England, where Fell reported 137 pharyngeal infections in patients aged 15 to 25 years.[4] Most of these patients had sore throats and 65 had an "irritant" maculopapular rash. Two recent reports emphasize other aspects of *C hemolyticum* infections: Wickremesinghe reported 16 cases from Sri Lanka and noted the rarity with which *C hemolyticum* is isolated in pure culture—a feature shared with other species of *Corynebacterium*[5]; and Green reported a single case of pharyngitis associated with a greyish-yellow membrane mimicking pharyngeal diphtheria.[6]

The three cases described here are consistent with the reported experience in several ways. Although none of the patients had a skin rash, all fell within the 15- to 25-year-old age group, which appears to be at greatest risk for *C hemolyticum* infection. All three had initial symptoms of nonspecific tonsillitis and pharyngitis, and all eventually responded to penicillin in combination with drainage. Leukocytosis, reported to be uncommon in uncomplicated pharyngitis, was present in all of our patients. However, despite the frequent association of *C hemolyticum* with pharyngeal infection, the organism has not previously been implicated in the local suppurative complications of acute mucosal infection of the oral cavity. In past series[15,16] of the microbial flora of peritonsillar abscesses, *Streptococcus* sp (alpha and beta hemolytic) have been the most common isolates, with *Bacteroides* sp the next most frequent. *Staphylococcus aureus, Hemophilus influenzae, Klebsiella pneumoniae* and *Streptococcus pneumoniae* were found in rare instances as well. No isolate of any species of *Corynebacterium* has been reported.

This report further substantiates the pathogenic potential of *C hemolyticum* in health, young adult hosts. Sepsis with this organism has been described and the present study provides evidence of local invasiveness. Awareness of the pathogenicity of *C hemolyticum* and the use of appropriate media to optimally demonstrate the characteristic β-hemolysis (for example, rabbit or human blood agar) will facilitate identification of these bacteria in oropharyngeal infections. Fortunately the strains described in the literature and those seen in our patients have been uniformly sensitive to the antibiotics commonly used for bacterial tonsillitis. The major concern is that use of sheep-blood containing agar media on which hemolysis is minimal and delayed may lead to an incorrect diagnosis of viral pharyngitis with the result that antibiotic therapy is withheld. This may lead to progressive and invasive infection such as that observed in these three cases.

Addendum

One additional case of peritonsillar abscess associated with *C hemolyticum* was reported after the preparation of this manuscript.[17]

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Multiple Synchronous Lesions of Acral Metastasis

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METASTASIS to the hands and feet (acral metastasis) is rare. Recognition of such lesions as metastatic is often difficult and a degree of clinical suspicion is required. These lesions almost inevitably foretell an ominous prognosis. One small subgroup of these patients has multiple synchronous acral metastatic lesions, rather than single lesions. Not only is their prognosis poor but, due to their unusual presentation, the lesions may be even less likely to be recognized for what they are and other disorders, including osteomyelitis or cardiac embolic phenomena, may be considered and evaluated first. We report a case of multiple synchronous acral metastatic lesions in a patient who had lung cancer.

Report of a Case

The patient, a 63-year-old man, had had a left upper lobectomy for poorly differentiated squamous cell carcinoma of the lung seven years before the present admission. Liver-spleen scan, brain scan and bone scan

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showed no abnormalities at that time. The patient refused postoperative radiation therapy.

His subsequent course was unremarkable until three weeks before the present admission when shortness of breath developed and he was noted to have a right middle lobe pneumonia. He was treated with antibiotics with good clinical response. Because of his history, the patient underwent bronchoscopy, which showed a tumor in the right bronchus intermedius. A biopsy specimen showed poorly differentiated squamous cell carcinoma, believed to be a second primary. Computed tomographic (CT) scan of the head and liver-spleen scan showed no evidence of metastasis. The patient was not a surgical candidate because of poor pulmonary function and was treated with irradiation to the lung tumor and hilum.

