

Surgical Management of Cutaneous Mastocytosis: A Systematic Review

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BACKGROUND: Surgical intervention is rarely used in managing cutaneous mast cell disorders. **OBJECTIVE:** To analyze studies on surgical management of cutaneous mast cell disorders in humans and review practical considerations for these surgeries. **METHODS:** We conducted a literature search of major medical databases using terms related to mast cell disease and surgical treatment in human patients from inception of the databases to April 20, 2026. **RESULTS:** Nineteen of 981 screened articles met inclusion criteria. There were 13 cases of solitary mastocytomas: 3 mast cell sarcomas (MCS), 1 multilocalized mastocytomas, 1 solitary mastocytoma that transformed into MCS, and 1 atypical mastocytoma to borderline MCS. For localized mastocytomas, wide local excision achieved adequate symptom control in most cases. Systemic disease carried a poor prognosis overall despite both surgical and adjuvant therapies. Tryptase was more likely to be elevated in more severe systemic, recurrent, or malignant disease. **CONCLUSION:** Surgical intervention has both diagnostic and therapeutic value for isolated solitary mastocytomas and in certain cases of MCS. Careful perioperative management is crucial. Further research is necessary to determine the value of premedication. **KEYWORDS:** Mastocytosis, mastocytoma, tryptase, mast cell disease, mast cell sarcoma

Mastocytosis is characterized by an inappropriate proliferation of mast cells in the skin, gastrointestinal tract, kidneys, bone marrow, or other organs. The most current diagnostic guidelines adopted by the World Health Organization in 2021 divide this disease into overarching subtypes: cutaneous mastocytosis (CM) and systemic mastocytosis (SM), each of which is further stratified by prognostic and clinical criteria.¹ CM, the focus of this review, is characterized by neoplastic mast cells limited to the skin and is the more common presenting subtype in pediatric patients, carrying a good prognosis with possible resolution at puberty. The cutaneous lesions of CM are categorized by their morphology, and the commonly described variants include monomorphic and polymorphic maculopapular CM, also known as urticaria pigmentosa, as well as cutaneous mastocytoma and diffuse CM.² Adult patients are more likely to experience SM, which frequently presents with cutaneous lesions. Cutaneous lesions can be the first sign of SM and carry a poor prognosis, specifically for nonindolent SM, due to internal organ involvement.¹ Both forms can exhibit Darier's sign and may appear similar on histology with increased numbers of mast cells in the dermis and perivascularly.

Mast cell degranulation can be triggered by various stimuli, including crosslinking of immunoglobulin E, via toll-like receptors, stem cell factor receptors, specific ligand-mediated G protein-coupled receptor activation, the *KIT* receptor, and more.³ Subsequent degranulation then causes the release of preformed mediators including histamine and tryptase, which is followed within a few minutes by the synthesis of prostaglandin D₂, leukotrienes, and platelet activating factor, and finally by the generation

of numerous cytokines with both pro- and anti-inflammatory effects.⁴ Symptoms of mast cell activation are heterogenous in both CM and SM and can range vastly from bothersome pruritus or flushing to life-threatening anaphylaxis.^{5–7}

Surgical procedures, specifically to alleviate the cutaneous manifestations for isolated mastocytoma or mast cell sarcoma (MCS) via surgical excision, are rarely performed in humans with mastocytosis. This is possibly due to concerns about perioperative complications such as mast cell degranulation or anaphylaxis, though surgical recommendations are largely derived from case reports and expert opinions rather than controlled trials.⁸ However, there exists abundant veterinary literature describing surgical management of CM in animals. By extrapolation, surgery may provide a therapeutic option in certain human populations.

The objectives of this review are to identify appropriate patient types for surgical management of cutaneous manifestations of mastocytosis and MCS and define the best practices to minimize perioperative complications.

