

Acrometastasis: a literature review

D. STOMEIO¹, A. TULLI², A. ZIRANU¹, C. PERISANO¹, V. DE SANTIS¹, G. MACCAURO¹

¹Orthopedic Oncologic Unit; and ²Hand Surgery Unit, Department of Geriatrics, Neuroscience and Orthopedics; Catholic University of the Sacred Heart, School of Medicine, Rome, Italy

Abstract. – OBJECTIVE: Acrometastases are a rare observation, and account for approximately 0.1% of metastases. Every age can be affected, with a male predominance. The most common primary cancer site is the lung, followed by the colo-rectal, breast and genito-urinary tract.

They are most commonly seen in pre-terminal patients with wide-spread disseminated disease. Rarely, they may be the first presentation of occult silent cancer, mimicking a benign condition. There is no standard treatment. We reviewed last 20 years literature in order to describe the most common sites of primary tumours and the more commonly used treatments.

MATERIALS AND METHODS: We searched the Cochrane Central Library (CENTRAL), MEDLINE/PubMed (from 1940 to February 2014), SCOPUS database, and EMBASE/Ovid using a combination of controlled vocabulary and text word terms.

RESULTS: Lung cancer was the first most common cause of acrometastases both in hands and feet, with 32.9% of all the cases; 20% of cases were renal cell cancer (RCC) metastases, followed by breast (12.9%) and colon (10%). Primary malignancies and site of metastasis (hand vs foot) suggest that the tumour cells reach the bones through the circulation and not the lymphatic system; in foot acrometastases Batson's plexus may play a fundamental role in dissemination.

CONCLUSIONS: Treatment depends on staging and tumor extent. Amputation or disarticulation is the most common approach. It allows a wide margin resection and pain control. In some cases palliative treatment with radiation therapy, bisphosphonates and chemotherapy have been attempted with good results. The prognosis of the patients with acrometastases is poor; the mean survival time after diagnosis is 7 (\pm 7) months. Special reference needs to be made to metastasis from renal cell carcinoma; if treated with radical surgical resection and nephrectomy a better outcome and survival rate shall be expected.

Key Words:

Acrometastasis, Extremities, Hand, Foot, Metastasis, Bone, Small bones.

Introduction

Acrometastases are metastases located distal to the elbow and knee¹. While metastatic bone disease is a common observation in a cancer patient natural history, metastases in hands and feet are a very rare occurrence, and represent the 0.1% of all metastatic bone lesions². Since they are usually found in widespread cancer disease, hand and foot metastases are indicators of poor prognosis. Generally, mean life expectancy after acrometastasis diagnosis is about 6 months¹. The most common primary malignancy is lung cancer, followed by gastro-intestinal e and genito-urinary tracts tumours³.

There is an increase of reports in literature, since a better life expectancy in cancer patients brought along an increased risk of bony metastases, and acrometastases as well.

They are generally diagnosed in patients with a well-known tumour history, but in 10% of the reported cases they represented the first sign of an occult malignancy⁴.

They present with soft tissue swelling, erythema, functional impairment of the affected ray, and intermittent pain, generally at rest and not modified by movements. Differential diagnoses include: inflammatory lesions, cysts, gout, ganglia, osteomyelitis, tuberculous dactylitis, pyogenic granuloma and primary skin tumours².

In this article we revise the new cases reported in literature since 1987 and add them to previous database present in literature. Because of the bizarre nature of acrometastases, we focus on the physiopathology of this disease.

Epidemiology

Bone metastases are a common finding in the natural history of cancer patients; on the contrary acrometastases are very rare. They account approximately for 0.1% of all metastatic osseous involvement².

Current advances in cancer therapy have increased patients' life expectancy though increas-

ing the risk of metastases and acrometastases, as well. Finding acrometastases is considered a sign of poor prognosis, since they usually appear in patients with widespread disease¹; even though in 10% of cases acrometastases are the first sign of an occult cancer^{4,5}.

The first to describe this rare manifestation in the hand was Handley in 1906⁶. In 1920 Bloodgood⁷ published the first report of a metastasis in the foot. In the reported series men are affected two times more than women, and lung cancer is the most common malignancy. In order to explain this male predominance, the strong relationship between cigarette smoking and lung cancer has been advocated⁸. Even though smoking attitude in women is increasing, though increasing lung cancer incidence in female sex, and perhaps acrometastases.

Healey et al⁹ noted a predilection for the dominant hand when the metastases were located in the upper limb; on the contrary, Hayden et al¹⁰ noted no relationship between hand dominance and incidence of metastases, since both hands were equally affected in their series.

Lung cancer is the primary malignancy in almost half acrometastases, followed by renal cell carcinoma, colorectum and breast².

Materials and Methods

We based our review on the papers by Kerin et al² and Libson et al¹¹. The latter published in 1986 a review of all the cases of acrometastases reported in literature until that moment.

The following electronic databases have been searched: The Cochrane Central Library (CENTRAL), MEDLINE/Pubmed (from 1940 to February 2014), SCOPUS database, and EMBASE/Ovid. The search strategies for the different electronic databases (using a combination of controlled vocabulary and text word terms) were: acrometastasis OR acrometastases OR hands metastases OR hand metastasis OR foot metastasis OR feet metastases OR extremity metastasis OR extremities metastases OR small bone metastasis OR small bones metastases; Hand OR Finger OR Metacarpal OR Digit OR Phalanx OR small bones.

Articles not written in English, French or Spanish were excluded. We collected 118 case reports and review articles. 70 patients were reported¹²⁻⁹¹ (Table I). These cases have been added to those previously recorded in the literature. Table II

records the primary malignancies of the 70 new cases reported in the literature since 1987; Table III reports the new 49 cases of metastases to the hand by site of origin. Table IV deals similarly with the 21 cases of foot metastases. In Tables V and VI there is the total amount of metastases in the hand and foot, respectively.

