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Pulmonary Metastasis of Benign Giant Cell Tumor of Bone

Six Histologically Confirmed Cases, Including One of Spontaneous Regression

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Benign giant cell tumor of bone, despite being classified as benign, has the unusual ability to metastasize. Metastasis of such a tumor has been thought to be rare, with only approximately 50 such cases having been reported. However, as awareness of the metastatic potential of these tumors has increased, and methods of detection have improved, metastasis of benign giant cell tumor has been increasingly recognized. Six patients with pulmonary metastasis of giant cell tumor have been treated at a Los Angeles hospital since 1980. This represents 9.1% of all patients treated for benign giant cell tumor of bone over the same period at this institution, a higher rate than that encountered in previously published series. The early detection and treatment of this tumor is important, because those with complete resection of tumor have the best prognosis. The nature of these pulmonary metastases remains unpredictable, however, as evidenced by two of the cases in this series: one of spontaneous regression, and another of death caused by pulmonary failure.

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Giant cell tumor accounts for approximately 20% of primary bone tumors in China, and 4–5% of all primary bone tumors in the Western world.[5,10,13,19,34,46] Although classified as benign, this tumor has the unusual tendencies of local aggressiveness, recurrence, and metastasis. Approximately 50 cases of benign giant cell tumor with pulmonary metastasis have been reported in the literature.[1,7,10,15,18–22,24,26,28,30,45,47] Many are case reports with one to three cases. This is the fourth largest series of histologically confirmed benign pulmonary metastasis. The results of this series are addressed in the context of the previously reported series.

MATERIALS AND METHODS

Sixty-six patients with benign giant cell tumor of bone were treated between 1980 and 1991. Their demographics and clinical characteristics are listed in Table 1. Six of these patients (9.1%) had a course complicated by pulmonary metasta-

TABLE 1. Demographics and Clinical Characteristics of Patients With Giant Cell Tumor

Site of Initial Surgery	Number of Patients	M:F*	% Female	Age** (years)	Stage I (%)	Stage II (%)	Stage III (%)	Recurrence (%)	Metastasis (%)
UCLA	47	22:25	53.2%	36.7	6 (12.8%)	13 (27.7%)	28 (59.6%)	4 (8.5%)	2 (4.3%)
Not UCLA	19	7:12	63.2%	30.8	0 (0%)	0 (0%)	19 (100%)	14 (73.7%)	4 (21.1%)
All sites	66	29:37	56.1%	34.6	6 (9.1%)	13 (19.7%)	47 (71.2%)	18 (27.3%)	6 (9.1%)

* M:F = male to female ratio.
** Age = age at initial observation.

sis (Table 2). These six patients ranged in age from 17 to 42 years (mean 28.2) at the time of diagnosis. There were four males and two females.

Radiographic studies of the primary site and lungs of all six patients were reviewed by both the orthopaedic oncology surgeon and a musculoskeletal radiologist at the authors' institution. The pathology was evaluated by both the orthopaedic oncology surgeon and a pathologist specializing in musculoskeletal pathology.

CASE REPORTS

Case 1

A 17-year-old boy presented to his local physician with an expansile lytic lesion of the right proximal tibia extending to subchondral bone, and was referred to the authors' institution. Open biopsy, aggressive curettage of the tibial lesion, and wide excision of the soft tissue extension were performed. The tibial defect was then cauterized with phenol and filled with iliac crest bone graft. Pathology showed conventional giant cell tumor.

Routine follow-up examination two months postoperatively showed no evidence of local recurrence; chest radiographs were normal (Fig. 1-A). Despite repeated efforts to have him return to the clinic, the patient was lost to follow-up evaluation. Twelve months postoperatively, he was admitted to an outside hospital with right lower leg pain and chronic cough; radiographs of the patient's right leg and chest showed a local recurrence, as well as bilateral pulmonary masses (Figs. 1B and 1C). Percutaneous needle biopsy of a lung lesion showed metastatic giant cell tumor (Fig. 1D).