METHODS

A literature search using PubMed, PubMed Central, Google Scholar, and the Cochrane Library was performed for the terms “mast cell disease,” “mastocytosis,” or “mastocytoma,” in association with the terms “surgical,” “surgery,” “excision,” or “surgical treatment” from database inception to April 20, 2026. The search was conducted adhering to the updated 2020 standards of the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) statement (**Figure 1**). Cases were

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included if they involved human patients, cutaneous forms of mast cell disease were diagnosed, and surgical intervention was performed for isolated CM or cutaneous MCS. During the review process, articles describing animal cases and cases of SM without cutaneous involvement were excluded. Two reviewers (author AH and author TK) independently reviewed the studies, and discrepancies were resolved through consensus.

RESULTS

A total of 981 unique articles were screened, and 31 met criteria to have the full text screened. Of these, 16 met eligibility criteria for inclusion. Supplementary searching identified 3 additional eligible case reports with the addition of the search terms “surgical intervention,” for a final total of 19 included cases. There were 13 cases of CMs, 3 MCSs, 1 multilocalized mastocytoma, 1 CM that transformed into MCS, and 1 atypical mastocytoma to borderline MCS. Eight of the patients were women, 10 were men, and 1 case did not specify a gender. The cases exhibited a broad age distribution ranging from 13 days to 71 years. Tryptase levels were available in 2 MCS cases (range: 18–28 ng/mL in 1 case and >122 ng/mL in the other) and 3 CM cases (5.3–14.0 ng/mL); there was also a case of an atypical CM to borderline MCS (2.9 ng/mL). Each case is detailed in **Table 1**.

Patients experienced a full resolution of symptoms in 10 of the 13 cases of solitary mastocytoma treated with surgical resection or excisional biopsy. One patient had resolution of systemic symptoms but mild localized recurrent blistering after excision, and 2 patients did not have follow-up information available. Surgery was performed to confirm the diagnosis (excisional biopsy) or for debulking in patients with an MCS and solitary mastocytoma transforming into MCS. These aggressive tumors were treated with multimodal therapy including imatinib (3 cases), systemic corticosteroids (1 case), radiation therapy (3 cases), and stem cell transplant (1 case). Two cases of MCS presented in childhood (ages 12 and 19) and 1 presented in adulthood (age 71), with the additional case of malignant transformation into MCS occurring at age 40; the pediatric cases were both alive at follow up while both adults were deceased. Of note, none of the cases in this review were associated with SM.

