) tests were performed, resulting in positive results for thimerosal, balsam of Peru, and menthol. A prick test with paracetamol syrup 1:1 gave a positive reaction with a wheal that increased in size up to 30 mm in diameter after 30 minutes, when he developed face and neck erythema and a mild throat closure feeling, at which point he was treated with ebastine (20 mg) and methylprednisolone (40 mg) with rapid resolution of symptoms. One month later, skin prick tests with injectable paracetamol (Perfalgan; Bristol-Myers Squibb, New York, New York), which does not contain any macrogol, from 1/10,000 to 1/1 were performed, with negative results. The graduated oral challenge with paracetamol tablets was tolerated up to a cumulative dose of 1 g. Specific ethylene oxide IgE (ImmunoCAP; Phadia, Uppsala, Sweden) test results were negative. Afterward, a skin prick test with macrogol 400 (100 mg/mL starting from 1/10,000 to 1/1) was performed with negative results, whereas skin prick test results with macrogol 4,000 and 6,000 (100 mg/mL at 1/10,000 dilution) were positive (wheal diameter, 6 mm). The results of skin prick tests with paracetamol syrup and macrogols 400, 4,000, and 6,000 were negative in 10 nonatopic controls. The CD203 basophil activation test result was positive for macrogol 4,000 and 6,000 at a 1:100,000 dilution and negative for macrogol 400 for all the tested dilutions

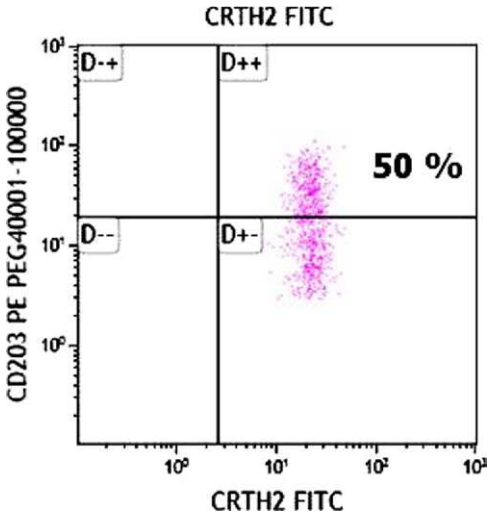

Figure 1. Basophil activation test shows a positive result for macrogol 4,000.

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(Figure 1), in agreement with the cutaneous test results. Low-molecular-weight (200-700) macrogols are liquid and have been reported to cause contact dermatitis or contact urticaria. High-molecular-weight (1,000-7,500) macrogols are solid and, although generally poorly absorbed (approximately 0.2%) by the gastrointestinal tract, have been implicated in some cases of anaphylaxis. A peculiar case of anaphylaxis after oral drug intake and of contact urticaria due to polyethylene glycols of high and low molecular weight, respectively, has been reported.[5]

The systemic reactions reported by our patient seem to be IgE dependent. Positive skin prick test results and a positive basophil activation test result for macrogols 4,000 and 6,000, along with the positive skin prick test result for paracetamol syrup (containing macrogol 6,000), suggest a type 1 reaction. The patient was advised to systematically check drugs and products potentially containing macrogol, including cosmetics and conserved foods. Allergy to excipients should be considered, particularly in cases of multiple allergic reactions to multiple drugs. We suspect that allergic reactions to macrogols may be underreported.