The patient was transferred to the authors' institution. Chest computed tomography (CT) scan showed extensive bilateral parenchymal metastases and mediastinal metastases, in addition to tracheal encasement and slight narrowing of the left mainstem bronchus by tumor. Because of this very extensive pulmonary involvement, the patient was a poor candidate for either radiation therapy or thoracic surgery. He underwent curettage and drilling of the tibial recurrence with phenol cauterization and polymethylmethacryalate placement. Pathology was, again, conventional giant cell tumor.

The patient was last seen in the authors' clinic 14 months after initial presentation. Chemotherapy was recommended, but the patient refused. He died 23 months after his initial presentation (and 11 months after diagnosis of the lung metastases) because of his extensive pulmonary disease.

Case 2

An 18-year-old man presented to an outside orthopaedic surgeon with a destructive lesion in the right lateral femoral condyle with impending pathologic fracture, and the patient was referred to the authors' institution for treatment.

Open biopsy, curettage, cauterization with hydrogen peroxide and betadine, and allografting of the defect were performed. Pathology showed conventional giant cell tumor.

Six months after his initial surgery, multiple bilateral pulmonary nodules were noted on a routine chest radiograph. Computed tomography scan demonstrated more than 100 nodules, most measuring 1–3 mm in diameter. The extent of lung involvement precluded complete tumor excision, and the patient had approximately ten

of these resected from each lung via a median sternotomy. Pathology showed benign giant cell tumors with peripheral bone deposition (Fig. 2A).

No adjuvant therapy was administered. The patient did well clinically, and resumed sporting activities, including basketball and tennis. Twenty-six months after lung resection, he had no evidence of local recurrence in the femur, but still had multiple bilateral lung and extrapleural nodules, the largest being a 7-cm parenchymal nodule and a 6-cm extrapleural mass (Figs. 2B and 2C).

The patient remained asymptomatic from both a pulmonary and musculoskeletal standpoint, and did not return to the clinic for another 24 months. At that time, his range of motion of the right knee was 0°–90° flexion, with no extensor lag. There was no evidence of local recurrence, either clinically or radiographically. Chest radiographs and CT scan showed a marked decrease in the size of the lung parenchymal and extrapleural nodules in the two years since his previous studies (Figs. 2D and 2E). Further regression of the pulmonary nodules was evident on the next set of chest radiographs an additional ten months later (five years after median sternotomy).

Case 3

A 42-year-old woman fell on her right knee. After three months of continuing knee pain, the woman finally sought orthopaedic attention. Physical examination at that time showed a slight fullness and tenderness over the right fibular head. Plain radiographs showed a lytic lesion of the right proximal fibula, and curettage of the fibular lesion was performed. Pathology demonstrated benign giant cell tumor. *En bloc* resection of the fibular head was performed three years later for local recurrence. Pathology again showed conventional giant cell tumor. Preoperative chest radiographs showed multiple bilateral lung nodules. Percutaneous needle biopsy of one of the lung lesions showed conventional giant cell tumor.

The patient was referred to the authors' institution and underwent resection of four right lung metastases. Left lower lobectomy and lingulectomy for three left lung metastases were performed the next month. Pathology from each of these specimens was also benign giant cell tumor.

The patient has remained asymptomatic and without any clinical or radiographic evidence of local or pulmonary recurrence for more than ten years after pulmonary resection.

RESULTS

Six of the 66 patients (9.1%) with giant cell tumor of bone who were treated from 1980 to 1991 had pulmonary metastasis of the tumor. The initial presentation of the primary tumor included pain in all six patients. Pain alone was found in two patients; pain with a palpable mass in two others; pain and a limp in one patient; and a pathologic fracture in the sixth patient. The primary tumor was located in the proximal tibia in three of six cases (50%), with one involving the distal femur, one in the proximal fibula, and the other being multicentric. All six patients had Stage III lesions by the time pulmonary metastasis was diagnosed. The average time until diagnosis of metastasis was 23 months (range six to 45), and one patient had pulmonary symptoms (persistent cough) at the time of diagnosis of pulmonary metastasis.

