Multitool Approach for High-Risk Aspirin Desensitization in a Pregnant Woman

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Pre-eclampsia is a condition that affects pregnant women. It is characterized by high blood pressure and proteinuria, leads to miscarriage, and is life-threatening for the mother. Low doses of aspirin started at 16 weeks of gestation have proven to be helpful in preventing eclampsia in women at risk. Omalizumab is a humanized anti-IgE monoclonal antibody approved for severe allergic asthma and chronic urticaria, although it has been used off-label for several other conditions, including drug allergy and aspirin-induced asthma.

We present the case of a woman with previous fetal loss due to eclampsia and cross-hypersensitivity with nonsteroidal anti-inflammatory drugs (NSAIDs) who was desensitized to aspirin using both omalizumab and a nasal challenge protocol.

The patient was a 36-year-old pregnant woman (13th week after in vitro fertilization) with a previous history of allergic dust mite–induced rhinitis and asthma, oral mite anaphylaxis, and an NSAID-induced blended reaction with periorbital angioedema and asthma exacerbation. She was referred to our Allergy Department because she had been prescribed aspirin to prevent eclampsia. Since she had experienced a miscarriage at week 31 in her previous pregnancy because of pre-eclampsia, she was prescribed aspirin 100 mg for prophylaxis. NSAIDs cross-hypersensitivity had been studied years before, and tolerance to paracetamol, COX2 inhibitors, and meloxicam had been confirmed. In addition, tolerance to aspirin 100 mg had been tested in another hospital before in vitro fertilization. However, while pregnant, she developed mild bronchospasm and palpebral angioedema 4 hours after the first dose. Symptoms resolved with antihistamine and salbutamol at home. A second attempt to take the medication resulted in the same symptoms; therefore, she was referred for desensitization.

Because of her high-risk pregnancy and sensitivity to aspirin, we decided to use omalizumab as premedication combined with a cautious protocol based on a nasal challenge with ketorolac to create a threshold for desensitization, as described elsewhere [1,2]. The patient was informed of the risks and benefits and signed an informed consent document.

Omalizumab 300 mg was given 2 weeks and 48 hours before starting the desensitization protocol. Control of asthma was assessed, and montelukast 10 mg daily was added.

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

On the first day, doses of 1, 2, 4, and 6 mg of nasal ketorolac were given at 30-minute intervals until a cumulative dose of 13 mg was reached. Half an hour after the last dose, the patient complained of cough, mild chest tightness, and nasal blockage, with a 33% fall in $Vol_{2\text{-}8}$. Her physical examination and vital signs were normal. The symptoms resolved with oral dexchlorpheniramine 6 mg. She remained under observation for 4 hours after the last dose and was asymptomatic at discharge.

On the second day, a 12-mg full-dose nasal challenge was performed with no reaction. One hour later, the patient tolerated aspirin 25 mg given orally. On days 3 and 4, doses of 25 plus 25 mg and 50 plus 50 mg were administered with a 1-hour interval between the doses. On the fifth day, she tolerated the full 100-mg dose. She continued taking aspirin 100 mg, together with omalizumab 300 mg at 4-week intervals and daily montelukast until the 36th week of her pregnancy, when her obstetrician advised her to stop aspirin. She underwent a cesarean delivery at week 38 and gave birth to a healthy girl.

Adjuvant omalizumab therapy for IgE-mediated drug desensitization has been reported [4]. NSAID-exacerbated respiratory disease (NERD) is caused by an imbalance in the arachidonic acid pathways, leading to overproduction of cysteinyl leukotrienes, with no involvement of specific IgE against NSAIDs [5]. However, omalizumab not only reduces IgE levels and expression of FcεRI on mast cells, but is also associated with a depletion on eosinophils and reduction in urinary leukotriene E4 (LTE4) concentrations, which are higher in NERD patients and increase in response to aspirin challenge. One recent study with 16 patients showed that omalizumab was able to reduce urinary levels of LTE4 and upper and lower respiratory symptoms after aspirin challenge [6]. In addition, data from case reports and a randomized, double-blind, placebo-controlled study of 11 individuals with NERD have shown that adding omalizumab 16 weeks prior to an aspirin desensitization protocol was associated with a significant reduction in the frequency of reactions during desensitization in the omalizumab arm [7]. Clinical observations suggest that omalizumab may also be useful for aspirin-induced urticaria [8]. Given that the symptoms in the present case were mixed (respiratory and angioedema), we expected omalizumab to be helpful for both.

Safety is a major concern when we prescribe a drug during pregnancy. Data from the EXPECT study suggest that omalizumab is not associated with fetal anomalies [9]. Montelukast has been shown to prevent reactions during desensitization [10].

Nasal challenge with ketorolac has proven to be safe and useful both for diagnosis of NERD and for enhancing desensitization. Theoretically, when performing a nasal challenge, the reaction should be limited to the upper airways, thus reducing the risk of a systemic or pulmonary involvement, although the procedure remains risky. 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 to run a desensitization protocol was made after discussing all options with the patient and because she was at high risk of developing eclampsia again.

In conclusion, we report the case of a high-risk patient who had to undergo desensitization to aspirin in a narrow time interval. The goal was achieved by combining various tools, namely, standard drugs (montelukast) and biologic drugs (omalizumab), as well as a slow desensitization protocol following a nasal challenge.

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Conflicts of Interest

The authors declare that they have no conflicts of interest.

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