Malignant and Metastatic Tumors of the Hand

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Malignant tumors of the hand are rare, although there remain many instances in which marginal excisions are performed for unsuspected malignant hand lesions. Suboptimal biopsy incisions and inadvertent contamination during these excisions may result in larger resections or amputations being necessary to ensure complete removal of the tumor with negative margins. This article provides an update for the current management of patients with primary malignant and metastatic tumors of the hand, including the roles of adjuvant radiotherapy and chemotherapy for the more common hand tumors. *(J Hand Surg 2010;35A:1895–1900. © 2010 Published by Elsevier Inc. on behalf of the American Society for Surgery of the Hand.)*

Key words Malignant tumors, hand, soft tissue sarcoma, bone tumors, acrometastases.

CME Continuing Medical Education

Most hand surgeons routinely manage patients who present with tumors of the hand. The vast majority are benign ganglions, giant cell tumors of tendon sheath and lipoma. Malignant tumors are rarely seen in the hand. Unfortunately, this leads to a low index of suspicion of malignancy and may result in a delay in diagnosis or suboptimal biopsies, the hazards of which have been well covered by many authors.[1] The fact that so few patients with malignant tumors of the hand present initially to cancer centers[2] highlights the need for all hand surgeons to be aware of the clinical signs of malignancy and the principles of performing an optimal biopsy.

Because of the rarity of malignant tumors of the hand, much of our knowledge is either extrapolated from larger series from other sites or from small case series of tumors within the hand.[3] Thus, information on prognosis must be interpreted in this context. The purpose of this review is to provide an update on the developments in treatment of malignant hand tumors, including current diagnostic, staging, and treatment modalities.

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SOFT TISSUE SARCOMA

It was once believed that soft tissue sarcomas of the hand had a poorer prognosis than those elsewhere in the extremities.[4] More recent publications suggest that the reverse is possibly true, with patients with tumors of the hand having better survival than do those with similar tumors at other sites.[5] Part of the reason could be that patients with hand tumors tend to present with small tumors. The challenge is to balance the need for complete excision of the tumor with negative margins with the desire to preserve maximum hand function. To this end, continuing improvements in magnetic resonance imaging allow better imaging and delineation of the tumor and have greatly assisted surgical planning.

STAGING STUDIES

The workup for patients with soft tissue sarcomas of the hand should include the following imaging modalities: plain radiographs and magnetic resonance imaging of the hand, and computed tomography scan of the chest. Positron emission tomography scans have been shown to be useful in detecting extrapulmonary sites of tumor involvement in pediatric sarcoma patients.[6] Positron emission tomography has also been shown to be useful in helping differentiate between benign and malignant

tumors in patients with neurofibromatosis.[7] However, indications for using positron emission tomography remain to be determined, and must be balanced against factors such as cost, availability, and the dose of radiation required for each scan, especially positron emission tomography/computed tomography scans. In addition, other modalities such as magnetic resonance imaging of the spine may be indicated for patients with high-risk myxoid liposarcomas, which have shown a predilection for metastasis to this region.[8]

EDUCATIONAL OBJECTIVES

- Describe the workup of patients with soft tissue sarcoma of the hand.
- Discuss the role of sentinel lymph node biopsy.
- List the role of radiotherapy with regards to local recurrence and patient survival.
- State the indications for radiotherapy.
- Compare and contrast chondrosarcoma and osteogenic sarcoma with respect to treatment, recurrence, and prognosis.
- Discuss the various tumors that metastasize to the hand.

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SENTINEL LYMPH NODE BIOPSY

Lymph node metastases for soft tissue sarcomas are uncommon and are seen most often in angiosarcoma, embryonal rhabdomyosarcoma, and epithelioid sarcoma.[9,10] Sentinel lymph node biopsy has been done for adult soft tissue sarcomas such as synovial, epithelioid, and clear cell sarcoma, but its utility has not been established.[11] There appears to be a survival benefit with aggressive local treatment and regional lymph node dissection for patients with soft tissue sarcoma, with regional lymph node involvement in the absence of other systemic disease.[10,12] This group of patients could potentially benefit from sentinel lymph node biopsy with completion lymphadenectomy performed when a positive sentinel node is identified. However, prophylactic lymph node dissection for epithelioid sarcoma, previously recommended by some authors, is probably not indicated in the absence of palpable lymph nodes or a positive sentinel lymph node biopsy.[13] Sentinel lymph node biopsy has also been used in pediatric patients.[14] In patients with rhabdomyosarcoma, it is a useful staging tool that helps indicate prognosis and helps determine the patient's treatment.[15]

SURGERY

Surgery remains the mainstay of treatment for soft tissue sarcoma. Aside from the known prognostic factors of size, grade, and depth, resection margins are especially important in the hand. Achieving negative margins appears to have a significant impact on local recurrence and patient survival[2,5] and should therefore be the goal of all surgical resections.