The follow-up period ranged from 23 months to more than 16 years after initial presentation (mean, 9.5 years), and from 11 months to more than 12 years (mean, 7.5 years) after initial pulmonary resection. All five surviving patients have been observed for at least five years since pulmonary resection.

Local recurrence was noted in five of the authors' six patients (83%) with pulmonary metastasis, either concurrent with, or before, diagnosis of the metastasis. All four patients who had their initial surgery elsewhere had a local recurrence, as did one of two patients who had their initial surgery at the authors' institution. No patient had pulmonary metastasis diagnosed at the time of initial presentation. The pathology of all primary lesions was conventional giant cell tumor without evidence of malignancy. The pa-

TABLE 2. Patients With Lung Metastases of Benign Giant Cell Tumor

Case	Gender, Age at Diagnosis	Primary Location	Treatment of Primary	Recurrence and Treatment	Time Until Metastasis Diagnosed (months)	Pulmonary Symptoms	Lung Involvement	Surgical Treatment of Metastases	Adjuvant/ Neoadjuvant Treatment of Metastases	Follow-Up Time (after detection of pulmonary metastases)
1	M, 17	Proximal tibia	Curettage, phenol, bone graft	Curettage, phenol, drilling, PPMA packing	12	Cough	Diffuse, bilateral lung involvement; mediastinal mass; tracheal encasement	—	—	Died at 11 months
2	M, 18	Distal femur	Curettage, hydrogen peroxide, betadine, allograft	—	6	—	>100 nodules, bilateral	Incomplete excision (~20 excised)	—	Alive with regression of bilateral pulmonary nodules at 5 years
3	F, 42	Proximal fibula	Curettage	Fibular head excision	37	—	4 right lung nodules 3 left lung nodules	Complete excision	— NED at 10 years	
4	M, 29	Proximal tibia	Curettage, bone graft	Curettage, bone graft and excise soft tissue mass Curettage, hydrogen peroxide, betadine, PMMA packing Proximal tibial replacement	16	—	Dozens of nodules, bilateral	Incomplete excision (28 right and 13 left lesions excised)	—	Alive with multiple, bilateral pulmonary nodules (stable size) at 5 years
5	F, 41	Proximal tibia	Curettage, bone graft	Curettage, cryosurgery, PMMA packing	45	—	3 right lung nodules	Complete excision	—	NED at 12 years
6	M, 22	Proximal phalanx of ring finger (multicentric)	Curettage, bone graft	Lt. 4th ray resection Soft-tissue resection (lt. palm) Radiation therapy (lt. hand)	27	—	1 right lung nodule <10 left lung nodules	Complete excision	Combination chemotherapy (after right and preceding left thoracotomy)	NED at 10 years

thology of the five recurrent primary tumors and the metastatic lesions was also benign giant cell tumor in all cases, and was similar to that of the primary tumors.

One patient had a locally recurrent tumor treated with 3000 rads of radiation before metastasis, but there was no evidence of malignant transformation, either locally or in the pulmonary nodules, at any time. The patient has been closely followed for more than ten years since receiving the radiation therapy.