Results

In our review of the new cases reported since 1987, we collected 49 metastases located in the hands and 21 in the feet. Lung cancer was the first most common cause of acrometastases both in hands and feet, with 32.9% of all the cases [Tables II, III, IV]. 20% of cases were Renal Cell Cancer (RCC) metastases, followed by Breast (12.9%) and Colon (10%). Even though RCC had a higher percentage in feet, we recorded a higher number of RCC metastases in hands. Though, this is not of statistical relevance, since the cases of hand metastases were more than twice the foot metastases.

In 30% of the new cases recorded, acrometastases was the first sign of malignancy. This is an interesting finding since, in the past literature, acrometastases percentage from occult malignancies is assessed about 10%. We don't know exactly the meaning of this evidence. Probably acrometastases have become more frequent during the years, and clinicians prefer to report rarer cases.

Subsequently, we discuss the main features of the principle types of acrometastases found in our review.

Carcinoma of the Lung

Metastases from lung cancer comprise almost half the recorded secondary lesions to the bones of the hand. This reflects both the prevalence of bronchial carcinoma and its predilection for the skeleton in metastatic spread. Metastases to the foot are much less common² (Tables V and VI). Lung metastases are generally osteolytic and interest a single bone of an affected extremity; multiple bony involvement may, however, occur².

Carcinoma of the breast. Breast metastases show an almost equal predilection for the hand and foot (Tables V and VI). Multiple bony involvement is characteristic. Their appearance in radiograms may be sclerotic, lytic, or mixed.

Genitourinary tumours. Examination of Table VI shows that renal carcinoma is the most com-

Table I. New cases reported in the literature since 1987.

Case	Author	Year	Primary Site	Metastatic Site	Age	Sex
1	Bucley	1987	Colon	Hand		
2			Colon	Hand		
3	Troncoso	1991	RCC	Foot - proximal phalanx toe		
4			RCC	Foot - distal phalanx		
5	Bloom	1992	Breast			
6	Bibi	1993	RCC	Hand		
7	Abrahams	1995	Occult - Lung	Hand - Right thumb	62	M
8			Occult - RCC	Hand - 4° MC	63	M
9			Occult - Lung	Hand - Lunate	59	F
10	De Maesener	1995	Breast	Simultaneous - hand foot		
11	Freedman	1995	Breast	Foot	47	F
12	Castello	1996	Lung	Hand		
13			RCC	Hand		
14			Hard palate	Hand		
15			Larynx	Hand		
16			Pharynx	Hand		
17	Kemnitz	1996	Lung	Foot - 1° MT	68	M
18	Saglike	1996	Lung	Hand - Phalanx		M
19	Viswanathan	1996	Lung	Hand - Phalanx		
20	Adegboyega	1999	RCC	Hand - Phalanx		
21	Shannon	2000	Timus	Hand - Phalanx	54	M
22	Kaufmann	2001	Lung	Foot - Calcaneus		M
23	Tolo	2002	RCC	Hand - Triquetrum	63	M
24	Slater	2003	RCC	Hand - Triquetrum		
25	Campa	2004	Lung	Hand - Right 4° distal phalanx	72	F
26	osterhouse	2004	Breast	Foot - Calcaneus	80	F
27	Riter	2004	RCC	Hand - 2° distal phalanx bilateral	53	F
28	Umebayashi	2004	Breast	Hand - Right 4° distal phalanx	68	M
29	Yadav	2004	Occult - RCC	Foot - Right	55	M
30	Keramidas	2005	Occult - Lung	Hand - Right 3° 4° 5° MC	66	F
31	Kouvaris	2005	Breast	Foot - Talus	59	F
32	Perdona	2005	Occult - RCC	Foot - Toe	72	M
33	Ramkumar	2005	Occult - Lung	Foot - Toe	60	F
34	Bahk	2006	Gastric	Hand - 1° 2° 3° 4° 5° digits	67	F
35	Maccauro	2006	Occult - Urothelial	Foot - Talus	64	F
36	Ozcanli	2006	CHS	Hand	47	M
37	Khan	2007	Occult - Bladder	Foot	76	M
38	Lai	2007	Occult - Lung	Foot - 1° Distal phalanx	57	F
39	Salesi	2007	RCC	Hand - Left 2° finger		
40	Flynn	2008	Occult - Lung	Hand - Left 2° MC	78	F
41			Breast	Hand - 3° MC	69	F
42	Miyamoto	2008	Gastric	Hand - Left 5° MC	72	F
43	Tzaveas	2008	Lung	Hand - Left 5° MC	68	M
44	Ellington	2009	Colon	Foot		
45			Colon	Foot		
46			Colon	Foot		
47	Otsuji	2009	HCC	Hand - Left 5° distal phalanx	49	F
48	Wavreille	2009	Breast	Hand - Right 5° distal phalanx	48	F
49	Anoop	2010	Occult - Colon	Hand - Right distal 5° phalanx	76	M
50	Long	2010	Lung	Hand - Left 3° distal phalanx	53	M
51	Lozic	2010	Lung	Hand - Right 1° distal phalanx		M
52	Bhandari	2011	Occult - Lung	Hand - Left 2° finger	52	M
53	Choufani	2011	Occult - RCC	Foot		
54	Dar	2011	Oesophageal	Hand - Bilateral all digits		
55	Sur	2011	Breast	Hand - Right 2° finger	63	F
56			Endometrium	Hand - Right 2° finger	52	F
57			Rectum	Hand - proximal phalanx	74	F
58			Lung	Hand - proximal phalanx	69	F

Table continued

Table I. (Continued). New cases reported in the literature since 1987.

