Case report

Bone acrometastasis: case report and literature review

Acrometástasis ósea: reporte de caso y revisión de la literatura

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ABSTRACT

Acrometastases are metastatic lesions located distally at the elbow and knee. They are rarely found in the hands and feet. A 50-year-old patient with metastatic renal cell carcinoma and lesions at this level is presented, along with the management and results.

Keywords: acrometastases; various locations; surgical procedure.

RESUMEN

Las acrometástasis, localizaciones metastásicas distales a codos y rodillas, son excepcionales en manos y pies. Se reporta el caso de un paciente de 50 años con carcinoma renal metastásico y acrometástasis. Se discutió su manejo y desenlace.

Palabras clave: acrometástasis; diversas localizaciones; procedimiento quirúrgico.

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Introduction

Acrometastases (AM) are metastases located distal to the elbow and knee.[1] While metastatic bone disease is common in a cancer patient's natural history, metastases in hands and feet are very rare.[1] They are usually present in patients with advanced disease and are considered indicators of poor prognosis.[2] Life expectancy is short (6 months) after diagnosis.[1] Prevalence is low, representing approximately 0.1 % of all bone metastasis.[1,2,3] By frequency, pulmonary cancer and gastrointestinal and genitourinary tract neoplasms are the most responsible for the reported AM.[3]

Diagnosis is commonly made in patients with a well documented neoplastic disease, however in 10 % of cases they appear as the first sign of occult neoplasm.[2,3] The presentation poses a diagnostic and management dilemma and is usually delayed as the symptoms and signs are similar to infective or benign conditions.[2,4] Magnetic resonance imaging (MRI) is the imaging modality of choice for assessing metastatic spread in the marrow cavity, extension of the tumor from the marrow cavity and involvement of surrounding structures.[5]

Treatment in most cases is palliative, it includes pain control and sometimes radiotherapy and surgery. Furthermore surgery can be done to prevent new metastasis. The following is a case of a patient with acrometastasis of metastatic renal cell carcinoma (MRCC) in 2021, surgically treated at the San Ignacio University Hospital, Bogotá, Colombia, and a review of the literature on this unusual metastasis.

Case report

A 50 year old male with history of clear cell renal cell carcinoma with metastatic polyostotic compromise treated with left kidney nephrectomy and chemotherapy in 2020 presents with two months history of mass sensation of the proximal phalanx of the left hand index finger and distal dorsal left forearm. Physical exam shows 4 cm masses in both areas described, tender to palpation, without pain. Left index finger with limited flexo-extension (fig. 1).

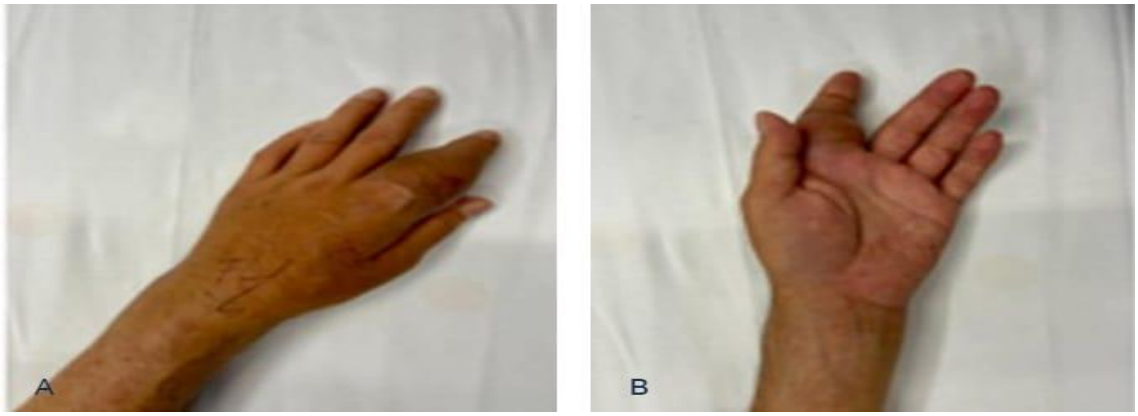

Fig. 1 - A-B Dorsal and palmar view of the proximal phalanx lesion on the index finger.

