Successful Desensitization of an Adult with Type I Hypersensitivity to Imatinib

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Citation

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Abstract

Cutaneous reactions to imatinib, an effective treatment for chronic myeloid leukemia, have been experienced by up to 30% of patients treated with 400 mg. Current protocols illustrate graded challenges that span up to 10 weeks. The following is a case in which a five-day graded challenge protocol was used for the administration of imatinib to a patient with a history of cutaneous reaction after starting therapy.

CASE PRESENTATION

Our patient is a 65-year-old Asian female with a history of chronic myeloid leukemia (CML), Philadelphia chromosome-positive, who was intolerant to interferon-alpha treatment. Her atopic history was significant for an allergy to amoxicillin (hives). Due to failure of interferon-alpha treatment, indicated by no significant cytogenetic improvement by fluorescent in situ hybrid analysis (FISH), she was switched to imatinib, 400 mg/daily. Three weeks later, she developed a pruritic, urticarial rash over her entire body, but no shortness of breath. No other cause for the rash could be found. The imatinib was discontinued and the urticaria gradually resolved. Additionally, the patient experienced leg edema which was thought to be a side effect of the imatinib itself. Approximately one month later, she was restarted on imatinib 300 mg/daily and again experienced the urticarial rash, in addition to periorbital edema after ten days of therapy. Again, the imatinib was discontinued and she improved on a tapering dose of prednisone over three days, with resolution of the skin findings. Since then, the patient has been treated with hydroxyurea.

After a lengthy discussion with the patient regarding the best therapy for the CML, it was agreed that desensitization to and subsequent continuation of imatinib therapy would be the most prudent course for her treatment of CML. Imatinib was an especially judicious course of treatment as she had failed interferon therapy and was Philadelphia chromosome-positive.

Literature on imatinib desensitization illustrates success with gradual dose escalation over 10 weeks ($_2$). As the patient had an understandable amount of anxiety regarding continuing her chemotherapy treatment expeditiously, we opted not to subject the patient to the ten-week course of desensitization. The patient was started on imatinib 0.005 mg on day one with incremental doses given over the five days (Table 1), and was monitored closely in the Medical Intensive Care Unit. After the 200 mg dose on day four, she experienced pruritis of her feet bilaterally, with no rash, erythema, or shortness of breath. The pruritis lasted ten minutes, and resolved on its own, without medications. The patient completed the graded challenge without further reactions and tolerated the challenge with minimal side effects. Since the graded challenge, the patient was followed up as an outpatient after one month, three months, and six months and was doing well on the imatinib. She had no further episodes of pruritus or rash, and did not experience erythema or shortness of breath.

Figure 1

Table I: Imatinib Oral Desensitization Protocol

Day	Time (hours)	Strength	Conc. (mg/mL)	Dose (mg)	Volume (mL)	Total Dose (mg)	Total mL
Day 1	0	1/1,000	0.001	0.005	5	0.005	5
	3	1/100	0.01	0.05	5	0.055	10
	6	1/10	0.1	0.5	5	0.555	15
	9	1	1	5	5	5.555	20
	12	10	*2	50	25	55.555	45
Day 2	0			50	25	50	25
	12			50	25	100	50
Day 3	0			100	50	100	50
	12			100	50	200	100
Day 4	0			200	100	200	100
	12			200	100	400	200
Day 5	0			400	200	400	200

*Dissolve film-coated tablets in apple juice or water

DISCUSSION

The Philadelphia chromosome translocation (9;11) is the initiating event in CML. The gene product of this translocation, BCR-ABL, is a tyrosine kinase protein with an integral role in oncogenic activity ([1]). Imatinib selectively inhibits the BCR-ABL tyrosine kinase resulting from the translocation and has been shown to be an effective treatment for CML ([1]).

Chemotherapeutic agents have the potential to initiate a hypersensitivity reaction. Up to 30% of patients treated with imatinib 400 mg/day have experienced skin manifestations ([3], [4]). Successful treatment of the reaction involves antihistamines, topical steroids, or a brief course of oral steroids for more severe cases ([2], [3]). Once the patient is successfully treated for the reaction, providers must reassess the risks and benefits of imatinib treatment. As demonstrated for patients such as ours with CML refractory to other chemotherapeutic agents, further treatment with imatinib is warranted. In such a case, desensitization to imatinib is required. The protocol for desensitization is varied ([2], [3], [4]). Rule, et al., demonstrated in case reports that imatinib treatment could be continued in patients with cutaneous reactions by using short-term oral steroids in conjunction with imatinib, or by reintroducing imatinib with gradual dose escalation over 10 weeks ([2]). We chose not to use pretreatment with steroids in our patient, as we did not wish to exacerbate the edema that she was experiencing - a side effect possibly related to imatinib ([5]). Tanvetaynon et al. illustrated a case report of a woman who required desensitization over 24 weeks and was subsequently maintained on a once-weekly imatinib dose due to recurrent cutaneous reactions ([3]).

Our experience demonstrates that desensitization to imatinib with a five-day protocol of dose escalation, without oral steroids (unless warranted by a hypersensitivity reaction), is a safe and effective option. Further studies are needed to determine if this procedure will be tolerated by most patients.

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