Three weeks after the radiation therapy was started, the patient noted a reddened soft tissue swelling of the fifth distal digit, left hand, and of the right palm, as well as erythema and mild swelling on the dorsum of the left foot. He stated that these had been slowly developing over the previous two weeks.

Past medical history and review of systems were unremarkable except for chronic obstructive lung disease. The patient was previously a construction worker and had a 150-pack-year history of smoking.

On physical examination, the patient's vital signs were stable and he was afebrile. He appeared mildly cachectic but in no acute distress and was alert, oriented and answered questions appropriately. The chest was clear to auscultation and percussion, with egophony heard at the right upper lung field. The cardiac examination elicited no abnormalities. Examination of the extremities showed pronounced clubbing of all digits. The fifth digit of the left hand had a violaceous enlargement of the central tuft of the distal phalanx. There was pustule formation and it was very tender with minimal warmth (Figure 1). The right hypothenar eminence had a similar lesion with a central, draining, tender ulcer (Figure 2). The left big toe had mild swelling, erythema and tenderness at the first metatarsophalangeal joint and proximal phalanx.

X-ray studies of the hands and feet showed lytic lesions at the left fifth distal phalanx and bone destruction at the medial distal aspect of the first proximal phalanx of the left foot (Figure 3). No bony abnormalities were noted in the right hand. Bone scan of the entire skeleton showed only focal areas of increased activity in the left foot.

Course

The lesions were originally believed to be infectious in origin or possibly thromboembolic phenomena. No clinical evidence of bacterial endocarditis or other cardiac pathologic process was found, though echocardiogram was not done. Incision and drainage of the left fifth digit lesion showed no bacteria or fungus on a Gram's stain and bacterial cultures were negative. There

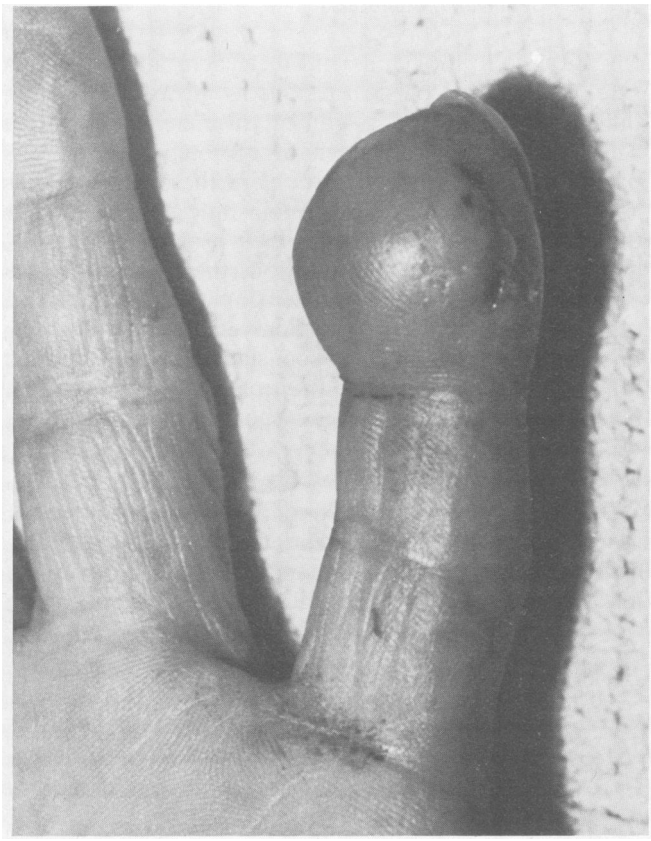

Figure 1.—Photograph of fifth digit of the left hand.