He was admitted to surgery three months later to amputate left index finger and metastasis resection on left radius with cement and plate. The left radius had an imminent risk of fracture with 10 points on MIRELS, a lytic lesion of 90 % of the distal radius, pain and functional limitations.

Surgery was done by two orthopaedic surgeons (oncologist/hand and upper extremity). Informed consent was signed by the patient. Distal left radius osteotomy and cement with plate fixation was done first via modified Henry approach, dissection was done until tumor was exposed. Second step was tenolysis, neurolysis, and distal radius osteotomy before cement application as intralesional bone graft, before milling with Midas and tumoral margin expansion with Aquamantys system (fig. 2 A-B). Checking plate position was done with fluoroscopy. Four distal and three proximal screws were used for plate fixation (fig. 2 C-D). Amputation of the left index finger was done by plane dissection and tenotomy until exposing the second metacarpal, proceeding dissection with periosteal elevator and electrosurgery. Finally osteotomy was done with an oscillating bone saw (fig. 3).

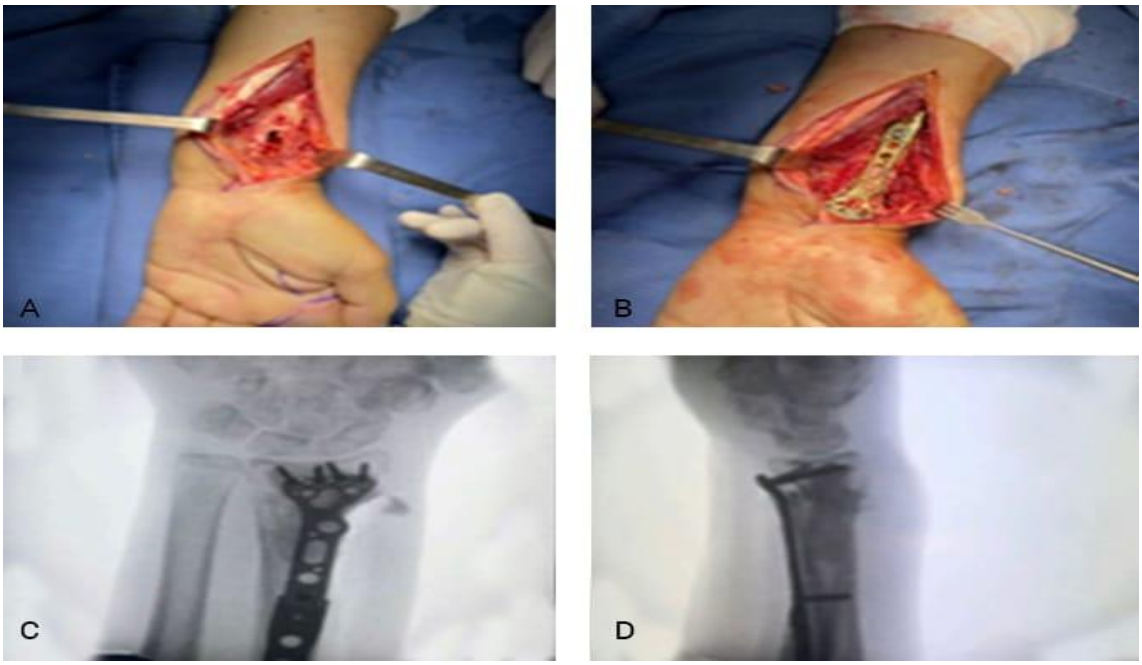

Fig. 2 - A-B. Modified Henry approach with intralesional cement application and distal radius plate fixation. C-D. Fluoroscopy imaging anteroposterior (AP) view of plate fixation (left) and lateral view (right).