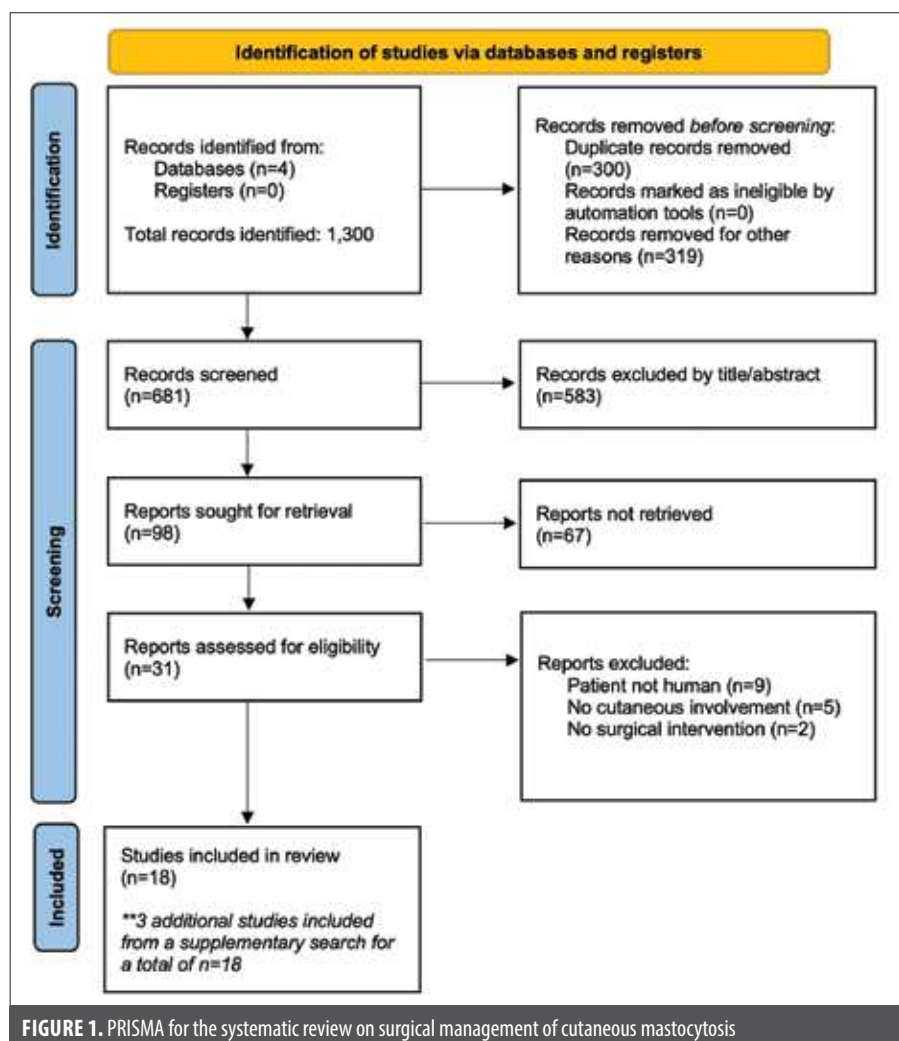


FIGURE 1. PRISMA for the systematic review on surgical management of cutaneous mastocytosis

DISCUSSION

For solitary mastocytomas, simple wide local excision appeared effective, with the majority of cases showing complete resolution of symptoms without recurrence. Of the 13 mastocytoma cases in this review, 10 achieved full symptom resolution following surgical resection or excisional biopsy.^{9–17} Adjuvant medical therapy was rarely required.

Two cases underscore the indications for surgical intervention. Ha et al¹⁵ described a 13-day-old neonate with a rapidly growing facial mastocytoma successfully treated with excisional biopsy and no postoperative complications or recurrence. Verma et al¹⁶ reported a 2-month-old infant in whom a solitary mastocytoma caused life-threatening recurrent apnea, respiratory distress, diarrhea, and limpness—all of which resolved completely following surgical excision at 6

months of age, representing the first reported case of surgical excision resolving such acute multisystem manifestations in a solitary cutaneous mastocytoma.

In contrast, outcomes were generally worse for more disseminated or aggressive subtypes, even those considered nonmalignant. Munro and Farr¹⁷ reported ongoing blistering at the surgical site after excising a solitary scalp lesion. Meanwhile, McDermott and Topol¹⁸ found some success in debulking several refractory tumors with an ultrasonic scalpel after localized radiotherapy, excision, and cautery failed.

The cases of transforming tumors may lower the threshold for excising even benign-behaving mastocytomas due to the exceedingly rare possibility of malignant degeneration to MCS. Poor surgical control and recurrence were seen for transforming tumors and primary MCSs. For example, Wardle et al¹⁹ described a man

TABLE 1. Systematic review articles on surgical management of cutaneous mastocytosis