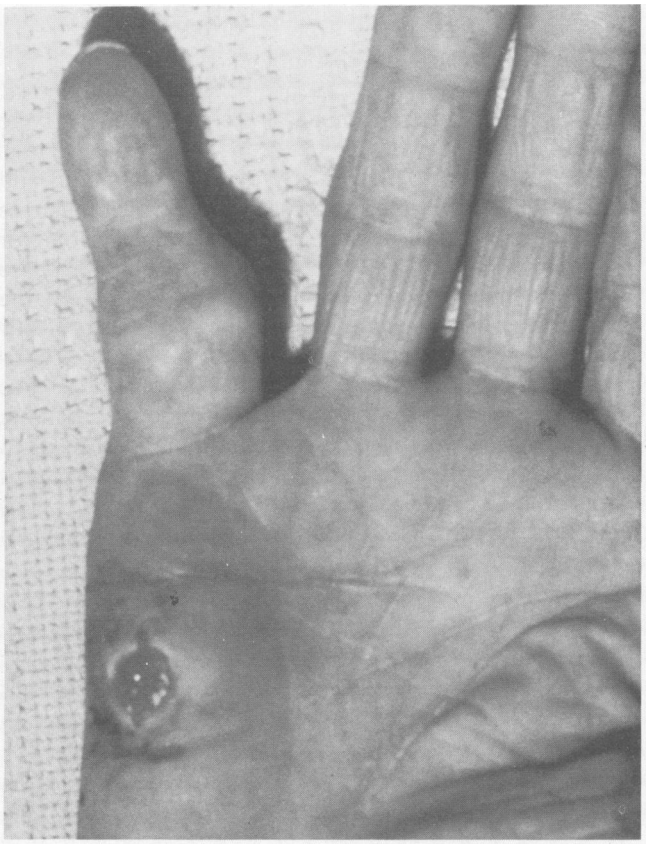

Figure 2.—Photograph of the right hypothenar eminence.

was no improvement after a course of antibiotics. The patient subsequently underwent amputation of the fifth digit at the proximal interphalangeal joint following a suspicion that this was metastasis. The bulbous mass removed (2.0 cm by 2.5 cm) was semisoft with a homogeneous grey appearance. The bone also was soft. On microscopic examination a deep, widely infiltrating, poor to moderately differentiated squamous cell carcinoma was seen, identical to that seen on the surgical slide of the primary pulmonary cancer (Figure 4).

The surgical site healed well and a course of radiation therapy to the right hand and left foot was begun. There was significant amelioration of the lesions but incomplete resolution. At the completion of irradiation the patient had a painful area in the midshaft of the right radius. On radiography there was a lytic lesion that had not been included in the previous irradiation

