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Adverse reaction to dextromethorphan

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Key words: adverse reaction; dextromethorphan; opiates.

Dextromethorphan is a nonrespiratory depressant opiate derivative used alone or in combination with other compounds as symptomatic treatment of cough and its efficacy is similar to that of codeine (1).

A 24-year-old woman presented at our outpatient clinic for a sensation of bolus in the throat with swallowing difficulty, erythema and hives with audible whistling immediately after the first dose of Romilar® (dextromethorphan hydrobromide), which was resolved after treatment with corticosteroids and antihistaminic agents. She had taken Algidol® (paracetamol and codeine) half an hour before the onset of the symptoms. She had previously tolerated Romilar, paracetamol and codeine without any problems.

An allergy study by prick test with Romilar (dextromethorphan) was positive. A skin prick test (SPT) with Romilar

was also performed in 10 controls, being positive in three of them.

The SPT with paracetamol and codeine was negative. Oral challenge with paracetamol and codeine was well tolerated. Oral challenge was also performed with another opioid agonist, tramadol, which was well tolerated.

After challenge with dextromethorphan (0.5 ml of the Romilar syrup solution), the patient immediately developed four hive lesions on her back that was resolved after antihistaminic treatment.

Given that the results of the challenge test were doubtful because it was not possible to disguise the taste of the preparation and as the adverse reaction was not severe and the patient requested this drug to control her symptoms, we decided to repeat the challenge test.

In the first place, a placebo having identical taste as Romilar was administered and was well tolerated. Then dextromethorphan was administered and after 0.5 ml of the solution, the patient developed generalized erythema with generalized pruritus and decreased blood pressure. Prompt treatment with adrenaline, steroids and antihistamines relieved the symptoms.

Dextromethorphan is used as an antitussive drug with the same efficacy as codeine but with less subjective or gastrointestinal abnormalities. Unlike other opiates, it has no analgesic power. Its toxicity is low and adverse reactions are rare, the most common being those that affect the central nervous system or psychiatric disorders; rash or urticaria type manifestations and anaphylaxis are totally rare (1).

We have not found any reports of allergic reaction to dextromethorphan with positive skin test. There is one case of anaphylaxis (2) due to dextromethorphan in which no skin test was performed and one case of fixed drug eruption with positive oral challenge but with negative epicutaneous test (3).

Opiate derivatives are nonspecific histamine releasers and induce nonallergic drug hypersensitivity (4).

In our case, it is interesting that the patient has tolerated codeine and tramadol, also nonspecific histamine releasers. Because of this, as well as the positivity of the prick and the rareness of reactions of

this type in spite of the wide use of the drug, a mechanism of IgE-mediated drug allergy cannot be ruled out (4).

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Exposure to methyl methacrylate and hypersensitivity pneumonitis in dental technicians

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Key words: dental technician; hypersensitivity pneumonitis; methyl methacrylate.

We report two cases of dental technicians with a diagnosis of hypersensitivity pneumonitis because of inhalation of methyl methacrylate (MMA), occur-

These observations demonstrate the risk of the development of not only pneumoconiosis or asthma, but also an hypersensitivity pneumonitis to MMA.

ring within the first weeks of exposure to MMA.

When polishing and grinding prosthesis, dental technicians are exposed to mineral dusts and chemicals. Pneumoconiosis, asthma and hypersensitivity pneumonitis (HP) have been described, linked to silica, silicon carbide, asbestos or metals (1). Methyl methacrylate (MMA) is a monomer, commonly used in dental clinics. Previously, MMA has been shown responsible for occupational asthma, rhinoconjunctivitis, contact dermatitis or stomatitis (2, 3). We report two cases of HP induced by an exposure to MMA in students working in a dental laboratory.