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HISTOPLASMOSIS IN THE OLECRANON BURSA OF A PATIENT WITH IDIOPATHIC CD4 LYMPHOCYTOPENIA

Idiopathic CD4 lymphocytopenia (ICL) is a rare, non–human immunodeficiency virus (HIV)–related syndrome with a decrease in absolute CD4 T-lymphocyte counts to less than 300/mm^3 or less than 20% of total T cells on more than 2 occasions at least 6 weeks apart. It was first defined in 1992 and later summarized in an updated review in the *New England Journal of Medicine* in 1993.[1] The absence of any other primary or secondary immunodeficiency causing a low CD4 T-cell count is also a requirement for diagnosis. This heterogeneous syndrome is most likely due to genetics and unrelated to HIV-1, HIV-2, human T-lymphotrophic virus, or other transmissible agents. It typically presents in adulthood, appears to have no sex predilection, and may be associated with autoimmunity. The pathogenesis of this syndrome is a decrease in the generation of T-cell precursors, abnormal T-cell apoptosis, biochemical failure of CD3 T-cell receptor, and defective cytokine production causing depressed T-cell immunity.[2] It can be differentiated from HIV based on the slow rate of decrease in CD4 cell counts and the lack of a compensatory increase in CD8 cell counts and immunoglobulin. Although clinical findings depend on the degree of immune suppression, these patients are often predisposed to opportunistic infections. A cohort study of 47 ICL patients showed that pulmonary and extrapulmonary cryptococcal, mycobacterial, pneumocystis, candidal, and cytomegaloviral infections were commonly seen in these individuals.[3] Cryptococcal meningitis is one of the most commonly described infections in the literature, but rare cases of progressive multifocal leukoencephalopathy and lymphoproliferative diseases have been reported.[1,3-5] Patients with ICL are also susceptible to fungal infections with *Histoplasma capsulatum.*[5]

Histoplasma capsulatum, a dimorphic fungus endemic to the tropics and the Ohio Mississippi River Valley areas of North America, is commonly implicated for its pulmonary involvement. T-cell immunity plays a predominant role in recovery from histoplasmosis. Primary histoplasmosis can cause immunologically mediated aseptic inflammatory arthritis, erythema nodosum, arthralgias, and cutaneous granulomas in individuals with altered T-cell–mediated immunity.[6,7] Primary cutaneous histoplasmosis manifests as papules, pustules, plaques, wartlike lesions, or granulomas. Cutaneous lesions, although extremely rare, occur in up to 17% of patients with disseminated histoplasmosis and in the immunocompetent population in endemic areas.[7]] Immunocompromised patients with a low CD4 cell count are more susceptible to disseminated and cutaneous histoplasmosis.[5,8] We present a unique case of histoplasmosis in the olecranon bursa of an individual with idiopathic CD4 lymphocytopenia.

A 34-year-old, heterosexual man with idiopathic CD4 lymphocytopenia had been receiving prophylactic trimethoprim-sulfamethoxazole, 800 mg twice a week, for his immunodeficiency. An evaluation at the time of diagnosis showed a CD4 cell count of 233/mm^3 and a CD4:CD8 ratio of 0.40. The most recent CD4 cell count and CD4/:CD8 ratio were 274/mm^3 and 0.30, respectively. The results of serologic testing and polymerase chain reaction for HIV-1 and HIV-2 were negative, and the patient was free of immunosuppressant therapy. The patient had a history of cryptococcal pneumonia and cutaneous histoplasmosis on the forehead and the proximal aspect of the thigh, which had both been treated in the past. He then presented with a posterior left elbow mass with numbness in the fourth and fifth digits of the left hand accompanied with significant weight loss. The initial magnetic resonance image was consistent with the physical and clinical assessment. The interpretation suggested nonspecific edema in the subcutaneous tissue and swelling overlying the olecranon process, confirming olecranon bursitis (image not shown). This fluctuant mass had gradually enlarged to approximately 5 cm in length and 4 cm in width during a period of 8 months with associated erythema and tenderness of the surrounding soft tissue (Fig 1A and B). The results of a *Histoplasma* urine antigen test to detect disseminated histoplasmosis were negative. Subsequent magnetic resonance imaging showed more prominent tissue changes with an interval enlargement of the previously noted lesion posterior to the olecranon process. The lesion was heterogeneous in appearance with nodular and peripheral enhancement (Fig 1C and D). Given the patient's history of immunosuppression, atypical infections or neoplasms such as Kaposi sarcoma

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