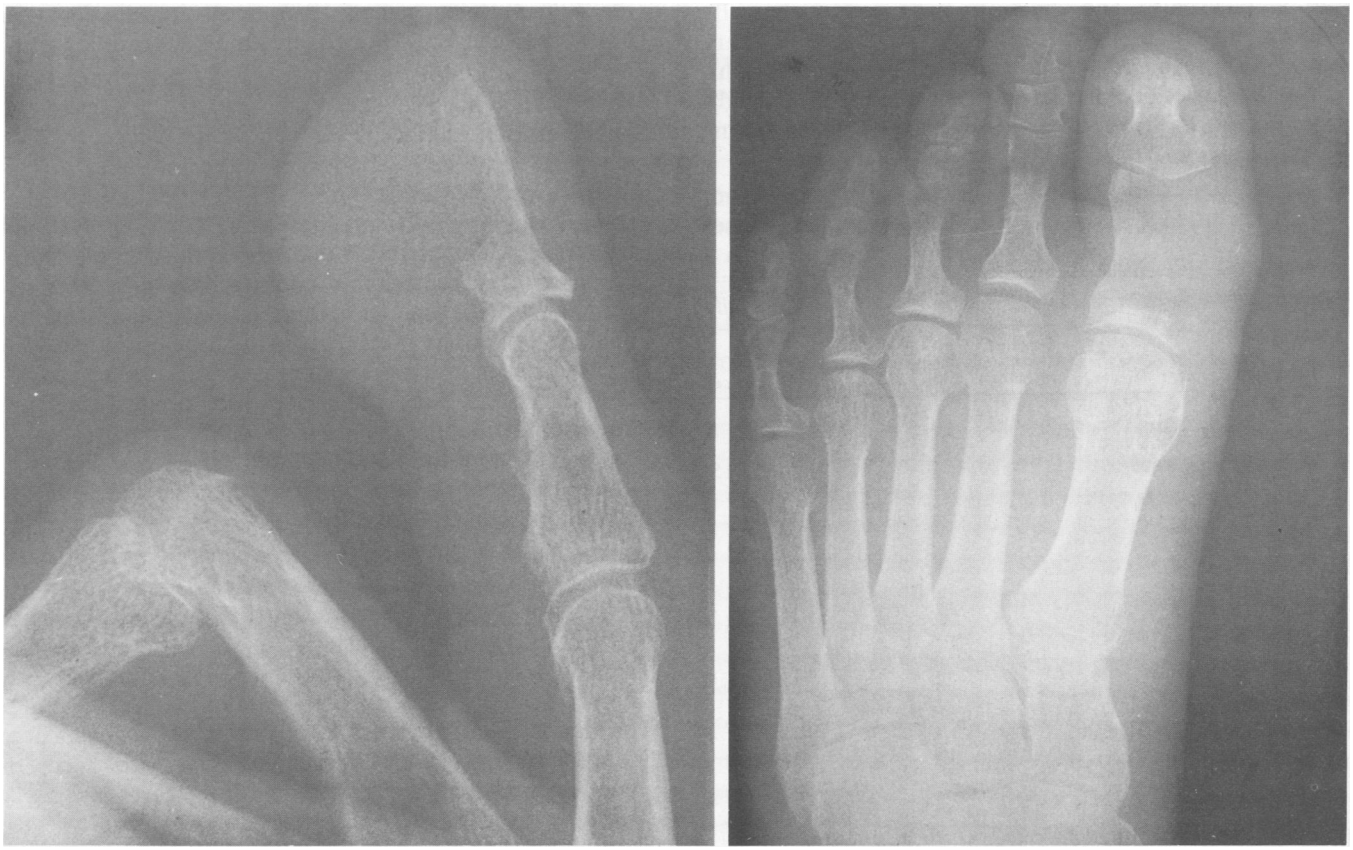

Figure 3.—Left, Radiograph of the fifth digit of the left hand, which shows soft tissue swelling and erosion of bone in the distal phalanx. **Right,** Radiograph of the left foot, which shows erosion of bone in the first proximal phalanx.