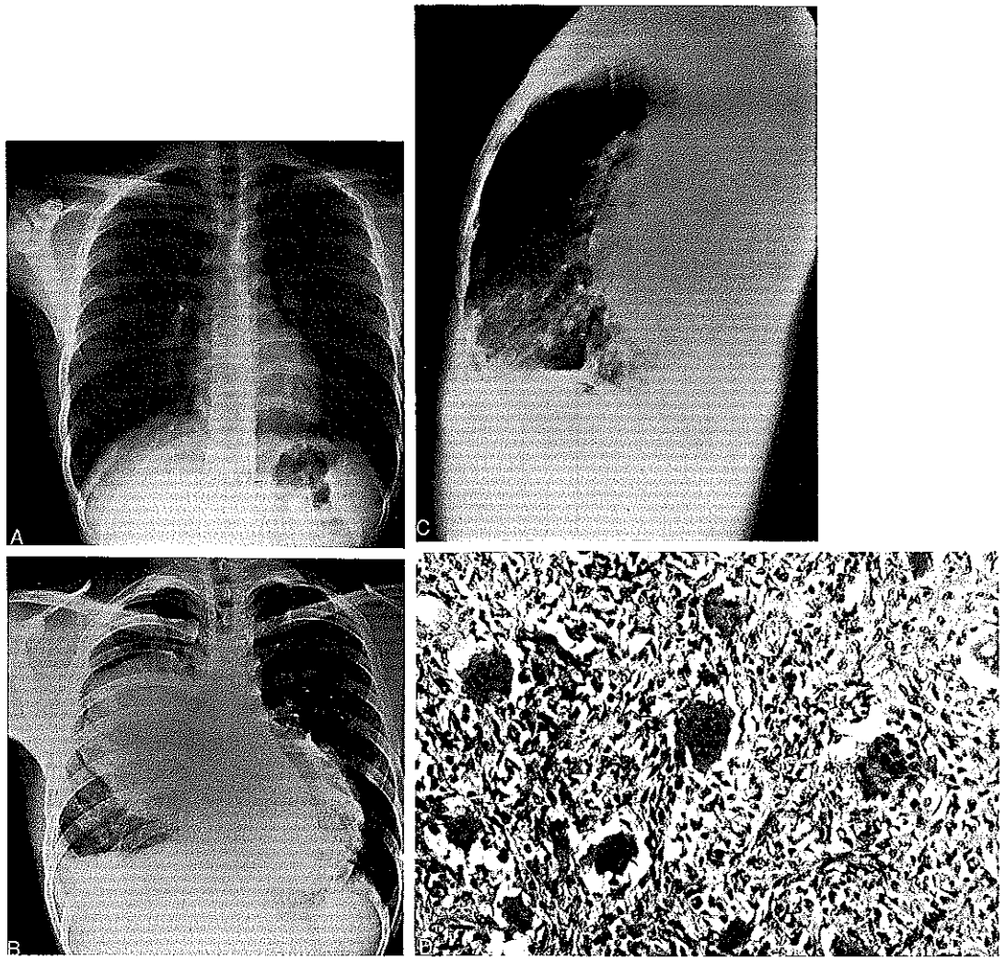
The lung lesions were treated with complete excision in three patients (one of whom also received adjuvant chemotherapy), partial excision in two patients, and no treatment in one patient.

The patient with extensive bilateral disease who received no treatment died 11 months after diagnosis of the metastases and 23 months after initial presentation. The three patients who underwent complete excision of all lung lesions remain alive and without any evidence of recurrent pulmonary disease at ten, ten, and 12 years after pulmonary resections and 13, 14, and 16 years after initial presentation, respectively. In two patients in whom complete resection of pulmonary metastases was impossible, incomplete excision was performed. These patients remain asymptomatic with presence of multiple bilateral pulmonary nodules five and 5.5 years after the pulmonary resections (and 5.5 and seven years after initial presentation), respectively. One of these patients, described in Case 2, had marked regression of his lung metastases over the ensuing years, despite no adjuvant treatment.

Lt. 3rd, 5th ray resections	2	2	NED, no evidence of disease.
Soft-tissue excision (rt. heel)	2	2	
Rt. BKA	2	2	
Lt. fibular head resection	2	2	
Rt. distal radius curettage, phenol, bone graft	2	2	
Lt. calcaneal curettage, phenol, bone graft	2	2	
Lt. femoral neck curettage, phenol, internal fixation	2	2	