Case	Author	Year	Primary Site	Metastatic Site	Age	Sex
59			Lung	Hand - proximal phalanx	54	M
60	Borgohain	2012	Occult - RCC	Hand - Right 2° MC trapezium Trapezoid	70	M
61	Gharwan	2012	Occult - Colon	Hand - Right 3° MC phalanx	54	M
62	Khosla	2012	Vaginal	Hand - °4 MC	65	F
63	Lamarca	2012	Occult - Lung	Foot - Left 3° MT	68	M
64	Ornetti	2012	Endometrium	Hand - Right 2° middle phalanx	68	F
65	Rauf	2012	Occult - HCC	Hand - Left 5° distal phalanx	66	M
66	Rinonapoli	2012	Occult - Lung	Hand - Left 1° MC thumb	74	M
67	Trinidad	2012	Lung	Foot - Right 1° MT	67	M
68	Gilardi	2013	Occult - Lung	Hand		
69	Ryder	2013	Occult - Urothelial	Foot - Left calcaneus	82	F
70	Van Veenendaal	2014	Occult - Lung	Hand - Right 3° proxiaml phalanx	83	F

mon primary in foot metastases (18.2%), equal in incidence to secondary lesions from large bowel. Renal carcinomatous metastases are also the third most common cause of metastases to the hand, constituting 18.4% of the total. A similar predilection in localization can be seen in urothelial, uterine and vaginal metastases; even though peripheral metastases from uterine carcinoma are rare¹¹.

Gastrointestinal carcinoma. Metastases from carcinoma of the large bowel show a tendency to involve the foot, where they are the second most commonly occurring metastases (16.5%) after RCC (18.2%). Metastases to the hand are much less frequent (10.2%).

Table II. New cases recorded by site of origin.

New cases recorded by site of origin	N°	%
Lung	23	32.9
Kidney	14	20.0
Breast	9	12.9
Colo-rectum	8	11.4
HCC	2	2.9
Endometrium	2	2.9
Gastric	2	2.9
Urothelial	2	2.9
Oesophagus	1	1.4
Vaginal	1	1.4
Pharynx	1	1.4
Larynx	1	1.4
Timus	1	1.4
CHS	1	1.4
Hard palate	1	1.4
Bladder	1	1.4
Total	70	100

Gastric and oesophageal tumours rarely metastasise to the extremities.

Discussion

Pathophysiology

Osseous secondary lesions generally affect bones rich in red marrow such as vertebral bodies⁹²; little bones of the extremities are very poor in red marrow²; this could be an explanation of why acrometastases are so rare.

The precise mechanism used by tumour cells to reach hands and feet has not been clearly understood; many hypotheses have been suggested.

It is accepted that tumour cells dissemination to acral regions occurs through circulation and not the lymphatic system^{1,93}. This would explain the high prevalence of lung cancer metastases, because they have direct access to systemic circulation through left atrium and ventricle. Other visceral tumour emboli cannot reach directly systemic arteries because they have to pass the filter of lungs and liver.

Table III. New cases of acrometastases to the hand.

New cases of acrometastases to the hand	N	%
Lung	17	34.7
Breast	5	10.2
Kidney	9	18.4
Colorectum	5	10.2
Uterus	2	4.1
Larynx	1	2.0
Other	10	20.4
Total	49	100.0

Table IV. New cases of acrometastases to the foot.

New cases of acrometastases to the foot	N	%
New cases of acrometastases to the foot	N°	%
Lung	6	28.6
Breast	3	14.3
Kidney	5	23.8
Colorectum	3	14.3
Uterus	0	0.0
Larynx	0	0.0
urothelial	2	9.5
vaginal	0	0.0
Other	2	9.5
Total	21	100.0

Healey et al⁹ reported that the dominant hand was more often affected. They postulated this was because the dominant hand receives a larger amount of blood supply, and is more likely to undergo injuries than the non-dominant one. Formerly, in 1923 Joll CA⁴¹ suggested a trauma-induced mechanism: repeated trauma may degrade the resistance of surrounding tissue, allowing tumour emboli to settle and grow within bone. Other authors, instead, support the theory that trauma would release chemotactic factors, such as prostaglandins, promoting tumour cells migration and adherence⁹³.

Localization

Metastases have been recorded in every bone of each hand.

In Flynn et al series⁸ the third digit was the most often affected, followed by the thumb. The distal phalanx was the preferential site. An explanation could be that tumour emboli need a reduced blood speed to settle⁸. The carpus has been

Table V. Total number of metastases to the hand with site of primary neoplasm.

TOT Metastases to the hand with site of primary neoplasm	N°	%
Lung	108	44.1
Breast	30	12.2
Kidney	30	12.2
Colorectum	15	6.1
Uterus	6	2.4
Larynx	4	1.6
Unknown	4	1.6
Other	48	19.6
Total	245	100.0

stated to be a most uncommon site of metastases. The most commonly affected bones in foot are talus and calcaneus.

As described by Kerin et al², the most common primary malignancies are lung, kidney, colo-rectal, followed by breast. The distribution of metastases from these primaries to hands and feet is not indifferent. Lung metastases affect usually the hand, while renal and colo-rectal metastases affect the foot; in breast cancer there is no significant difference between localizations in hands and feet. Lamarca et al⁹⁴ explained this phenomenon describing the diaphragm as a boundary: supradiaphragmatic tumours reach the systemic arterial circulation and, therefore, the hands, while infradiaphragmatic neoplasms use to metastasise to the feet in a retrograde manner through the valveless Batson's vertebral venous plexus⁹⁵. In breast cancer, dissemination occurs through lymphatic system.

A particular case of metastatic dissemination to the hand has been described by Bahk et al⁹⁶; they reported a case of a patient affected by humerus pathological fracture from gastric cancer metastasis; given the poor prognosis they performed intra-medullary nailing; after the procedure dissemination to all the five distal phalanges of one hand was observed.

Clinical Presentation and Differential Diagnosis

Acrometastases are generally diagnosed in patients with a well-known tumour history, but in 10% of the reported cases they represented the first sign of an occult malignancy⁴.

They present with pain, palpable mass, an enlarging digit or a mechanical dysfunction in the

Table VI. Total number of metastases to the foot with site of primary neoplasm.