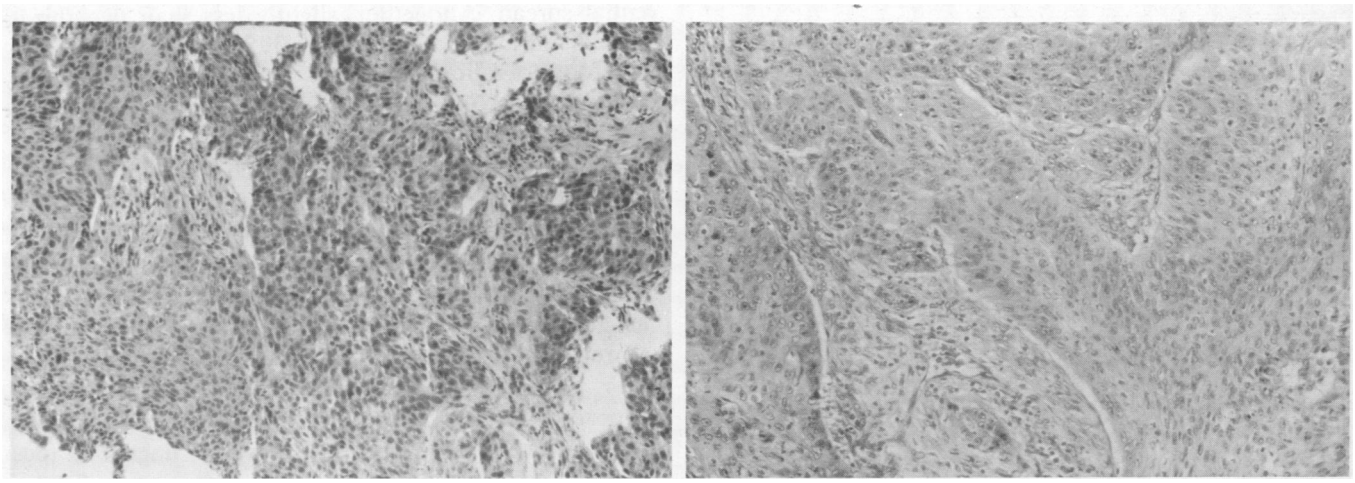

Figure 4.—Left, Photomicrograph of the bronchial biopsy specimen showing poorly differentiated squamous cell carcinoma. (Reduced from magnification ×40). **Right,** Photomicrograph of the soft tissue metastasis in the amputation specimen. The histologic pattern is identical to the bronchial biopsy material. (Reduced from magnification ×40.)

port. His condition gradually deteriorated, with increasing weakness and shortness of breath. He died three weeks after complete courses of palliative radiation treatment to both extremities, eight weeks following appearance of the acral metastasis. Autopsy was not done.

Discussion

The first description of acral metastasis was in 1906 by Handley,[1] in a case of breast cancer metastatic to the metacarpals. The diagnosis was made clinically without benefit of radiography. A year later, Massary and Weill[2] reported the first case of roentgenographically diagnosed acral metastasis. A number of additional reports have been published since, including several reviews.[3,4]

Kerin[4] reviewed 30 cases of metastasis to the hand, which included 7 new cases in addition to 23 cases from previously published reports. In all, 43% (13) of the patients had primary lung carcinoma, three had breast cancer, three had renal cancer, two had parotid cancer and there were nine single cases of various other primaries.

Bouvier and co-workers[3] in 1971 annotated 135 cases of metastasis to the hands and feet, most of which were found in the literature, as well as several cases not previously reported. Of these, 37% were from a bronchogenic carcinoma primary. Breast cancer accounted for 20%, uterine cancer 10%, gastrointestinal cancer 8%, renal cancer 7% and prostate cancer 3%.

Since 1971, 49 additional cases of acral metastasis have been reported. These include the case presented above and an additional patient we have recently seen who had large cell carcinoma of the lung and metastasis to the left middle finger. This patient's acral metastasis was originally manifested by swelling and joint tenderness thought to be due to trauma. Initial radiographs gave unremarkable findings, but on a later examination there was an erosive lesion in the proximal phalanx of the left third digit. A whole-body bone scan showed multiple areas of increased isotope concentration consistent with metastasis, but no lesions were noted in the hands. We then requested spot images of the hands and the lesion in the left third digit was identified. The patient died two months after initially complaining of the painful digit.

Tables 1 and 2 are updated versions of Bouvier's list of case histories. Metastasis from lung cancer accounts for 39% of all cases. Next is breast cancer with 19%, followed by metastatic lesions from the gastrointestinal tract (11%), uterus (8%), kidney (8%), prostate (3%) and parotid gland (2%). The other primaries account for 1% or less of cases. Three fourths of lung cancer acral metastasis, two thirds of the lesions from the gastrointestinal tract and 59% of those from breast are found in the hand. However, foot metastasis accounts for 93% of those from uterine cancer primaries. The number of cases from other primaries is too small to make conclusions about preferential spread. Altogether, slightly less than two thirds were hand metastasis, whereas 39% were metastatic to the foot (a ratio of 1.6:1).