DISCUSSION

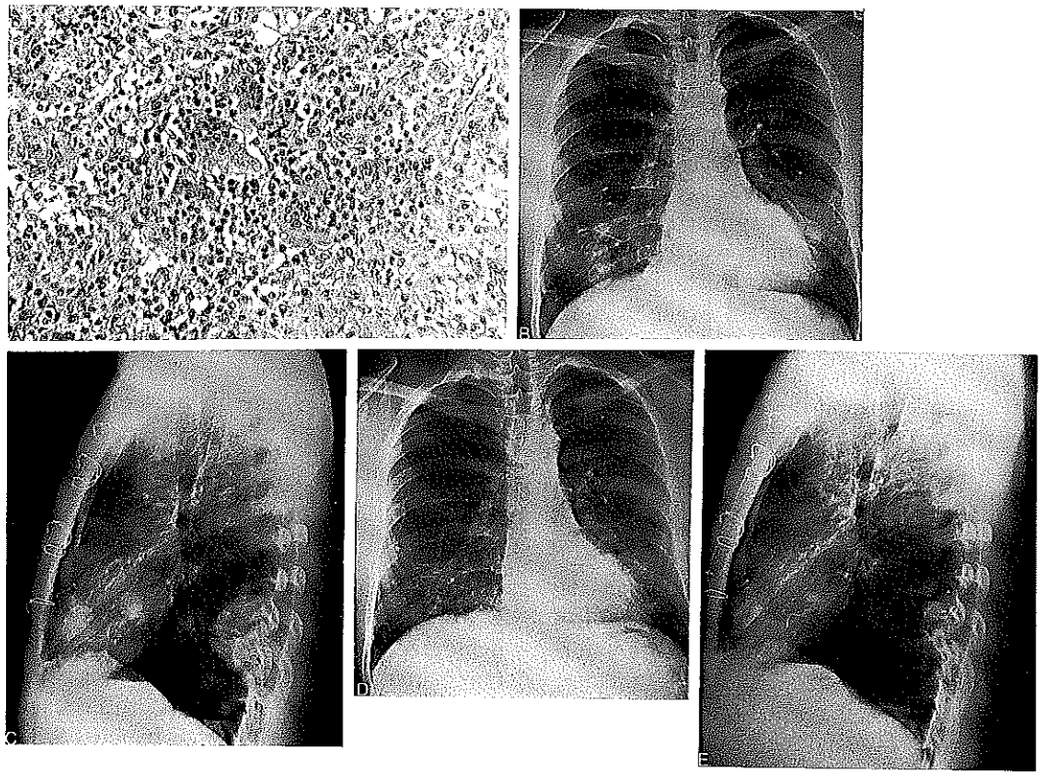
Like chondroblastoma, giant cell tumor is a benign bone tumor that may metastasize to the lung, and, on rare occasions, may even cause death.[25] A review of the literature puts the risk of local aggressiveness, recurrence,



Figs. 1A–1D. (A) Normal anteroposterior chest radiograph obtained two months after curettage, phenol cauterization, and bone grafting (Case 1). (B and C) Anteroposterior and lateral chest radiographs in Case 1 show extensive bilateral pulmonary metastasis. (D) Percutaneous needle biopsy of the lung demonstrates a conventional giant cell tumor (Case 1). (Stain, hematoxylin and eosin; original magnification, ×250.)

and pulmonary metastasis from giant cell tumor in perspective.

Metastasis of benign giant cell tumor occurs in 0–7% of large series.[2,3,7–9,16,26,32,33,39,42,46,47,49] The great preponderance of metastases are to the lung, although metastases to the brain, kidneys, adrenals, gastrointestinal tract, other bones, and skin have been described.[1,7,11,16,66,42,47,49] Pulmonary metastasis of benign giant cell tumor of bone was first reported in 1926 by Finch and Gleave.[15] Since that time, there have been approximately 50 cases reported in the literature.[1,4,10,16,18,20,22,24,26,27,49,36,43,47,49] Most of these have been case reports, although, in the last decade, larger series have been published from leading orthopaedic oncology centers in this country and Eu-



Figs. 2A–2E. (A) Photomicrograph of one of many removed lung nodules in Case 2 demonstrates conventional giant cell tumor. (Stain, hematoxylin and eosin; original magnification, ×250.) (B and C) Anteroposterior and lateral chest radiographs in Case 2 obtained 26 months after median sternotomy show the presence of multiple bilateral lung nodules and a large extrapleural mass. (D and E) Anteroposterior and lateral chest radiographs (Case 2) obtained four years after median sternotomy show a significant regression in the size of the parenchymal and extrapleural nodules in the preceding two years, despite no further treatment.