TOT Metastases to the hand with site of primary neoplasm	N°	%
Colorectum	19	16.5
Kidney	21	18.2
Lung	20	17.4
Urothelial	11	9.6
Breast	12	10.4
Uterus	6	5.2
Prostate	4	3.5
Ovary	2	1.8
Unknown	8	7
Other	12	10.4
Tot	115	100

hand causing impairment of daily activities; sometimes erythema and ulcerations can be noticed. Pain is generally deep and intermittent, present also at rest, not modified by movements and refractory to commonly used analgesics. Differential diagnoses include: inflammatory lesions, cysts, gout, ganglia, osteomyelitis, rheumatoid arthritis, tuberculous dactylitis, pyogenic granuloma and primary skin tumours².

Imaging

Appearance on roentnograms depends on tumour origin: lung and renal metastases are generally lytic, prostatic ones are sclerotic, while breast metastases are mixed, both lytic and sclerotic.

CT scan is of poor value in this region because it lacks resolution in this limited space. MRI is the gold standard; it helps evaluating bone marrow disease and extraosseus extension of the tumour³.

Treatment

When an acrometastasis is suspected, a complete staging is necessary in order to determine the primary lesion, its extension and prognosis. Considering these data and the patient's performance status, we can tailor the best treatment.

Staging must include radiographs and MRI of the region affected by metastases, CT of the chest and abdomen, and bone scan.

It is mandatory to obtain a tissue diagnosis, performing a biopsy: fine needle aspiration biopsy (FNAB) provides cytological diagnosis, while trocar biopsy and incisional biopsy provide histologic diagnosis. Some authors^{3,97} suggest not to use incisional biopsy for limited space in these regions and the risk of making the lesion extra-compartmental.

Since acrometastatic cancer is very rarely observed, there is no standard protocol for treatment; we shall evaluate case by case and tailor the therapy to that particular patient's needing. Because of the poor prognosis, treatment is aimed at palliation: adequate tumour resection, pain relief, rapid recovery and preservation of maximal hand function¹.

When possible, local curettage and tumour excision shall be performed in order to salvage the ray. Unfortunately, in the hand, normal soft tissue around the lesion is wanting, thus, limiting the possibility of resection. Most metastases occur in the distal phalanx; here the flexor tendon and its sheath is part of the compartment as proximally as the midpalmar space, while the extensor ten-

don is part of the compartment until the metacarpophalangeal joint⁹⁸. On this basis, disarticulation of the ray is often needed to obtain wide margins.

In the reported cases, curettage has been performed in lesions that could not be resected without a disfiguring amputation or an unacceptable degree of functional disability^{9,96}. The rate of local recurrence after curettage is 20%³.

Amputation is the most frequent treatment option in literature, above all when the lesion is located in the distal phalanx.

When disarticulation of the ray is performed, the functional outcome is generally acceptable: patients do not lose small objects from the hands, even though grip strength is weaker⁵⁸.

In the foot, amputation can be that of a ray, midfoot or transtibial, depending on the location and spread of the tumour.

Radiotherapy has been attempted also, in order to obtain either local control of the disease or pain palliation^{99,100}. The use of chemotherapy is still controversial since the poor performance status of these patients.

Treatment of single acrometastases from Renal Cancer deserves to be discussed apart. When a single bone metastasis is found, it is well known that patients undergoing simultaneous excision of primary renal cancer along with bony secondary lesion have a good prognosis¹⁰¹. This could be valid for acrometastases as well, but further evidences are needed.

Conclusions

Acrometastases are usually found in widespread cancer disease¹⁰². They are indicators of poor prognosis. In the review by Afshar et al¹⁰³ patients' mean life expectancy from the time of the diagnosis was 7 (± 7) months.

Generally they affect a single bone or a single extremity, but cases have been reported in which a simultaneous involvement of both upper and lower extremity is seen^{104, 105}.

Before assessing a treatment, a complete staging and a biopsy are needed.

Since they are very rare, there is no standard protocol for therapy. In the treatment of appendicular skeleton metastases, tumour sensitivity to adjuvant therapies must be considered, before proceeding to surgery¹⁰⁶. Chemotherapy and Radiotherapy have been both suggested, even though amputation and disarticulation are the

most commonly used treatment. When possible local excision shall be preferred; unfortunately, in the phalanges this is difficult to perform since here bone and tendons are part of the same compartment, though shifting the treatment towards resection/disarticulation.

There is no evidence in literature that acrometastases excision could improve patients' life expectancy. It can be speculated that it does not, since metastases to small bones are signs of widespread disease, but further studies are needed.

We found no prospective or retrospective study about quality of life after surgery. Nevertheless, many authors agree that removing acrometastases improves patients' quality of life, even though sacrificing a ray. It is the most efficient way to control the pain¹⁰⁷. Even when invasive surgery is performed, the aesthetic and functional outcome is acceptable^{3,58,108}.

Acrometastasis may be the first manifestation of malignancy¹⁰⁹⁻¹¹³. Given the poor prognosis, early diagnosis is important to offer adequate treatment. A delay in treatment can adversely affect the quality of life¹¹⁴⁻¹¹⁸.

Conflict of Interest

The Authors declare that they have no conflict of interests.