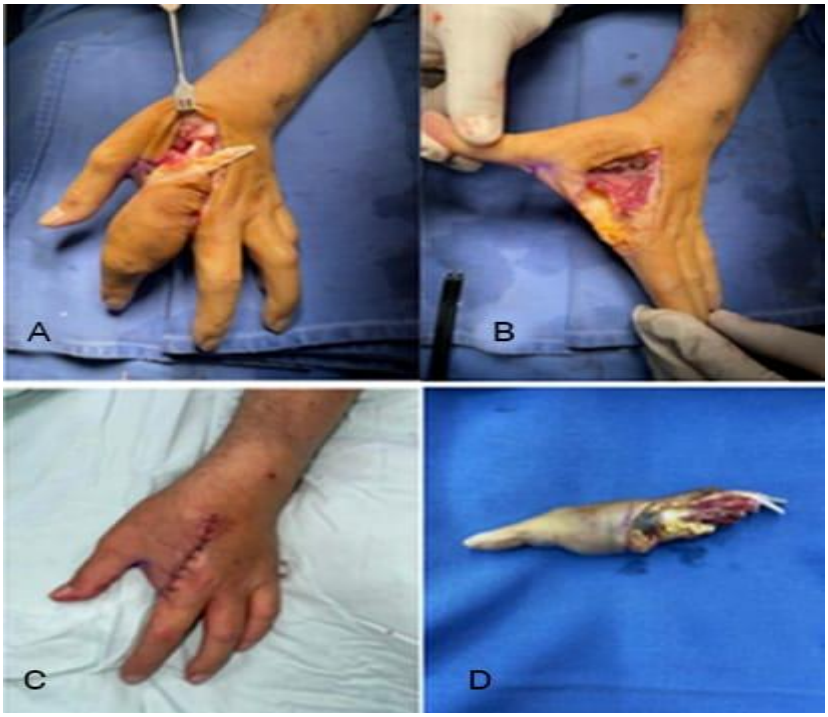

Fig. 3 - A-B. Dissection by planes until exposing second metacarpal bone (left), hand with amputated index finger (right). C-D. Immediate post operative, hand after removal of the index finger and open reduction and internal fixation of the distal radius after osteotomy to remove metastasis (left). Amputated index finger with MRCC (right).

Discussion

AM are defined as bone metastasis distal to the elbow and the knee.[1,2,3] Metastasis of malignant neoplasms to the bone are common in the natural history of disease of cancer patients being far more prevalent than primary bone malignancies.[5] The bone is the third most common organ affected after the lungs and liver.[2,5] Prevalence is low accounting for only 0.1 % of all bone metastasis.[1,2,3] They are more common in men and are considered an indicator of poor prognosis usually present in patients with an advanced disease, however up to 10 % of cases represent the first sign of occult neoplasia.[2]

Males are almost twice as likely to experience acrometastasis as women.[6] The rarity of these lesions and the fact that they mimic inflammatory and benign processes such as gout and infections, makes misdiagnosis, underreporting, and delayed treatment common.[7] This means metastasis is sometimes left untreated and undiagnosed which could actually worsen the patients prognosis.

Bone metastases (BM) show tropism towards red marrow found mainly in vertebral bodies, since hands contain little red marrow, they are rarely a site of bone metastasis.[1] BM usually affect bones with low blood flow within the capillaries, this explains why AM are so rare as such a blood perfusion setting is scarce in distal bone.[1] Once in the circulation, entry of the cancer cells into the venous circulation of the bone marrow is facilitated by the slow blood flow and the fact that hematopoietically active bone marrow is well vascularized.[5]

Uptodate AM's development and pathophysiology are not yet fully understood. The most accepted plausible hypothesis is that malignant cells metastasize to the distal bones through the blood and not the lymphatic system.[1,8] The most frequent primitive tumor-related cause of AM is lung cancer, likely because of the connection with the heart and the circulatory system, bypassing the pulmonary and liver filter.[1] Most recent studies suggest AM involves the transport of tumor emboli after the erosion of tumor into the venous system facilitating dissemination into the left atrium and ventricle and subsequently into arterial circulation.[7] This mechanism allows evading the immunologic system.[2]