rope.[2,3,26,39,49] The report of metastasis in two immunocompromised hosts has caused speculation that immunocompetence may help protect against metastasis.[3,29]

The 9.1% rate of metastasis in this study is higher than that found in the literature. This is because of the very high rate (21.1%) of pulmonary metastasis found in patients referred to this institution after primary treatment. The extremely high rate found in this group of referral patients is probably attributable to the fact that all 19 of them had Stage III lesions, three of which had already metastasized before referral. The rate of 4.3% pulmonary metastasis for lesions treated initially at this institution is similar to those found in the literature.

The cause of the metastases is unclear. The vascularity of giant cell tumors with frequent encroachment into peritumoral blood vessels is well described, with some authors having noted that the tumors may even be pulsatile.[3,6,7,12,17,31,40,44] Sladden[44] reported vascular invasion by five of 11 giant cell tumors (45%) in 1957, despite the fact that none of these tumors had metastasized. According to Dahlin and Unni, intravascular extension of giant cell tumor cells ''does not seem to correlate with increased risk'' to the patient.[10]

In cases of metastasis, there is, at times, vascular invasion by the primary tumor, but this is more often absent.[3,6,7,17,31,40] In the current study, only one of six patients (Case 3) with pulmonary metastases had encroachment of giant cell tumor cells on vascular lumina.

Most metastases are diagnosed within the first few years after diagnosis of the primary, although they may not be found for ten years or more.[31,39,47,49] Some authors have postulated that the metastases are the result of iatrogenic seeding of the blood stream and lungs at the time of surgery for the primary lesion.[19,26,37] However, several cases in the literature demonstrate that the pulmonary lesions may be detected simultaneous with, or even before, the detection of the osseous primary.[3,16,31,45,49] Katz *et al.*[23] did a growth rate analysis on a lung metastasis from giant cell tumor, and concluded that the metastasis was present for years before the primary was even diagnosed. Hematogenous metastasis is not the only pathway for giant cell metastasis; lymph node metastases have also been reported.[11,16,19]

The six patients at this institution had pulmonary metastasis diagnosed six to 45 months (mean, 23.8 months) after initial surgical treatment. All six patients had undergone curettage as part of the initial treatment of the primary lesion.

Although no isolated radiographic, clinical, or histologic grading system for giant cell tumor can give an accurate prognosis regarding the behavior of a particular giant cell tumor, the surgical staging system proposed by Enneking[14] does have some prognostic value. Stage I benign tumors generally account for 10–15% of giant cell tumors; treatment by curettage yields good results.[3,4,13,14] Stage II accounts for approximately 75% of all giant cell tumors; treatment may be either curettage or wide excision, both of which yield good results.[3,4,13,14] Stage III tumors are reported to account for 10–15% of giant cell tumors; wide resection is often performed for Stage III lesions, generally with good results.[3,4,13,14] Stage III tumors, despite their reported rarity, account for the majority of pulmonary metastases, although these may be seen with Stage II primaries, as well.[2,3,14,26]

At the authors' institution, the frequency of the stages of tumor is different from those generally reported (Table 1). Although *en bloc* resection is rarely performed, only four of 28 patients (14.3%) receiving initial treatment at the authors' institution for Stage III lesions have had local recurrence. One of these four had pulmonary metastases. Also, only two of the 28 patients presenting with Stage III giant cell tumor had pulmonary metastasis. There were no local recurrences or pulmonary metastases in the 19 patients undergoing initial treatment at this institution for Stage I or Stage II giant cell tumor of bone during the period of study.