AUTHOR	SEX	AGE	DIAGNOSIS	TRYPTASE LEVELS	SURGICAL TREATMENT	ADJUVANT TREATMENTS	OUTCOME
Ashinoff et al ⁸	M	33 years	Solitary mastocytoma	N/A	Surgical excision	N/A	No recurrence
Arik, Yilmaz et al ¹⁰	F	9 months	Solitary mastocytoma	Within normal limits, no exact number given	Excisional biopsy	N/A	Complete resolution
Khan et al ¹¹	F	30 years	Solitary mastocytoma	11 to 14 ng/mL	Surgical excision	N/A	Resolved
Pandhi et al ¹²	M	24 years	Solitary mastocytoma	N/A	Surgical excision	N/A	No recurrence at 1 year
Papanastasiou et al ¹³	Unknown	9.5 years	Solitary mastocytoma	N/A	Surgical excision	N/A	No generalized symptoms (flushing, tachycardia) after 24 months
Thappa et al ¹⁴	F	2.5 months	Solitary mastocytoma	N/A	Surgical excision	N/A	Resolved
Ha et al ¹⁵	F	1 month	Solitary mastocytoma	N/A	Surgical excision	N/A	No recurrence
Verma et al ¹⁶	F	6 months	Solitary mastocytoma	N/A	Surgical excision	N/A	No recurrence
Munro and Farr ¹⁷	M	6 months	Solitary mastocytoma	N/A	Excisional biopsy	N/A	Scalp lesion recurrence and continued blistering
McDermott and Topol ¹⁸	M	62 years	Urticaria pigmentosa progressing to multifocalized mastocytomas	N/A	Repeated surgical excisions	Localized radiotherapy, excision of skin graft, fulguration, cautery, ultrasonic scalpel	Refractory disease
Wardle et al ¹⁹	M	44 years	Atypical mastocytoma, borderline to mast cell sarcoma	Within normal limits (2.9 µg/L)	Repeated surgical excisions	N/A	Refractory disease within 2 years; re-excision with no refractory disease
Ryan et al ²⁰	F	12 years	Mast cell sarcoma	Ranged from 122 to >200 ng/mL throughout treatment course	2 debulking surgeries	Trialed 8+ different chemotherapy agents over 27 months, followed by radiation and imatinib mesylate with allogeneic hematopoietic stem cell transplantation	Alive with persistent disease 45 months following initial presentation
Ryan et al ²⁰	M	19 years	Mast cell sarcoma	18 ng/mL in initial workup, then returned to normal after first excision, then elevated to 28.2 ng/mL during recurrent disease	2 excisional biopsies	Imatinib 400 mg daily	Recurrent mast cell sarcoma by lymph node biopsy at 19 months
Horny et al ²¹	F	71 years	Mast cell sarcoma	N/A	Surgical excision	Corticosteroids, bleomycin, radiation therapy	Deceased due to hemorrhagic diathesis
Chang et al ²²	M	26 years	Solitary mastocytoma	N/A	Surgical excision	N/A	Not reported
Auquit-Auckbur et al ²³	M	40 years	Solitary mastocytoma transforming into mast cell sarcoma	8.6 ng/mL	Surgical excision	Localized radiotherapy, imatinib 400 mg daily	Deceased
McKinnon et al ²⁴	M	60 years	Solitary mastocytoma	Within normal limits (5.3 µg/L)	Surgical excision	N/A	No recurrence
Baraf et al ²⁵	M	18 years	Solitary mastocytoma	N/A	Surgical excision	N/A	N/A
Mylianus et al ²⁶	F	27 years	Solitary mastocytoma	N/A	Surgical excision	N/A	No recurrence

F: female; M: male; N/A: not applicable

with an atypical, morphologically high-grade cutaneous mast cell tumor (borderline between mastocytoma and MCS) managed by serial excision following recurrence more than 6 years after diagnosis, with persistently normal serum tryptase throughout. Additionally, 2 cases of MCS described by Ryan et al²⁰ demonstrated failed surgical control even with multi-agent chemotherapy regimens after initial mass debulking. Moreover, Horny et al²¹ described patient death secondary to intractable bleeding after resection of cutaneous metastases from an aggressive subglottic mass. It is important to note that these cases represent rare and severe manifestations of the disease, and the outcomes may not be generalizable to all patients with cutaneous mastocytomas.