Case 1. A 24-year-old female, with no medical history, was admitted for progressive severe dyspnoea and cough for 3 weeks. She had been exposed to MMA during her dental technician training in the laboratory, which had started 6 months ago. Physical examination revealed diffuse bilateral crackles. Biological results showed hypoxemia (55 mmHg). Pulmonary function tests (PFT) revealed a major diffusion alteration (45% of predicted value). Computed tomography (CT) showed a ground glass pattern (Fig. 1). An occupational HP to MMA was suspected. The patient improved in a few days under systemic corticosteroids treatment. One month later, 3 days after her return in the laboratory, she was hospitalized again for a severe dyspnoea, which reappeared the first day of re-exposure. CT-scan showed ground glass pattern again. Bronchoalveolar lavage (BAL) found a cell count of

570 000 cells/ml (10% macrophages, 60% lymphocytes, 25% neutrophils). Hypoxemia was 58 mmHg. PFT found a forced vital capacity (FVC) of 2.0l (50%) and a forced expiratory volume in 1 s (FEV1) of 0.85l (24%). Again, the patient rapidly recovered after a short oral corticosteroid therapy, and decided to definitely quit her job.

Case 2. A 20-year-old female was hospitalised for acute respiratory distress. She trained as dental technician for a few weeks. Physical examination revealed major dyspnoea associated with cough, and diffuse bilateral crackles. Blood analysis indicated hypoxemia (65 mmHg). PFT revealed a restrictive pattern (total lung capacity at 67% of predicted value) and pulmonary diffusion alteration. Chest X-ray showed diffuse and bilateral condensations associated with ground-glass attenuation zones. Occupational HP to MMA was suspected. A favourable outcome was slowly obtained under oral corticosteroid treatment and occupational eviction. Two months later, she was exposed, under medical care, to aerolized particles of MMA in a glass cage to confirm the diagnosis. Moderate dyspnoea was observed. BAL and PFT performed after the provocation test showed abnormalities compared with normal values obtained just before the test: increase of lymphocytes, 30% of total cell count, and decrease of carbon monoxide transfer coefficient (TLCO) (-20%).

We described two cases of HP related to MMA exposure occurring in dental

technician students, and confirmed after re-exposure. Dental technicians are exposed to many mineral particles or acrylic dusts potentially involved in pneumoconiosis (asbestos, silica, chromium, etc.) (4), asthma (nickel, palladium, cobalt, acrylic resin) (1, 2) and/or HP (cobalt, beryllium) (2, 4), chronic obstructive pulmonary disease (COPD), lung cancer and fibrosis (5). The diagnosis of HP deserves to be considered in so far as exposure to MMA was responsible for clinical symptoms and resulted in biological, chest X-ray and PFT abnormalities consistent with HP (6). Differential diagnosis (infection...) were first eliminated. Duration of exposure allowed to exclude pneumoconiosis to mineral or metal particles. The exposure to the causative antigen (i.e. MMA) may result in acute, subacute, and chronic forms of HP. An acute episode usually follows a previous sensitization, as illustrated in case 1, and the intensity of the reaction (alveolitis) is related to the amount of inhaled antigen and the duration of exposure (7). The provocation tests with MMA alone reproduced the characteristic features of HP, suggesting the diagnosis of HP by inhalation of MMA rather than by other mineral particles also used in the laboratory.

MMA is an acrylic resin used for its resistance and lightness. Resins are reconstituted by mixture of powder (polymeric form of MMA) and liquid (monomeric form of MMA) for the preparation of prosthesis. Inhalation of the powder, or of the vapour produced