Review of the literature shows that the demographics for metastatic giant cell tumor patients differ slightly from those for giant cell tumor patients overall. The age at presentation is similar; the patients with pulmonary metastasis from benign giant cell tumor of bone range in age from 12 to 61 years (mean, 29 years). There is, however, a slight male predominance (55%). Fewer than one half of the primaries with lung metastases are around the knee; the most common sites for the primary are the distal femur (28%), distal radius (17%), and proximal tibia (12%), although other sites include the proximal femur, distal tibia, distal ulna, metacarpals, phalanges, pelvis, sacrum, coccyx, and proximal and distal humerus. Hand primaries tend to metastasize more frequently than do primaries in other sites (two of 21 cases in the study by Averill *et al.*[1] study). Recurrence is also seen somewhat more frequently in the tumors that metastasize (66%).

The differences in patient demographics and tumor characteristics between giant cell tumor patients in general and those with pulmonary metastases may be because of the relatively small number of reported cases

of pulmonary metastasis. Location of the primary tumor in this series of patients with pulmonary metastases more closely resembles the overall giant cell tumor experience, with three tumors found in the proximal tibia, one in the distal femur, and one in the proximal fibula. The case of metastasis of the multicentric giant cell tumor is difficult to categorize because of its rarity. Recurrence was seen in five of the six patients before, or synchronous with, the diagnosis of pulmonary metastasis. Flow cytometry, previously thought to be promising, is of little value in assessing the likelihood of metastasis in benign giant cell tumor.[41,51]

Obtaining a tissue diagnosis of a suspected pulmonary metastasis is very important. Such a lesion could be the result of many processes: metastasis of the benign primary, metastasis after the primary undergoes malignant degeneration, or an unrelated process. As well as being of intellectual interest, this also has important therapeutic and prognostic ramifications. Although open biopsy is usually performed in such cases, transthoracic needle aspiration has also been described,[47] and was used in two cases in the current series.

Pulmonary metastases from giant cell tumor have been treated in various ways throughout the years. Although, initially, many such metastases went untreated, the treatment of choice is now felt to be surgical extirpation.[2,3,16,17,19,20,26,31,35] Complete excision of benign giant cell tumor lung metastases, as was performed in the authors' third, fifth, and sixth cases, results in excellent long-term survival. The majority of such patients have no evident disease at two to ten years or more postoperatively.[2,3,20,21,30,-37,39,49,50] Some have recurrent metastases, and surgical excision is, again, the treatment of choice.[3,25,38,48] Unlike other types of pulmonary tumors, adjuvant therapy is not indicated when complete excision can be performed.[2,3,26]

However, complete excision of all lung metastases is often not possible because of the extent of pulmonary disease. In such cases, partial excision may be performed, as in the authors' second and fourth cases. Long-term results with incomplete excision have also been excellent, but, because many of these patients have undergone adjuvant chemotherapy or radiotherapy, the effect of incomplete excision alone is harder to ascertain.[3,16,39] The two patients treated with incomplete excision in this series (Cases 2 and 4) did not receive adjuvant therapy; both were alive with disease at five years after pulmonary resections. Neither was symptomatic at last follow-up examination, and one had had a marked decrease in the size of pulmonary metastases in the preceding three years.

Some patients are not diagnosed with metastases until they are unresectable. Adjuvant therapy may be used in such cases. Chemotherapy alone has been reported in two patients with pulmonary metastasis of benign giant cell tumor.[24,26] One of these patients had chest pain and hemoptysis resolve while receiving chemotherapy.[24] Both patients were alive with disease at 2.25 and 2.5 years after diagnosis of metastasis, although further follow-up evaluation has not been reported. One patient in the authors' series (Case 1) refused chemotherapy, although it was recommended for his inoperable pulmonary disease, and he died less than one year later.

Radiation therapy has also been reported as the sole treatment in two additional patients with pulmonary metastasis of benign giant cell tumor.[31,45,50] One patient was alive without evidence of disease 22 years after treatment, and the other was alive with disease at the completion of treatment. Radiation therapy was not used in this study.

Radiation therapy followed by chemotherapy has been tried in one patient with unresectable lung metastases.[39] The patient died of complications of the chemotherapy one year after diagnosis of the metastasis.