Partial hand preservation has proven possible even in large soft tissue sarcomas of the hand, with acceptable functional and oncologic outcomes.[16] Partial hand amputations, such as disarticulations for tumors localized to the finger, or modified single or double ray amputations, can be done with negative resection margins and low local and distant recurrence rates.[17] Functional outcomes are dependent on the amount of native tissue that is preserved, with poorer outcomes for more extensive amputations such as double ray amputations. However, double ray amputation still leaves a useful assistive hand that is superior to amputation and a hand prosthesis.[16] Aggressive tumor excision must be accompanied with good soft tissue reconstruction to maximize the functional and esthetic outcomes of hand salvage surgery. Reconstruction is performed by a different team in our practice, allowing the surgeon performing the resection to do whatever is necessary to ensure adequate wide tumor excision.[18]

RADIOTHERAPY

The role of radiotherapy in reducing local recurrence rates has been firmly established in previous randomized trials.[19,20] However, it has not been shown to improve patient survival. Preoperative radiotherapy has the advantage of using smaller doses of radiation as well as a smaller radiation field compared with postoperative radiation, potentially reducing the complications from radiation. When compared with postoperative radiation in a randomized trial,[21] preoperative radiotherapy resulted in more wound complications (35% for preoperative and 17% for postoperative radiotherapy), and had equivalent early functional outcomes.[22] However, there seems to be better late function.[23] Preoperative radiotherapy also can potentially improve the likelihood of hand preservation in large tumors close to vital structures by causing tumor shrinkage, although the converse may occur in radiotherapy-resistant tumors. Delivery of radiation has recently become more precise, using techniques such as image-modulated radiation therapy that may result in lower side effects because they spare normal tissue from radiation.[24] In the hand, radiotherapy would be indicated for high-grade tumors with close resection margins, tumors larger than 5 cm, or tumors lying close to vital struc-



FIGURE 1: A 70-year-old woman with a history of metastatic renal cell carcinoma to the distal phalanx of the small finger presenting with a 1-week history of pain and swelling of the pulp, appearing similar to a felon. Front view.



FIGURE 2: Side view of case in Figure 1.

tures to shrink the tumor and preserve these structures during tumor resection.

CHEMOTHERAPY

A recent meta-analysis of chemotherapy trials for localized soft tissue sarcoma confirms that chemotherapy reduces the local and distant recurrence rates and marginally improves overall survival. Adding ifosfamide to doxorubicin-based treatment improves the results but at the cost of greater toxicity.[25] In selected tumors such as rhabdomyosarcoma, chemotherapy greatly improves patient survival.[15] The emergence of target therapy may result in a better response to chemotherapy, similar to results for imatinib mesylate in the treatment of gastrointestinal stromal tumors.[26]

BONE SARCOMAS

Chondrosarcoma

Chondrosarcoma is the most common primary malignant bone tumor that occurs in the hand.[27,28] However, chondrosarcomas constitute less than 2% of all primary cartilaginous bone tumors of the hand.[27] The diagnosis of chondrosarcoma should be made in the context of radiologic findings because more cellular atypia is accepted in enchondromas of the hand than in other sites.[27,28] Chondrosarcomas of the hand appear to be locally aggressive tumors with a high rate of local recurrence after curettage alone, although they rarely metastasize. They can arise from pre-existing enchondromas.[27] It is still unclear whether curettage with or without local adjuvant treatment or wide excision and/or amputation is the treatment of choice,[27–30] as the risk of local recurrence must be balanced against the functional loss and life expectancy of the patient, espe-



FIGURE 3: Radiograph showing almost complete destruction of the distal phalanx.

cially because chondrosarcoma tends to occur in older patients. However, examination of the entire lesion is important to exclude rarer tumors such as dedifferentiated chondrosarcoma or chondroblastic osteogenic sarcoma, which require more aggressive treatment and carry a poorer prognosis.[27]

Osteogenic sarcoma

Primary osteogenic sarcoma of the hand is rare, accounting for as few as 0.18% of all cases of osteosarcoma. The prognosis for osteosarcomas of the hand may be better than at other sites.[31] Wide excision of osteosarcoma is essential because positive margins are strongly correlated with local recurrence, which carries a poor prognosis.[32] The role of chemotherapy in the treatment of high-grade osteosarcoma is already well established, and recent trials with the addition of muramyl tripeptide have shown a survival benefit in patients with nonmetastatic[33] and potentially those with metastatic disease.[34] Preoperative chemotherapy has

