Multi-tool approach for high risk aspirin desensitization in a pregnant woman

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Pre-eclampsia is a condition found in pregnant women, characterized by high blood pressure and proteinuria. It can be a cause of miscarriage and maternal life risk. Low doses of aspirin given since the 16 weeks of pregnancy have proven to be helpful in preventing eclampsia in women at risk. Omalizumab is a humanized anti-Ig E monoclonal antibody approved for severe allergic asthma and chronic urticaria, but it has been used out of label for several other conditions including drug allergy and aspirin induced asthma.

Here we present a case of a woman with previous foetal loss due to eclampsia and NSAIDs cross-hypersensitivity who has been desensitized to aspirin using both omalizumab and a nasal challenge protocol.

A 36-years old pregnant woman (13th week after in vitro fertilization procedure), with previous history of allergic dust mite rhinitis and asthma, oral mite anaphylaxis and a NSAID induced blended reaction with periorbital angioedema and asthma exacerbation, was referred to our Allergy Unit because she should take aspirin to prevent eclampsia. She had suffered an abortion at 31st week because pre- eclampsia in her previous pregnancy, so she was prescribed aspirin 100 mg for prophylaxis. Her NSAIDs cross-hypersensitivity had been studied years before, and tolerance to paracetamol, COX2 inhibitors and meloxicam had been confirmed. Besides this, tolerance to aspirin 100 mg had been tested in other hospital before the IVF. However, once pregnant, four hours after she took the first dose, mild bronchospasm and palpebral angioedema appeared. Symptoms resolved with antihistamine and salbutamol at home. A second attempt to take the medication resulted in the same symptoms so she was referred for desensitization.

Because her high-risk pregnancy and sensitivity to aspirin, we decided to use omalizumab as premedication plus a cautious protocol using a ketorolac nasal challenge to create a threshold for desensitization as has been described by others[1], [2]. The patient was informed of risks and benefits and signed an informed consent.

Omalizumab 300 mg was given two weeks and 48 hours before starting the desensitization. Control asthma was assessed and montelukast 10 mg daily was added.

Acoustic rhinometry controlled nasal challenge was performed with ketorolac 10 mg/ mL given with a nasal spray for a dose of 0.1 mL or 1 mg in each puff following guidelines recommendations for NSAID nasal challenge[3].

In the first day, doses of 1, 2, 4 and 6 mg of nasal ketorolac were given at 30 minutes intervals, until a cumulative dose of 13 mg was reached. Half an hour after the last dose she referred cough, mild chest tightness and nasal blockage with a 33% fall in Vol_{2-8} but normal physical

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examination and vital signs. Symptoms resolved with oral dexchlorpheniramine 6 mg. She remained under observation for four hours after the last dose and was asymptomatic at discharge.

The second day a 12 mg full dose nasal challenge was performed with no reaction. One hour later, aspirin 25 mg was given orally with good tolerance. On day 3 and 4 doses of 25 plus 25 mg and 50 plus 50 mg with one-hour interval between doses were given. In the fifth day she tolerated the 100 mg full dose. She continued taking aspirin 100 mg, together with omalizumab 300 mg at four weeks intervals and daily montelukast, until the 36th week of her pregnancy, when her obstetrician advised to stop aspirin. She underwent a c-section at 38th week and gave birth to a healthy female baby.

Adjuvant omalizumab therapy for Ig E-mediated drug desensitization has been described previously[4]. NSAID exacerbated respiratory disease (NERD) is caused by a disbalance in the arachidonic acid pathways, leading to an overproduction of cysteinyl leukotrienes, with no involvement of specific Ig E against NSAID drugs[5]. However, omalizumab not only reduces Ig E levels and FcΣRI expression on mast cells but also is associated with a depletion on eosinophils and reduction in urinary leukotriene E4 (LTE4) concentration- which are higher in NERD patients and increases in response to aspirin challenge. One recent study with sixteen subjects showed that omalizumab was able to reduce urinary levels of LTE4 and upper and lower respiratory symptoms after an aspirin challenge[6]. Besides several case reports, a randomized, double-blind, placebo-controlled study of eleven subjects with NERD, showed that adding omalizumab 16 weeks prior to an aspirin desensitization was associated with a significative reduction in reactions during the desensitization in the omalizumab arm[7]. Clinical observations suggest that omalizumab may be useful for aspirin-induced urticaria too[8]. Our patient symptoms were mixed- respiratory and angioedema- so we expected omalizumab to be helpful for both.

Safety is a major concern when we prescribe a drug in the pregnancy. Data from the EXPECT study suggest that omalizumab does not relates with foetal anomalies[9]. Montelukast use for preventing reactions during desensitization is well documented[10].

Ketorolac nasal challenge has showed to be safe and useful both for NERD diagnosis and for enhancing desensitization. Theoretically, when performing a nasal challenge, the reaction should be limited to the upper airways and the risk of a systemic or pulmonary reaction is lower, although it remains a risk procedure. Previous observations of NERD patients who tolerated oral aspirin after a positive nasal challenge led to the development of these protocols[1], [2]. However, to the best of our knowledge, this is the first report of this procedure in a pregnant woman. The decision of desensitization was made after discussing all options with the patient and because she was in high risk of developing eclampsia again.

In conclusion, this is a case of a high-risk patient who needed aspirin desensitization in a narrow time interval. The goal was achieved by combining different tools, both traditional (montelukast) and biologic drugs (omalizumab), and a slow desensitization protocol with previous nasal challenge.

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