References

- 1) MAVROGENIS AF, MIMIDIS G, KOKKALIS ZT, KARAMPI ES, KARAMPELA I, PAPAGELOPOULOS PG, ARMAGANIDIS PG. Acrometastases. *Eur J Orthop Surg Traumatol* 2014; 24: 279-283.
- 2) KERIN R. Metastatic tumors of the hand. *J Bone Joint Surg Am* 1983; 65: 1331-1335.
- 3) SPITERI V, BIBRA A, ASHWOOD N, COBB J. Managing acrometastases treatment strategy with a case illustration. *Ann R Coll Surg Engl* 2008; 90: 8-11.
- 4) ABRAHAMS TG. Occult malignancy presenting as metastatic disease to the hand and wrist. *Skeletal Radiol* 1995; 24: 135-137.
- 5) MACCAURO G, ESPOSITO M, MURATORI F, GEBERT C, GOSHEGER G, LOGROSCINO CA. A report of a very rare localization of bone metastasis to the talus. *Eur J Orthop Surg Trauma* 2006; 16: 67-69.
- 6) HANDLEY WS. *Cancer of the Breast and its Operative Treatment*. London: John Murray, 1906.
- 7) BLOODGOOD JC. Bone tumours, benign and malignant. *Am J Surg* 1920; 34: 229-237.
- 8) FLYNN CJ, DANJOUX C, WONG J, CHRISTAKIS M, RUBENSTEIN J, YEE A, YIP D, CHOW E. Two cases of acrometastasis to the hands and review of the literature. *Curr Oncol* 2008; 15: 51-58.
- 9) HEALEY JH, TURNBULL AD, MIEDEMA B, LANE JM. ACROMETASTASES. A study of twenty-nine patients with osseous involvement of the hands and feet. *J Bone Joint Surg Am* 1986; 68: 743-746.
- 10) HAYDEN RG, SULLIVAN LG, JEBSON PJ. The hand in metastatic disease and acral manifestations of paraneoplastic syndromes. *Hand Clin* 2004; 20: 335-343.
- 11) LIBSON E, BLOOM RA, HUSBAND JE, STOKER DJ. Metastatic tumours of bones of the hand and foot. A comparative review and report of 43 additional cases. *Skeletal Radiol* 1987; 16: 387-392.
- 12) ADEGBOYEGA PA, ADESOKAN A, VIEGAS SF. Acrometastasis in renal cell carcinoma. *South Med J* 1999; 92: 1009-1012.
- 13) ANOOP TM, GEORGE S, DIVYA KP, JABBAR PK. Metastatic phalangeal osteolysis as an initial presentation of carcinoma colon. *Am J Surg* 2010; 200: 61-63.
- 14) BARNETT LS, MORRIS JM. Metastases of renal-cell carcinoma simultaneously to a finger and a toe. A case report. *J Bone Joint Surg Am* 1969; 51: 772-774.
- 15) BHANDARI T, BROWN E. Acrometastasis and the potential benefits of early positron emission tomography scanning. *Ann Plast Surg* 2011; 67: 189-192.
- 16) BIBI C, BENMEIR P, MAOR E, SAGI A. Hand metastasis from renal cell carcinoma with no bone involvement. *Ann Plast Surg* 1993; 31: 377-378.
- 17) BLOOM RA, SULKES A, FREILICK G, LIBSON E. Breast metastases to bones of the extremities: simultaneous involvement of all four limbs. *Clin Oncol (R Coll Radiol)* 1992; 4: 58-59.
- 18) BORGHAIN B, BORGHAIN N, KHONGLAH T, BAREH J. Occult renal cell carcinoma with acrometastasis and ipsilateral juxta-articular knee lesions mimicking acute inflammation. *Adv Biomed Res* 2012; 1: 48.
- 19) BRICOUT PB. Acrometastases. *J Natl Med Assoc* 1981; 73: 325-329.
- 20) BRYAN RS, SOULE EH, DOBYNS JH, PRITCHARD DJ, LINSCHIED R. Metastatic lesions of the hand and forearm. *Clin Orthop Relat Res* 1974; 101: 167-170.
- 21) BUCKLEY N, PEEBLES BROWN DA. Metastatic tumors in the hand from adenocarcinoma of the colon. *Dis Colon Rectum* 1987; 30: 141-143.
- 22) CAMPAT, FAGNONI E, RIPAMONTI C. Palliative surgery of acrometastases from lung cancer: a case report. *Support Care Cancer* 2004; 12: 202-204.
- 23) CASTELLOJR, GARRO L, ROMERO F, CAMPO M, NAJERA A. Metastatic tumours of the hand. Report of six additional cases. *J Hand Surg Br* 1996; 21: 547-550.
- 24) CASTIGLIANO SG. Metastasis to the distal phalanx from a primary malignancy of the oral cavity: report of case. *J Oral Surg* 1996; 24: 467-469.
- 25) CHIRODIAN N, DICKSON MG, KERR PS. Fingertip metastasis presenting with a history of trauma. *Hosp Med* 1998; 59: 819.
- 26) CHOUFANI E, DILIGENT J, GALOIS L, MAINARD D. Metastatic renal cell carcinoma presenting as foot