In 1 interesting case, initial excision of a benign primary MCS preceded the appearance of a more aggressive sarcoma at the surgical site by 4 years, despite clear margins at the time of the initial excision.²⁷ Unfortunately, following re-excision of the sarcoma with clear margins and adjuvant radiotherapy, the patient still developed lymph node and bone metastases within a few months and ultimately succumbed to lethal hemorrhage of the metastases. While this description of malignant transformation in this disease process is exceptionally rare, further studies may be necessary to understand the epidemiology of and molecular events underpinning malignant degeneration of presumed-benign mast cell tumors.

THE ROLE OF TRYPTASE

Tryptase levels were reported infrequently but provided some insight into disease extent when available. For the 2 mastocytoma cases with levels, Arik Yilmaz et al¹⁰ and Khan et al¹¹ described normal preoperative serum tryptase, suggestive of isolated solitary cutaneous disease. Both were effectively treated with surgical excision. Meanwhile, tryptase was elevated intermittently throughout the treatment course of 2 MCSs, with levels fluctuating from 122 ng/mL to >200 ng/mL (normal range: 1–15 ng/mL), in the cases reported by Ryan et al.²⁰ Persistently high tryptase mirrored aggressive biology and heralded subsequent relapse and mortality. Normal levels may indicate truly localized pathology where surgery may succeed as monotherapy for primary cutaneous disease.

Tryptase has a low intra-individual variability

and can be helpful for risk stratifying for anaphylactic reactions.²⁸ Additionally, tryptase levels can help differentiate CM from SM. World Health Organization guidelines include tryptase levels >20 ng/mL as a minor criterion for SM; however, this is nuanced, as pediatric patients with diffuse disease may exhibit serum tryptase levels >100 ng/mL without having SM.¹ Furthermore, trending tryptase levels following the excision of lesions with a history or examination concerning for more aggressive disease may be prudent.

THE ROLE OF ddPCR FOR THE *KIT* D816V MUTATION

Droplet digital polymerase chain reaction (ddPCR) is a highly sensitive molecular diagnostic tool that can detect low levels of the *KIT* D816V mutation in peripheral blood.²⁹ Given the strong association between *KIT* D816V and SM, ddPCR may be helpful in the workup for patients with CM to rule out SM, potentially reducing the need for more invasive diagnostic testing in selected cases.²⁸ Collins et al³⁰ reported a case of MCS with a *KIT* p.D816V, detected with ddPCR, with the individual consequently found to have underlying SM. As such, ddPCR has emerged as a useful adjunct in distinguishing isolated cutaneous disease from SM.

CONSIDERATIONS FOR SURGERY

Surgical treatment may be reserved for patients who fail medical therapies including antihistamines, antileukotrienes, topical corticosteroids, or targeted *KIT* inhibitors such as avapritinib or for patients with localized skin disease that causes them significant distress.⁴ Importantly, before surgical management, symptomatic CM should be worked up to exclude SM. Not every patient may be appropriate for operative management, especially asymptomatic patients or pediatric patients for whom surgical treatment may require sedation or restraint.³¹ Indications to operate include the presence of a lesion on an area that experiences friction or pressure potentially leading to mast cell degranulation and systemic symptoms, such as flexural areas, palms, soles, and scalp.⁴ Some tips for procedural management are included in **Figure 2**.³²

Of the 19 cases evaluated in our review, none reported perioperative complications, such as

hypotension or anaphylactic shock, even when multiple large tumors were surgically operated on such as in the case described by McDermott and Topol.¹⁸ Notably, of the 19 cases, none of the patients received special preoperative treatment. However, given the paucity of literature describing surgical treatment of these lesions, a thorough history, physical examination, and laboratory markers such as tryptase may still be warranted to gauge the risk of perioperative complications. Even in the absence of positive findings, it is prudent to consider preoperative mast cell–inhibiting medications, as there is the rare possibility of anaphylaxis even in patients with CM.⁷ Further research may evaluate what indications might exist for triaging patients to higher-acuity surgical centers as opposed to excision in the dermatology office.

