Safe and Successful Protocol for Desensitization to Abiraterone

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Abiraterone acetate is used for the treatment of castration-resistant metastatic prostate cancer. It acts as a selective inhibitor of the enzyme 17 α-hydroxylase/C17,20-lyase (CYP17). Expression of this enzyme is necessary for the synthesis of androgens in the testicles, adrenal glands, and prostate tumor tissue; therefore, inhibition leads to reduced production of androgens. Given that inhibition of CYP17 also leads to increased production of mineralocorticoids by the adrenal glands, abiraterone should be taken with prednisone. While abiraterone is generally well tolerated, the summary of product characteristics and various studies list hypertension, hypokalemia, and hepatotoxicity as common adverse effects [1,2]. We present the case of a 63-year-old man with a personal history of hypothyroidism and sleep apnea hypopnea syndrome treated with continuous positive airway pressure who was diagnosed with prostate cancer (Gleason 4+5) and bone metastasis (T10 and left iliac spine). The patient had an initial clinical response to treatment with enzalutamide. As he remained asymptomatic, his urologist decided to maintain hormone treatment instead of taxane-based therapy, starting with abiraterone 1000 mg every 24 hours, together with prednisone 5 mg every 12 hours. After 4 days of treatment, the patient developed a fairly symmetrically distributed micropapular rash on the trunk (mainly the abdomen), both groins, and the root of the upper limbs. He also complained of axillary pruritus, although no lesions were visible at this level. There was no fever or mucous membrane involvement. He was evaluated in the urology department, where treatment was suspended. The rash resolved 4 days later, with minimum fine desquamation and no residual lesions.

We carried out an allergological work-up starting with skin prick tests at 200 mg/mL, although the result was negative. We decided not to perform patch tests, because standardized options with abiraterone are lacking. Even though the rash was indicative of a drug reaction, the fact that it was not severe led us to assess oral tolerance after adding ebastine 20 mg as premedication in an attempt to reintroduce the drug with tolerance. A provocation test was programmed for 2 days to achieve a total dose of 1000 mg of abiraterone. The protocol on the first day comprised 50 mg, 150 mg, and 300 mg, with a 1-hour interval between doses and 2 hours of observation after the last dose (cumulative dose, 500 mg). Ten hours after the challenge was completed, the patient developed a pruriginous micropapular rash on the thorax, affecting the groins and the axillas (Supplementary Material, Photo). Once the Urology Department confirmed that abiraterone was the first-choice agent for this patient, we developed a desensitization protocol (Table) in collaboration with the Pharmacy Department. Doses were prepared by weighing the corresponding amount of powder (10 mg, 30 mg, and 125 mg) and filling empty gelatine capsules. Dextrin maltose was used as the excipient. The desensitization protocol was stepped up every 3 days at the hospital, starting with the 10-mg dose; the patient maintained the maximum tolerated dose at home (Table). We decided to premedicate the patient with ebastine 20 mg/24 h and prednisone 15 mg/12 h. Once the total dose was reached, ebastine was stopped, and prednisone was stepped down, continuing with 10 mg/12 h during the following 2 days and maintaining 5 mg/12 h, as per the summary of product characteristics of abiraterone. The patient did not experience any problems or adverse events during the protocol, which was fully tolerated. Allergic reactions to anticancer drugs are a growing problem in allergology clinics, and desensitization protocols are useful when the drug involved is a first-choice option [3]. Rapid desensitization in IgE-mediated reactions has well-defined pathophysiological mechanisms, and while the procedure is risky, it has proven to be safe and efficacious [4]. In the case of late reactions (ie, more than 1 hour after administration), which are similar to those in the present case and are also frequently managed with rapid desensitization [5], there is no consensus on the ideal protocol,

Table. Desensitization Protocol

Day 1	
Doses administered at hospital with 30-minute intervals	10 mg 20 mg 40 mg 60 mg 125 mg
Day 2 and Day 3	
Dose at home	125 mg
Day 4	
Dose at hospital	250 mg
Day 5 and Day 6	
Doses at home	250 mg
Day 7	
Dose at hospital	500 mg
Day 8 and 9	
Doses at home	500 mg
Day 10	
Dose at hospital	1000 mg

with those published ranging from hours to several weeks [6,7]. While it is desirable to reach the therapeutic dose as soon as possible, rapid protocols are commonly associated with a greater risk of adverse reactions [8]. Verdu et al [9] reported a case of desensitization to abiraterone without previous oral challenge in a patient who experienced 2 reactions to the drug. The authors designed a rapid 1-day protocol. The patient experienced mild skin rash on the thorax; therefore, the protocol was extended to 4 days and completed with premedication comprising antihistamines and corticosteroids. In the case we report, we selected an intermediate protocol in order to reach the therapeutic dose as quickly as possible and with the minimum risk of reactions. After 10 days of desensitization, the patient was able to tolerate the complete dose without reactions or adverse events, and excellent tolerance was maintained after 2 months of treatment, with normal eosinophil counts and liver enzyme values. We present the case of a patient with allergy to abiraterone confirmed using controlled oral challenge. The patient managed to tolerate the full dose of the drug after a slow desensitization procedure with no reactions. It is remarkable that owing to the desensitization protocol, abiraterone could be used to avoid the toxicity induced by docetaxel—the alternative chemotherapy agent in this patient—while maintaining first-line therapy. We highlight the need for oral challenge in patients who experience nonsevere drug reactions in order to confirm hypersensitivity and consider our protocol to be a safe and effective option for achieving tolerance.

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Conflicts of Interest

The authors declare that they have no conflicts of interest.

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