Even those with residual pulmonary tumors after treatment may live for many

years.[3,26,31,39] In fact, authors have previously noted the fact that the pulmonary metastases may be self limited.[3,26,34,35] In addition, spontaneous regression of all, or some, of the metastases may be seen. This was first described in 1970 by Goldenberg *et al.*, and has since been described in four additional cases with biopsy-proven benign giant cell tumor metastases.[31,45,49] Complete regression in three cases of apparent giant cell tumor metastases that were not biopsy proven has also been reported.[2,28] The authors' second case represents the fifth patient with biopsy-proven pulmonary metastases from benign giant cell tumor of bone with spontaneous regression.

Overall, the pulmonary metastases are fatal in approximately 10–20% of cases.[2,3,31,49] Although there have been few reported cases of untreated pulmonary metastases of benign giant cell tumor, the majority of these patients died quite rapidly from their disease.[1,11,15,16] Others who underwent partial or complete excision also died from this condition.[3,16,39,42,49] Although the overall survival rate is certainly better than that for other types of metastatic tumors to the lung, this mortality underscores the fact that this is far from a ''typical'' benign tumor or a typical metastatic malignant tumor. The biologic behavior of giant cell tumor appears to fall between that of a conventional benign tumor and that of a conventional malignant tumor. The terms ''aggressive'' or ''low-grade neoplastic'' would appear to apply best to the giant cell tumor with a wide biologic range, varying from apparently completely benign to rare examples leading to patient demise after lung dissemination. The unpredictable behavior of giant cell tumor is highlighted by the fact that one of the authors' patients (Case 2), despite the presence of over 100 pulmonary nodules in 1988 and the resection of only approximately 20 of these, is alive and physically well five years later (with radiographic evidence of significant regression of the metastases). In contrast, when this disease proves fatal, it often does so within one year of diagnosis of pulmonary metastasis, as was seen in the current authors' first case.[1,11,15,16]

As awareness of the potential for pulmonary spread has increased, routine chest radiographs are now generally performed after diagnosis of the primary giant cell tumor. As a result, the presentation of pulmonary metastasis is now more commonly a subclinical, radiographic one. The three patients in the authors' series most recently diagnosed with pulmonary metastasis (Cases 1, 2, and 4) were diagnosed in this institution at six to 16 months (mean, 11.3 months) after diagnosis of the primary, in contrast to a range of 27–45 months (mean, 36.3 months) in the earlier patients diagnosed at outside institutions.

The lesions may first be noted on plain radiographs or chest CT scans, and may even be evident on bone scan.[22] Radiographic findings include pulmonary nodules (sometimes calcified) or masses (usually basilar, peripheral, or both in location), mediastinal masses, and pleural effusion.[3,12,18,19,49] Although most pulmonary metastases are subclinical, some patients do manifest pulmonary symptoms, such as cough, hemoptysis, dyspnea, dysphagia, or chest pain.[11,14,20,22,23,31,45,47,50] Systemic symptoms, such as weight loss, may also be present.[47,50] One of the patients in this series (Case 1) had pulmonary symptoms (a persistent cough), and none had systemic symptoms.

Close follow-up evaluation of all giant cell tumor patients with both clinical and radiographic evaluations is essential. In addition to radiographic evaluation of the primary tumor, baseline plain radiographs and CT scan of the chest should be performed at the time of presentation. Plain radiographs of the primary site and chest should then be obtained every three months for the first two years, with CT scans of these areas and bone scans every six months during the first two years, as well. For the next two years, plain films and clinical follow-up

evaluation should be obtained every six months, with annual CT scans and bone scans. Plain films and clinical examinations should be performed annually thereafter. Although the authors have seen local recurrences as long as five years after primary treatment (and others have reported them even later), the vast majority of all local recurrences and metastases will occur within the first two to three years, and treatment is much more easily accomplished, with less morbidity and greater success, if undertaken early. Their study and others support the view that, although 1–2% of patients with giant cell tumor may succumb to lung dissemination, it remains impossible to predict by any known means to whom this will occur. The authors do not, therefore, believe that this relatively rare tragic circumstance should dictate overly aggressive treatment, such as amputation, for the usual or even locally recurrent giant cell tumor.

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