- metastasis: case report and review of the literature. *J Am Podiatr Med Assoc* 2011; 101: 265-268.
- 27) DAR AM, KAWOOSA NU, SHARMA ML, BHAT MA Unusual metastasis to all the digits of both hands in a patient previously operated on for esophageal carcinoma. *Gen Thorac Cardiovasc Surg* 2011; 59: 225-227.
 - 28) DE MAESENEER M, MACHIELS F, NAEGELS S, VERHAEGHE W Hand and foot acrometastases in a patient with bronchial carcinoma. *J Belge Radiol* 1995; 78: 274-275.
 - 29) DE OLIVEIRA FILHO JA, SILVEIRA E, MARINS JL. Metastasis from renal carcinoma to a phalanx of the hand. *Br J Urol* 1978; 50: 280.
 - 30) ELLINGTON JK, KNEISL JS. Acrometastasis to the foot: three case reports with primary colon cancer. *Foot Ankle Spec* 2009; 2: 140-145.
 - 31) FLYNN CJ, DANJOUX C, WONG J, CHRISTAKIS M, RUBENSTEIN J, YEE A, YIP D, CHOW E. Two cases of acrometastasis to the hands and review of the literature. *Curr Oncol* 2008; 15: 51-58.
 - 32) FREEDMAN DM, HENDERSON RC. Metastatic breast carcinoma to the os calcis presenting as heel pain. *South Med J* 1995; 88: 232-234.
 - 33) GHARWAN H, YARLAGADDA L, DUFFY A. Acrometastasis as the Initial Presentation of a KRAS-Positive Colon Cancer. *Case Rep Oncol* 2012; 5: 404-408.
 - 34) GILARDI R, DELLA ROSA N, PANCALDI G, LANDI A. Acrometastasis showing an occult lung cancer. *J Plast Surg Hand Surg* 2013; 47: 550-552.
 - 35) GOLD GL, REEFE WE. Carcinoma and metastases to the bones of the hand. *JAMA* 1963; 184: 237-239
 - 36) GOYAL S, PURI T, GUPTA R, SURI V, JULKA PK, RATH GK. Tibial involvement in breast cancer: issues in diagnosis and management. *Foot (Edinb)* 2010; 20: 35-38.
 - 37) GRAHAM WP, KILGORE ES, WILLIAMS EH, GORDON SL. Metastatic tumours of the hand. *Hand* 1973; 5: 177-179.
 - 38) GRANT KB, ROLLER GJ. Metastasis of bronchogenic carcinoma to the terminal phalanx of a finger. *J Iowa Med Soc* 1966; 56: 1132-1135.
 - 39) HICKS MC, KALMON EH, JR., GLASSER SM. Metastatic Malignancy to Phalanges. *South Med J* 1964; 57: 85-88.
 - 40) IOIA JV, SUMNER JM, GALLAGHER T. Presentation of malignancy by metastasis to the carpal navicular bone. *Clin Orthop Relat Res* 1984; (188): 230-233.
 - 41) JOLL CA. Metastatic tumors of bone. *Br J Surg* 1923; 11: 38-72.
 - 42) KARTEN I. Phalangeal metastases from bronchogenic carcinoma. *JAMA* 1978; 239: 2449.
 - 43) KAUFMANN J, SCHULZE E, HEIN G. Monarthritis of the ankle as manifestation of a calcaneal metastasis of bronchogenic carcinoma. *Scand J Rheumatol* 2001; 30: 363-365.
 - 44) KEMNITZ MJ, ERDMANN BB, JULSRUD ME, JACOBS PM, RINGSTROM JB. Adenocarcinoma of the lung with metatarsal metastasis. *J Foot Ankle Surg* 1996; 35: 210-212.
 - 45) KERAMIDAS E, BROTHERSTON M. Extensive metastasis to the hand from undiagnosed adenocarcinoma of the lung. *Scand J Plast Reconstr Surg Hand Surg* 2005; 39: 113-115.
 - 46) KHAN S, WIN Z, LLOYD CR, NERIMAN D, SZYSZKO TA, SVENSSON WE, AL-NAHHAS A. Acrometastasis to the foot: an unusual presentation of transitional cell carcinoma of the bladder. *Nucl Med Rev Cent East Eur* 2007; 10: 26-28.
 - 47) KHOSLA D, RAI B, PATEL FD, SAPKOTA S, SRINIVASAN R, SHARMA SC. Acrometastasis to hand in vaginal carcinoma: a rare entity. *J Cancer Res Ther* 2012; 8: 430-432.
 - 48) KOUVARIS JR, KOULOULIAS VE, PAPACHARALAMPOUS XN, KOUTSELINI HA, GENNATAS CS, LIMOURIS GS, VLAHOS LJ. Isolated talus metastasis from breast carcinoma: a case report and review of the literature. *Onkologie* 2005; 28: 141-143.
 - 49) KUMAR PP, KOVI J. Metastases to bones of the hands and feet. *J Natl Med Assoc* 1978; 70: 837-840.
 - 50) LAI CC, TAN CK, SHIH JY. Acrometastasis from squamous cell lung cancer. *CMAJ* 2007; 177: 249-250.
 - 51) EONHEART EE, DiSTAZIO J. Acrometastases. Initial presentation as diffuse ankle pain. *J Am Podiatr Med Assoc* 1994; 84: 625-627.
 - 52) LONG LS, BRICKNER L, HELFEND L, WONG T, KUBOTA D. Lung cancer presenting as acrometastasis to the finger: a case report. *Case Rep Med* 2010; 2010: 234289.
 - 53) LOZIC AA, SILCONI ZB, MISLJENOVIC N. Metastases to rare locations as the initial manifestation of non-small cell lung cancer: two case reports. *Coll Antropol* 2010; 34: 609-612.
 - 54) MAHESHWARI AV, CHIAPPETTA G, KUGLER CD, PITCHER JD, JR., TEMPLE HT. Metastatic skeletal disease of the foot: case reports and literature review. *Foot Ankle Int* 2008; 29: 699-710.
 - 55) MIYAMOTO W, YAMAMOTO S, UCHIO Y. Metastasis of gastric cancer to the fifth metacarpal bone. *Hand Surg* 2008; 13: 193-195.
 - 56) MOHANTY S, FEDEROWICZ TE, UEHARRA H. Metastatic lesions of the fingers. *Surgery* 1968; 64: 411-415.
 - 57) NISSENBAUM M, KUTZ JE, LISTER GD. Clear-cell carcinoma of the lung metastatic to the hamate: a case report. *Clin Orthop Relat Res* 1978; (134): 293-296.
 - 58) NUZUMLALI E, ORHUN E, OTZTURK K, CEPER S, POLATKAN S. Results of ray resection and amputation for ring avulsion injuries at the proximal interphalangeal joint. *J Hand Surg Br* 2003; 28: 578-581.
 - 59) ORNETTI P, FAVIER L, VARBEDIAN O, ANSEMANT T. Clinical images: digital acrometastasis revealing en-