Acral metastasis may be significantly more common than is clinically recognized. It has been suggested that in advanced metastatic cancer little attention is given to the feet of patients who are not ambulatory[20] and the hands and feet are usually not included in radiographic studies of the skeleton.[4] In addition, unless definitely suspected, these lesions are not searched for at autopsy. Bone scans are commonly used in the search for bony metastasis. Many institutions, however, do not include the hands and feet in the area of exposure. Even in those institutions where total body scans are routinely done, lesions in the fingers or toes may not be detected unless specific spot images of those areas are made. This underreporting is probably even more significant when attempting to document the per-

TABLE 1.—*Reports of Metastasis to the Hand By Primary Site*

Site of Primary Cancer	*Cases of Metastasis to Hand*	*Percentage of Total**	*References*
Lung	55	30	3,5-14
Breast	20	11	3,14-17
Gastrointestinal tract	12	7	3,8,14,15
Kidney	6	3	3,14,15
Parotid	4	2	3
Prostate	3	2	3
Oral cavity	2	1	3,18
Lymphosarcoma	2	1	3
Uterus	1	< 1	3
Bladder	1	< 1	3
Tonsil	1	< 1	3
Skin	1	< 1	3
Brain tumor	1	< 1	3
Testicle	1	< 1	14
Sympathoblastoma	1	< 1	3
Cervix	1	< 1	19
Osteosarcoma	1	< 1	14
Chondrosarcoma	1	< 1	13
TOTAL	114	62	

*Total number of cases of acral metastasis—184.

TABLE 2.—*Reports of Metastasis to the Foot by Primary Site*

Site of Primary Cancer	*Cases of Metastasis to Foot*	*Percentage of Total**	*References*
Lung	16	9	3,6,8,17,20,21
Breast	14	8	3,20
Uterus	13	8	3
Kidney	9	5	3,20
Gastrointestinal tract	7	4	3,13,20,22
Prostate	3	2	3,6
Bladder	2	1	3,20
Thyroid	1	< 1	3
Vagina	1	< 1	3
Ovary	1	< 1	3
Submaxillary gland	1	< 1	23
Epipharynx	1	< 1	3
Unknown primary	1	< 1	20
TOTAL	48	38	

*Total number of cases of acral metastasis—184.

centage of metastatic lesions occurring in the upper versus the lower extremities.

There are few studies describing the overall incidence of primary cancers metastasizing acrally. In one study[24] 4 out of 2,532 patients (0.16%) with bronchogenic carcinoma had phalangeal metastasis, whereas 67% had metastasis to vertebrae. All the patients were examined radiologically, but it is unclear when in the course of the disease the studies were done or the relative incidence of metastasis during the course of each patient's time at risk. DePass and Roswit[25] found 2 patients out of 800 with bronchogenic cancer who had metastatic lesions to the bones of the hand.

Early diagnosis of acral metastasis may be very difficult. The site can be swollen, erythematous, warm and painful and may resemble a felon[26] or osteomyelitis.[27] The symptoms may also resemble monoarticular arthritis, including gout,[5,28] rheumatoid arthritis,[29] sympathetic dystrophy, tenosynovitis, tuberculous dactylitis (spina ventosa), enchondroma, epidermoid cyst, giant cell tumor, osteoid osteoma, sarcoidosis and other conditions.[4,30] In the case presented here, the lesions appeared to be consistent with osteomyelitis, but because of the sudden and multiple site presentations, the possibility of a cardiac embolic event was also entertained.

Usually, as in this case, the metastatic lesions are noted following the discovery of the primary carcinoma. There have been, however, several reports of the lesions being discovered before the diagnosis, or even suspicion, of cancer.[4,6,20,27] Gall and associates[20] report that five of the eight patients in their series had foot pain as the presenting symptom of visceral malignancy.

The vast majority of cases of acral metastasis occur directly in bone. In only a small percentage of patients does metastasis of soft tissue develop, which subsequently may or may not invade adjacent bone. Only 2 of the 30 cases reviewed by Kerin[4] had metastasis to acral soft tissue. Since his article in 1958, several other cases have been reported. Primaries for this type of metastasis include kidney,[2] testis[31] and parotid,[32] though most were from lung.[6,7,33,34] Our case is one such example, showing secondary invasion of bone at two different sites simultaneously with an additional soft tissue site.