Patients with both CM and SM may be at an increased risk of anaphylaxis when undergoing certain general anesthesia, and it is recommended that surgically managed patients be postoperatively monitored for at least 24 hours since delayed anaphylaxis has occurred hours after surgery in some patients.^{7,33–35} Additionally, friction and pressure are known causes of irritation and degranulation of cutaneous mastocytomas and may precipitate anaphylaxis. In vitro studies have shown stabilization of rat mast cells with direct injection of lidocaine, and local anesthesia has been shown to be safe overall in mastocytosis; however, the safety of injecting directly into mast cell lesions in humans is uncertain.^{36,37} Systemic lidocaine is not recommended in patients with mastocytosis, though lidocaine injections can be safely used in these patients. Regarding general anesthesia, in a cohort of 219 procedures, 91.8% of known mastocytosis cases used chronic antimediator therapy and/or preoperative prophylaxis and 10 required intraoperative treatment for potential mast cell activation.³⁸ This suggests that this protocol may be effective with a relatively low-risk profile if general anesthesia is necessary, such as in pediatric patients.

As mentioned in the previous section, tryptase levels have an undetermined significance in benign solitary lesions; however, they may have some utility in gauging the progression of malignant lesions. In patients with excised masses demonstrating mast cell infiltration or myeloid features on

tips for procedural management of cutaneous mastocytosis

Preoperative	Perioperative	Postoperative
- Evaluate for systemic mastocytosis, specifically, in patients with widespread, symptomatic, or atypical presentations. - Premedicate with H1 and H2 antihistamines, corticosteroids, and/or leukotriene modulators to stabilize mast cells. - If prior history of anaphylactic episodes, ensure easy access to intramuscular epinephrine during the procedure	- Avoid irritating lesions with overly aggressive topical sterilization - Actively monitor for any signs of acute anaphylaxis. - Avoid NSAIDs unless patient has been able to take them in the past without adverse effects - If using general anesthesia, the opiate medications morphine and codeine should be avoided, plus certain muscle relaxants including succinylcholine and rocuronium. - Fentanyl and vecuronium have been shown to be better tolerated in this patient population	Trend tryptase and assess for a <i>KIT</i> D816V mutation using ddPCR if there is any suspicion for malignancy or systemic progression
		

FIGURE 2. Tips for procedural management of cutaneous mastocytosis
ddPCR: droplet digital polymerase chain reaction; NSAID: nonsteroidal anti-inflammatory drug

histopathology, trending serum tryptase levels postexcision can help identify residual systemic disease, progression to SM, or an associated neoplasm, though the likelihood of an event is low. Additionally, ddPCR of *KIT* D816V offers a promising new molecular tool to evaluate for the presence or development of SM.

This study was limited by the small sample size of case reports and lack of outcome data in some cases. Tryptase levels were unavailable for many patients, which limited the ability to analyze the utility of this biomarker across different presentations. Cutaneous mast cell tumors, especially malignant forms, are quite rare, which makes the generalizability of the findings difficult. However, this review aimed to synthesize the available evidence on surgical management of these lesions and spark a multidisciplinary conversation that could potentially lead to better guidelines

and protocols for surgical treatment in the future. Further large-scale studies with robust data collection on outcomes are needed to develop higher-quality evidence-based recommendations.

CONCLUSION

Although rarely performed, surgical intervention has both diagnostic and therapeutic value for isolated mastocytomas. Careful triaging of procedures in addition to preoperative medication and perioperative management will help to minimize possible adverse outcomes. Transformation from mastocytoma to MCS was reported in 1 case, suggesting that surgical removal may be warranted for persistent isolated mastocytomas. The prognosis for MCS remains poor, and debulking surgery may be used among other multimodal approaches. The degree of tryptase

level spike or persistence of high levels on serial measurements may directly relate to prognosis. Further study should examine tryptase trends as a way to help tailor and monitor treatment across the spectrum of presentations. This study was limited by the small sample size of case reports and lack of outcome data in some cases. Further studies and multidisciplinary input from numerous specialties are needed to devise surgical management guidelines.

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