- dometrial cancer relapse. *Arthritis Rheum* 2012; 64:3167.
- 60) OSTERHOUSE MD, GUEBERT GM. Bilateral acrometastasis secondary to breast cancer. *J Manipulative Physiol Ther* 2004; 27: 275-279.
 - 61) OTSUJI M, MATSUNAGA S, KOGA H, KAWABATA N, IMAKI-IRE T, HIWAKI T, TASHIRO Y, SHIRAHAMA H, KOMIYA S. An atypical extrahepatic metastasis of the distal phalanx from hepatocellular carcinoma. *Int J Clin Oncol* 2009; 14: 159-162.
 - 62) OZCANLI H, ORUC F, AYDIN AT. Bilateral multiple cutaneous hand metastases of chondrosarcoma. *J Eur Acad Dermatol Venereol* 2006; 20: 893-894.
 - 63) PANTOJA E, CROSS VF, VITALE P, WENDTH AJ. Neoplastic involvement of terminal digits masquerading clinically as benign disease. *Rev Interam Radiol* 1976; 1: 9-13.
 - 64) PATEL MR, ANAND VS, DESAI SS. Metastatic tumor of the hand from malignant cystosarcoma phylloides of the breast. A case report. *Orthopedics* 1985; 8:373-375.
 - 65) PATEL MR, SANCHEZ HJ, SILVER JW, PEARLMAN HS. Metastatic carcinoma of hand. Clinical manifestations of occult or overt bronchogenic carcinoma. *N Y State J Med* 1978; 78: 2233-2237.
 - 66) PERDONA S, AUTORINO R, GALLO L, DE SIO M, MARRA L, CLAUDIO L, CARACÒ C, FRANCO R, FAZZIOLI F, GALLO A. Renal cell carcinoma with solitary toe metastasis. *Int J Urol* 2005; 12: 401-404.
 - 67) RAMKUMAR U, MUNSHI NI, EL-JABBOUR JN. Occult carcinoma of the lung presenting as pain in the hallux: a case report. *J Foot Ankle Surg* 2005; 44: 483-486.
 - 68) RAUF MS, MOTTA L, CONNOLLY C. Digital acrometastases as first sign of hepatocellular carcinoma. *Scott Med J* 2012; 57: 247.
 - 69) RINONAPOLI G, CARAFFA A, ANTENUCCI R. Lung cancer presenting as a metastasis to the carpal bones: a case report. *J Med Case Rep* 2012; 6: 384.
 - 70) RITER HG, GHOBRIAL IM. Renal cell carcinoma with acrometastasis and scalp metastasis. *Mayo Clin Proc* 2004; 79: 76.
 - 71) RYDER JH, MCGARRY SV, WANG J. Calcaneal acrometastasis from urothelial carcinoma of the ureter: a case report and literature review. *Clin Interv Aging* 2013; 8: 395-399.
 - 72) SAGLIKE Y, DEMIRTAS M, DEMIRORS H. Metastatic tumours of the hand. A case report. *Int Orthop* 1996; 20: 123-124.
 - 73) SALESI N, RUSSILLO M, MARANDINO F, RUGGERI EM, METRO G, COGNETTI F, FABI A. Bone of the hands as unusual metastatic site of renal cell carcinoma. *J Exp Clin Cancer Res* 2007; 26: 595-597.
 - 74) SHANNON FJ, ANTONESCU CR, ATHANASIAN EA. Metastatic thymic carcinoma in a digit: a case report. *J Hand Surg Am* 2000; 25: 1169-1172.
 - 75) SHAW KA, BALOG TP, GRASSBAUGH JA. Radiologic case study. Acrometastasis of the thumb. *Orthopedics* 2013; 36: 903, 64-66.
 - 76) SLATER RR, JR. Renal cell carcinoma with metastases to the triquetrum: case report. *J Hand Surg Am* 2003; 28: 532-533.
 - 77) SMITH RJ. Involvement of the carpal bones with metastatic tumor. *Am J Roentgenol Radium Ther Nucl Med* 1963; 89: 1253-1255.
 - 78) SNEDDON J. Painless metastatic deposit in a finger presenting as a pulp infection with osteitis. *Br J Clin Pract* 1969; 23: 511-513.
 - 79) SUR YJ, KANG YK, BAHK WJ, CHANG DK, RHEE SK. Metastatic malignant tumour in the hand. *J Plast Surg Hand Surg* 2011; 45: 90-95.
 - 80) TOMAS X, CONILL C, COMBALIA A, POMES J, CASTEL T, NICOLAU C. Malignant melanoma with metastasis into the capitate. *Eur J Radiol* 2005; 56: 362-364.
 - 81) TRINIDAD J, KAPLANSKY D, NERONE V, SPRINGER K. Metastatic adenosquamous carcinoma of the foot: a case report. *J Foot Ankle Surg* 2012; 51: 345-351.
 - 82) TZAVEAS A, PARASKEVAS G, PAZIS I, DIMITRIADIS A, KITSOULIS P, VRETTAKOS A. Metastasis of bronchogenic carcinoma to the 5th metacarpal bone: a case report. *Cases J* 2008; 1: 284.
 - 83) UMEBAYASHI Y. Distal phalangeal metastasis of extramammary Paget's disease. *J Dermatol* 2004; 31: 63-65.
 - 84) VAEZY A, BUDSON DC. Phalangeal metastases from bronchogenic carcinoma. *JAMA* 1978; 239: 226-227.
 - 85) VISWANATHAN PN, RANGAD F, ROUL RK. Metastases to the hand from carcinoma of the lower alveolus. *J Hand Surg Br* 1996; 21: 544-546.
 - 86) WAVREILLE G, BARONCINI M, RTAIMATE M. [A rare cause of pseudoclubbing (pseudohippocratic finger): the acrometastasis. A case report]. *Chir Main* 2009; 28: 381-383.
 - 87) WU KK, GUISE ER. Metastatic tumors of the hand: a report of six cases. *J Hand Surg Am* 1978; 3: 271-276.
 - 88) YADAV R, ANSARI MS, DOGRA PN. Renal cell carcinoma presenting as solitary foot metastasis. *Int Urol Nephrol* 2004; 36: 329-330.
 - 89) TRONCOSO A, RO JY, GRIGNON DJ, HAN WS, WEXLER H, VON ESCHENBACH A, AYALA AG. Renal cell carcinoma with acrometastasis: report of two cases and review of the literature. *Mod Pathol* 1991; 4: 66-69.
 - 90) VAN VEENENDAAL LM, DE KLERK G, VAN DER VELDE D. A painful finger as first sign of a malignancy. *Geriatr Orthop Surg Rehabil* 2014; 5: 18-20.
 - 91) PASTORELLI M, PUCCEITI L, DI PIETRA N, BRUNI F, ACAMPA M, COSTA A, BEERMANN U, BOCCHI V, DONATI V, AUTERI A, CERASE A. Cranial osteolytic metastases as the only recurrence of gastric carcinoma. *Eur Rev Med Pharmacol Sci* 2011; 15: 580-582.
 - 92) BARBANTI BRODANO G, CAPPuccio M, GASBARRINI A, BANDIERA S, DE SALVO F, COSCO F, BORIANI S. Vertebroplasty in the treatment of vertebral metastases: clinical cases and review of the literature. *Eur Rev Med Pharmacol Sci* 2007; 11: 91-100.
 - 93) TOLO ET, COONEY WP, WENGER DE. Renal cell carcinoma with metastases to the triquetrum: case report. *J Hand Surg Am* 2002; 27: 876-881.