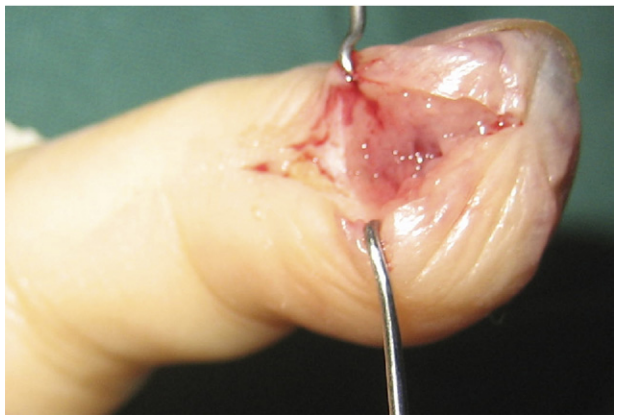


FIGURE 4: A fleshy tumor was seen at the time of biopsy. The patient underwent subsequent disarticulation of the distal phalanx once the diagnosis of metastasis was confirmed.

the potential benefit of shrinking the tumor to preserve critical structures during surgical resection but must be restarted soon after surgery, preferably within 21 days, because delays result in poorer overall survival for patients.[35] This study by Imran et al.[35] highlights the need to avoid surgical complications such as infections that could lead to delays in resumption of chemotherapy. Even in patients who develop multiple tumor recurrences, there is still a chance of salvage with aggressive combined surgery and chemotherapy.[36]

Ewing's sarcoma

A contemporary series showed that the prognosis for Ewing's sarcoma of the hand was no different from that in other extremity sites.[3] Currently, patients with localized tumors have a 5-year overall survival of up to 78% on current chemotherapy regimens combined with surgery and/or radiotherapy for local tumor control.[37] Recently, primitive neuroectodermal tumors have been classified by the World Health Organization together with Ewing's sarcoma and Askin tumors as Ewing's sarcoma family tumors, given the similar histologic appearance, molecular translocations, and response to treatment. The ideal method of achieving local control—whether radiotherapy alone, surgery alone, or combined modalities—remains to be demonstrated in a randomized trial. Surgery avoids the complications of stiffness, fibrosis, and radiation sarcoma in the long term, whereas radiotherapy preserves structures that would otherwise be sacrificed during surgical resection of the tumor. The prognosis for patients who develop local tumor recurrence or those with metastatic Ewing's sarcoma family tumors remains poor. Research involving inhibiting insulin-like growth factor, mammalian target of rapamycin, and angiogenesis are ongoing and

could potentially improve the prognosis for this group of patients.[38]

Hand metastases

Hand metastases constitute an estimated 0.1% of all osseous metastases.[39] The most common primary site is the lung, which accounts for about 40% of cases, followed by renal and breast primary cancers.[39–41] The true incidence of hand metastases may be higher, as many may go unnoticed with minimal symptoms. The mechanism of metastasis to the hand is unknown, although some have suggested that trauma and increased blood flow may explain why metastatic lesions are seen more commonly in the dominant hand.[41] At times, tumors can embolize from a proximal site during surgical manipulation.[42] Current theories on the mechanism of metastases focus on the "seed and soil" theory first proposed by Stephen Paget.[43] As our understanding of the mechanisms improves, we may be able to prevent a localized primary cancer from metastasizing. Hand metastases can present insidiously and mimic infections[40,41] (Figs. 1 to 4), and can be the initial presentation of an occult malignancy.[41] Treatment options include palliative radiation as well as amputations for fungating lesions. In addition, systemic treatment with bisphosphonates can reduce skeletal events for other sites of bone metastases.[44] Another agent with potential includes denosumab, a human monoclonal antibody that specifically inhibits receptor activator for nuclear factor kappa-B ligand, inhibiting osteoclast-mediated bone destruction. Denosumab is currently undergoing clinical trials.[45]

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JOURNAL CME QUESTIONS

Malignant and Metastatic Tumors of the Hand

For tumors in the hand, radiotherapy is indicated for what parameters?

a. High-grade tumors
b. Close resection margins
c. Tumors larger than 5 cm
d. Tumors lying close to vital structures
e. All of the above

Following preoperative chemotherapy for osteogenic sarcoma, what is the optimum time to restart chemotherapy after surgical resection?

a. Immediately postoperative
b. Within 3 weeks
c. Within 6 weeks
d. Within 3 months
e. Undetermined

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