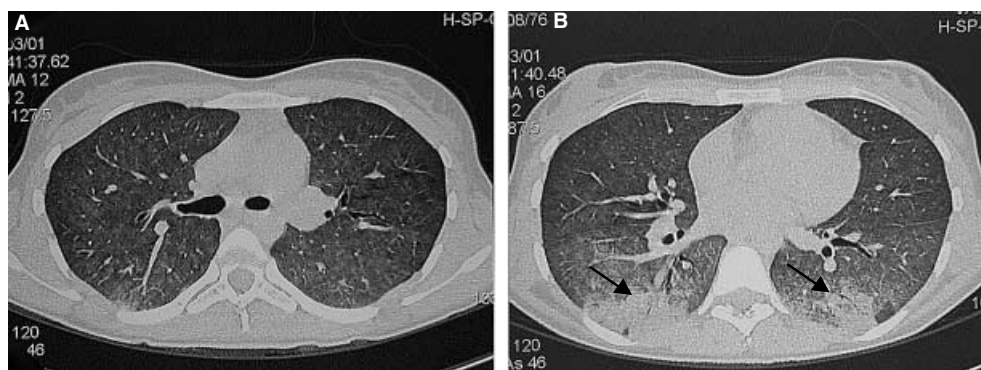


Figure 1. Chest HRCT scan obtained in a 24-year-old female presenting with progressive worsening of dyspnoea (case 1): at the level of the upper lobes: presence of ground glass opacities diffusely distributed throughout both lungs (A); at the level of the lower lobes: note the concurrent presence of ground glass opacities in the anterior parts of the lungs and areas of airspace consolidation in the right and left lower lobes, sparing a few secondary pulmonary lobules (B) (arrows).

by the volatile monomeric form during mixing is the first situation potentially dangerous for dental technicians. The second situation is linked to the environmental liberation of the polymeric form when polishing the solid plastic. Barrett (5) described the first case of interstitial lung disease related to an exposure to aerolized acrylic polymer of methacrylate in a dental student.

Even if this case was described as a pneumoconiosis, it showed usual characteristics of HP, and as in our two patients, clinical symptoms appeared within the first year of exposition to MMA during dental training. Confirming Barrett's case (5), the present two cases showed that MMA is potentially responsible for hypersensitivity pneumonitis. These data underlined the need for dental staff exposed to this substance to avoid direct contact with MMA, and to profit by adequate technical prevention measures, such as masks and local exhaust ventilation systems (8).

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Non-right-handedness and asthma

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Key words: asthma; adults; left-handedness; hormones.

This preliminary study aimed to estimate the evolution of asthma from adolescence to adulthood in a subgroup of left-handed and ambidextrous individuals with asthma.

All the 274 students of the Faculty of Health Science of the Technical Education Institute in Larissa, aged 18–35 years were enrolled in the study. A total of 268 questionnaires were completed. An adapted version of the ECRHS questionnaire was used for the assessment of asthma (1). Left-handedness was examined by the Edinburgh Handedness Inventory. The score ranges from –100 for extreme left-handedness to +100 for extreme right-handedness. The criterion of $LQ \leq 60$ was used to indicate non-right-handedness (2).

The data were examined using contingency tables and the Fisher's exact probability test, which is suitable for small numbers of observations (3).

Female : male ratio in the sample of the 268 students was 239 : 29. The mean age of the students was 21 years. Twenty-nine women reported an asthma diagnosis. Non-right-handedness was traced in six women (aged 19–20 years) among the 29 asthmatic individuals. LQ range was between –80 and 50. None of these six non-right-handed women reported asthma symptoms after 18 years of age and they were all free of symptoms for at least the past 2 years. On the contrary, 13 of the 23 right-handed women reported persistence of asthma symptoms after 18 years of age. A statistically significant difference was established between the two groups of right- and non-right-handed women (see Table 1).

Non-right-handedness has been associated with immune and allergic diseases, including asthma (4). Testosterone or some other substances, which are thought to be responsible for left-handedness may have a crucial effect in the development of asthma even since fetal life (4). Non-right-handed asthmatic children may represent a subgroup with special pathophysiological features and a different prognosis (5, 6). Despite the fact that non-right-handed asthmatics may experience more asthma attacks in childhood than right-handed (6), a non-right-handed asthmatic child might be expected to turn into a healthy adult. As for possible underlying pathophysiological mechanisms, it has been documented that central nervous system can modulate in various ways the immune response and there has been some evidence from animal experiments that brain laterality is associated with changes in lymphocyte function (7). If

Table 1. Asthmatic attacks after 18 years of age in non-right-handed students with asthma

Handedness	Asthmatic attacks after 18 years		
	Yes	No	Total
LQ > 60	13	10	23
LQ ≤ 60	0	6	6
Total	13	16	29

$P < 0.05$ (Fisher's exact $P = 0.02$).