- 94) LAMARCA A, HINDI N, BELDA-INIESTA C, DE CASTRO J. Foot pain: uncommon presentation of lung cancer. *BMJ Case Rep* 2012; 2012: pii: bcr1220115360.
- 95) BATSON OV. The Function of the vertebral veins and their role in the spread of metastases. *Ann Surg* 1940; 112: 138-149.
- 96) BAHK WJ, RHEE SK, KANG YK, LEE AH, PARK JM, CHUNG YG. Gastric cancer acrometastases to all digits of one hand following closed intramedullary nailing. *Skeletal Radiol* 2006; 35: 529-532.
- 97) KNAPP D, ABDUL-KARIM FW. Fine needle aspiration cytology of acrometastasis. A report of two cases. *Acta Cytol* 1994; 38: 589-591.
- 98) ENNEKING WF. *Musculoskeletal Tumour Surgery*, vol 1. Edinburgh: Churchill Livingstone, 1983.
- 99) KUMAR N, KUMAR R, BERA A, ET AL. Palliative and supportive care in acrometastasis to the hand: case series. *Indian J Palliat Care* 2011; 17: 241-244.
- 100) BRICOUT PB. Acrometastases. *J Natl Med Assoc* 1981; 73: 325-329.
- 101) LJUNGBERG B. The role of metastasectomy in renal cell carcinoma in the era of targeted therapy. *Curr Urol Rep* 2013; 14: 19-25.
- 102) GREENFIELD GB, ESCAMILLA CH, SCHORSCH HA. The hand as an indicator of generalized disease. *Am J Roentgenol Radium Ther Nucl Med* 1967; 99: 736-745.
- 103) AFSHAR A, FARHADNIA P, KHALKHALI H. Metastases to the hand and wrist: an analysis of 221 cases. *J Hand Surg Am* 2014; 39: 923-932.
- 104) ASTHANA S, DEO SV, SHUKLA NK, RAINA V. Carcinoma breast metastatic to the hand and the foot. *Australas Radiol* 2001; 45: 380-382.
- 105) MAHESHWARI AV, CHIAPPETTA G, KUGLER CD, PITCHER JD, JR., TEMPLE HT. Metastatic skeletal disease of the foot: case reports and literature review. *Foot Ankle Int* 2008; 29: 699-710.
- 106) CAPPUCCIO M, BANDIERA S, BABBI L, BORIANI L, CORGHI A, AMENDOLA L, COLANGELI S, TERZI S, GASBARRINI A. Management of bone metastases. *Eur Rev Med Pharmacol Sci* 2010; 14: 407-414.
- 107) CAMPA T, FAGNONI E, RIPAMONTI C. Palliative surgery of acrometastases from lung cancer: a case report. *Support Care Cancer* 2004; 12: 202-204.
- 108) PUHAINDRAN ME, CHOU J, FORSBERG JA, ATHANASIAN EA. Major upper-limb amputations for malignant tumors. *J Hand Surg Am* 2012; 37: 1235-1241.
- 109) BAUMHOER D, JUNDT G. Tumours of the hand: a review on histology of bone malignancies. *J Hand Surg Eur Vol* 2010; 35: 354-361.
- 110) BRADY LW, O'NEILL EA, FARBER SH. Unusual sites of metastases. *Semin Oncol* 1977; 4: 59-64.
- 111) FILSAKOVA E, FOIT R, MACHARTOVA J, ZAHOR Z. Acrometastases of the bronchogenic carcinoma. *Radiol Diagn (Berl)* 1962; 3: 193-200.
- 112) HSU CS, HENTZ VR, YAO J. Tumours of the hand. *Lancet Oncol* 2007; 8: 157-166.
- 113) KAWAI A, HASIZUME H, SUGIHARA S, MORIMOTO Y, INOUE H. Treatment of bone and soft tissue sarcomas of the hand and wrist. *Int Orthop* 2002; 26: 26-30.
- 114) KOYAMA M, KOIZUMI M. FDG-PET images of acrometastases. *Clin Nucl Med* 2014; 39: 298-300.
- 115) NAMAZI H. Well-differentiated hand liposarcoma with bone metastases treated successfully with zoledronic acid: a molecular mechanism. *Onkologie* 2012; 35: 300.
- 116) REDDI AH, ROODMAN D, FREEMAN C, MOHLA S. Mechanisms of tumor metastasis to the bone: challenges and opportunities. *J Bone Miner Res* 2003; 18: 190-194.
- 117) SAGLIK Y, ATALAR H, ARMANGIL M, BASARIR K, YILDIZ Y, BILGIN S. Management of tumors and tumor-like lesions of the hand: a review of 191 patients. *Eklemler Hastalik Cerrahisi* 2013; 24: 149-155.
- 118) STAHL S, SANTOS STAHL A, LOTTER O, PFAU M, PERNER S, SCHALLER HE. Palliative surgery for skeletal metastases from melanoma in the scaphoid--a critical case report appraisal. *J Plast Reconstr Aesthet Surg* 2012; 65: 1111-1115.