When bone is affected, it is almost invariably osteolytic in nature. One case of prostate cancer[8] had an osteoblastic lesion. Adjacent joints are rarely invaded. Periosteal reaction, often seen with inflammatory processes, is rare with metastasis and there is a lack of limiting sclerosis. Occasionally, in those cases wherein the metastasis originates in bone, there may be invasion of the overlying soft tissue.[4] The adjacent tissue is usually homogeneous and, in contrast to diffuse involvement during an inflammatory process, it is well defined.

Why is acral metastasis such a rare finding? Tumor emboli require certain conditions for metastatic development in a site distant from the primary tumor.[35] As Galasko[36] suggests, there are many possible factors including tumor-cell surface properties, embolic size and homogeneity, host immune system, host blood-clotting mechanisms, platelet activity and endothelial wall properties. One variable in this equation may be the lower temperature gradient in the acral areas that may be inhospitable for tumor growth.[20] Another factor may be that deposition of tumor emboli in bone occurs mainly in hematopoietically active sites,[37] which have a rich capillary network and sluggish blood flow. The femur, fibula, radius and ulnar bones contain only a small percentage of the red bone marrow, and bones distal to them are virtually devoid of it in a healthy adult.[38]

Mulvey[27] suggests that the process of hematogenous spread may be critical. Primary malignant lesions often erode veins and tumor emboli can thus travel to the capillary filter beds of the lung or liver (or both).[39] The communications with the vertebral venous plexus may then allow for deposition of the tumor emboli in sites of the axial skeleton as described by Batson,[40,41] but not in the peripheral bones. This venous anastomotic system is not developed peripherally.[42] In the case of bronchogenic cancer, venous erosion may allow tumor emboli to be carried to the left side of the heart and from there to the systemic arterial circulation.[27] This may theoretically also apply to metastasis to the lung from other primary lesions. As this situation occurs only rarely, it may also contribute to the rarity of acral metastasis. Studies with radioactively labeled tumor cells suggest that transpulmonary passage of cells into the systemic arterial system takes place and that from there metastasis to the systemic viscera may occur.[43] Mangini[15] suggests that the rapidity of the arterial circulation is another factor that may serve to hinder metastasis in the bones of the hands and feet. In the periphery, circulation speed is increased by the contracting muscular action of the extremities, which accelerates the return of the blood to the heart.

Acral metastasis is usually associated with advanced metastatic disease.[3,44] The average survival of these patients is two months, with very few reaching eight to nine months.[45] Many authors[3,4,16,46] therefore feel that the characteristic rapid evolution does not justify a reconstructive surgical procedure and treatment should be palliative to relieve pain and discomfort. Basora and Fery[16] suggest amputation of a finger because this can be done under local anesthesia with little risk and generally short postoperative care. Nissenbaum and colleagues[9] agree that amputation is better as palliative treatment and state that radiation therapy is usually not helpful. Bricout,[8] however, reports excellent relief of pain in four out of his five patients receiving radiation therapy to the affected extremities. Similarly, Gall and co-workers[20] used radiation therapy and weight-bearing short-leg casts and braces to restore weight-bearing function and increase activity in patients with metastasis to the feet. In some cases radiation therapy can result in new bone formation and disappearance

of a lytic lesion.[19] Of course, amputation of an involved part may be advisable in the rare situation when the primary lesion is resectable and there are no other metastatic lesions.[4] Systemic treatment with endocrine or antineoplastic chemotherapy should be considered in any patient with a neoplasm responsive to such therapy, such as breast cancer or lymphoma; however, this literature review suggests that acral metastasis portends a very poor outcome, and it is unlikely that systemic therapy would reverse the underlying disease completely, making local palliative interventions appropriate.

In the case reported here, we chose to combine both methods of treatment, amputating the affected finger and irradiating the palm of the right hand and the left foot. Amputation of the latter two sites would have been more problematic in terms of the procedure itself, the postoperative care and the function and emotional effect on the patient, while having no proved advantage. This patient was extremely debilitated at the time his acral metastasis was diagnosed and he declined systemic chemotherapy.

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