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CASE REPORT

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A case of indolent systemic mastocytosis responding to treatment with Avapritinib

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Key Clinical Message

Low dose Avapritinib is a new medication that is a potential treatment option not just for advanced systemic mastocytosis, but also for the indolent form.

KEYWORDS

Avapritinib, hematology, immunology, oncology, systemic mastocytosis

1 | INTRODUCTION

Systemic Mastocytosis (SM) is a rare disorder in which mast cells build up pathologically within organs and tissue. The involvement of mast cells can be restricted to the skin, or they can be systemic. One subtype of SM is called indolent SM, a less aggressive form of the disease compared to advanced SM, presenting with organ impairment due to mast cell infiltration.[1,2] Multi-kinase inhibitors such as Midostaurin and Imatinib have been used in the treatment of KIT D816V mutation-negative advanced SM or indolent SM that is refractory to conservative treatment,[3,4] but Avapritinib is currently reserved for treatment of advanced SM. Here is a case of a KIT D816 mutation-positive indolent SM responding to treatment with a lower dose of Avapritinib.

2 | CASE DESCRIPTION

A 51-year-old female was diagnosed with indolent SM in 2013. She initially had nonspecific symptoms such as nasal congestion, rhinorrhea, cough, and wheezing during childhood. Within the past 10 years, she continued to develop additional symptoms like flushing, itching, telangiectasias, hives, and bloating. The various triggers for these symptoms included heat, friction, and diet, and occasionally improved with Cetirizine. In April 2013, a skin biopsy revealed telangiectasia macularis eruptive perstans, and was positive for c-kit and tryptase. In July 2013, a bone marrow biopsy revealed atypical mast cells with spindle morphology, negative for KIT D816V mutation, and positive for CD117, CD25, and CD2. Despite conservative treatment, the patient experienced diarrhea, itchiness, hives, and headaches, so Cromolyn, Hydroxyzine, and injectable Omalizumab were prescribed. Injectable epinephrine was also provided for possible anaphylaxis, though the patient never reported any anaphylactic episodes. Since her bloating and diarrhea were still not optimally controlled and the patient was diagnosed with wild type KIT, Imatinib was started in 2015. Although the bloating and diarrhea did improve, the medication caused significant transaminitis and Imatinib had to be discontinued. Midostaurin was the next treatment of choice, but the patient had several adverse reactions including

rash, hepatotoxicity, and nausea so it was discontinued in December 2018. In 2019, the patient's serum KIT mutation was found to be positive, and she was enrolled in an expanded access clinical trial. At the time, Avapritinib 200 mg daily was only used to treat aggressive SM,[5] but the dosage was not yet established for indolent SM. Because of her history of hepatotoxicity to other tyrosine kinase inhibitors, the patient was started on a decreased dose of Avapritinib at 100 mg daily in April 2020. As time progressed, there were three subsequent dose reductions of Avapritinib as the patient had gastrointestinal adverse events. In August 2020, Avapritinib frequency was decreased from 100 mg daily to 100 mg every other day because of nausea, mental fog, and burning tongue ulcers. The mental fog resolved, and the gastrointestinal distress, skin flushing, and nausea decreased with Avapritinib at 100 mg every other day. In March 2021, the dosage was readjusted to 75 mg daily since the patient was able to tolerate it well for a few months. However, in July 2021, she developed COVID-19 infection in addition to neck, shoulder, and chest pain, so she discontinued Avapritinib for several weeks. After recovering from the infection and musculoskeletal pain, the medication was reintroduced at 25 mg daily. This dosage and frequency have been controlling the patient's serum tryptase levels, itchiness, and gastrointestinal symptoms well with no toxicities to the medication. Currently, the patient is still taking Famotidine, Cromolyn and Hydroxyzine. She periodically takes Ondansetron and has discontinued Pantoprazole.

3 | DISCUSSION

SM is a rare disease that can be difficult to diagnose and stage, as seen in this patient who experienced symptoms for 10 years before the official diagnosis was made. Although the bone marrow biopsy performed in 2013 was negative for KIT D816V mutation, this was likely a false negative as the assessment for that mutation was less sensitive at the time. For patients with indolent SM, treatment often involves symptom control. In this case, the patient was appropriately on an antihistamine, Cromolyn, and Omalizumab to decrease symptoms of mast cell overactivation. However, the disease management was inadequate as she was still symptomatic despite more conservative treatment and other standard therapies were limited by transaminitis. Luckily, she was able to tolerate Avapritinib. As of 2021, this medication has been approved by the United States Food and Drug Administration for treatment of advanced SM. While Avapritinib has already been approved to treat aggressive SM at 200 mg,[5] research is still being done on its use for indolent SM. For this patient, the oral multikinase inhibitor is highly effective against indolent SM in improving quality of life, decreasing symptoms, and effectively controlling serum tryptase levels. The ideal dosage of Avapritinib for this patient appears to be 25 mg daily, which is coincidentally the same dose that the PIONEER study is investigating for the safety and efficacy of Avapritinib in patients with Indolent SM with moderate to severe symptoms.[6] Perhaps Avapritinib should be accepted as an indication for the indolent form of SM, rather than limit its use to solely the advanced form.

AUTHOR CONTRIBUTIONS

Terrence Sun: Writing – original draft. **Marin Xavier:** Project administration; supervision; validation; writing – review and editing.

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CONFLICT OF INTEREST STATEMENT

We have no conflicts of interest associated with this publication. We confirm that this work is original, has not been published elsewhere, and is not being considered for publication elsewhere.

DATA AVAILABILITY STATEMENT

Data sharing does not apply to this article as no new data was created or analyzed in this study.

CONSENT

Informed consent was obtained from the patient to publish this report by the journal's patient consent policy.

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REFERENCES

1. Swerdlow SH, Campo E, Harris NL, et al., eds. WHO classification of Tumours of Haematopoietic and lymphoid tissues. *International Agency for Research on Cancer (IARC)*. revised 4th ed. Leukemia; 2017.
2. Pardanani A. Systemic mastocytosis in adults: 2021 update on diagnosis, risk stratification and management. *Am J Hematol*. 2021;96(4):508-525. doi:10.1002/ajh.26118 Epub 2021 Feb 21. PMID: 33524167.
3. Vega-Ruiz A, Cortes JE, Sever M, et al. Phase II study of imatinib mesylate as therapy for patients with systemic mastocytosis. *Leuk. Res.* 2009;33(11) Epub 2009 Feb 3:1481-1484.
4. van Anrooij B, Oude Elberink JNG, Span LFR, et al. Midostaurin in patients with indolent systemic mastocytosis: an open-label phase 2 trial. *J Allergy Clin Immunol*. 2018;142(3):1006-1008.e7. doi:10.1016/j.jaci.2018.06.003 Epub 2018 Jun 8. PMID: 29890238.

5. DeAngelo DJ, Radia DH, George TI, et al. Safety and efficacy of avapritinib in advanced systemic mastocytosis: the phase 1 EXPLORER trial. *Nat. Med.* 2021;27:2183-2191. doi:10.1038/s41591-021-01538-9
6. Akin C, Elberink HO, Gotlib J, et al. Pioneer part 2: a randomized, double-blind, placebo-controlled, phase 2 study to evaluate safety and efficacy of Avapritinib in indolent systemic Mastocytosis. *Blood*. 2020;136:41-42. doi:10.1182/blood-2020-136632

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