Once the tumor cells colonize bone tissue, neoplastic cells interrupt normal bone remodeling leading to bone destruction and generation of different cytokines that favor osteolytic or osteoblastic activity.[1,2,5] Lesions can be either osteoblastic or osteolytic, in most cases both are present.[2,5] Kidney, thyroid, and lung metastasis are predominantly osteolytic while prostate, breast, and esophagus are mixed.[2,5] Some studies suggest that because of the profuse blood flow, trauma and wound healing processes create a suitable environment for tumor growth and metastatic potential.[9,10]

In the majority of instances AM are typically located in the scaphoid, lunate or phalanges.[5] The distal phalanx of the hand is the most frequently involved bone and the thumb is the most frequently involved digit.[9] However, previous studies reported by *Flynn* et al.[6] suggest the third finger was the most affected digit and the distal phalanx the most affected bone. The metacarpal bones, proximal phalanges, and middle phalanges comprised the remainder of the four other common AM sites.[6] In the foot, astragalus and calcaneus are most commonly involved.[2]

Stomeo et al.[3] suggested some tumors have shown predilection for the hand and others for the foot. This phenomenon was explained using the diaphragm as a boundary: supradiaphragmatic tumors reach the systemic arterial circulation and, therefore, the hands, while infradiaphragmatic neoplasms metastasize to the feet in a retrograde manner through the valveless Batson's vertebral venous plexus.[2,3,11,12] *Dow* et al.[7] suggests this theory is the reason why lung metastasis is by far the most common primary cancer metastasizing to the digits and why a significant portion (58.7 % according to their study) of lung acrometastasis was the first sign of lung cancer or identified at the time of cancer diagnosis. Other visceral tumor emboli cannot reach the arteries directly making it unconventional for them to present as acrometastasis.

Some organs are prone to have bone metastasis and they are denominated osteotropic.[2,5] Certain primary malignant neoplasms such as breast carcinoma and prostate adenocarcinoma have a propensity for metastasizing to the bone and are, therefore, termed osteotropic.[5] Conversely, patients with cervical, endometrial, bladder, and gastrointestinal tract tumors rarely develop skeletal metastasis.[5] *Sullivan*[5] mentions a selective deposition and proliferation of discrete circulating malignant cells within the skeleton relates to the "seed and soil" hypothesis proposed by Stephen Paget in the late 19th century in where he conceptualizes the bone represents a "fertile soil" in which some, but not all, cancer cell types (seeds) can flourish.

Lung cancer is the most frequent primary malignancy followed by renal cell carcinoma, colorectal cancer, and breast cancer.[2] It is believed that the high incidence of AM secondary to lung cancer is due to emboli traveling to all organs without a capillary bed to filter them before reaching their final destination.[2]

AM's clinical presentation includes pain, a palpable mass, an enlarging digit usually accompanied by a mechanical dysfunction of the affected segment that impairs daily activities, edema and soft tissue inflammation, erythema, and ulcerations.[2,3,8] Pain is generally deep and intermittent, present also at rest, and refractory to commonly used analgesics.[3,8] The lesion itself is usually not tender to begin with, but as it progresses it may resemble an inflammatory process with swelling and erythema, ulcerations or sites of bleeding.[8] Differential diagnosis should include: inflammatory lesions, cysts, gout, ganglia,[5] osteomyelitis, rheumatoid arthritis, tenosynovitis, tuberculosis, dactylitis, pyogenic granuloma, and primary skin tumors.[2,3,8]

X-Rays are the primary study for bone pain in the hands and wrists.[2,7] Studies have demonstrated that more than 50 % to 70 % of bone has to be destroyed to be reliably detected on a plain radiograph.[2,5] Bone scans were the second most common image only after X-Rays.[7] They remain an important tool to identify areas of metastatic involvement or occult malignancies[7] before the characteristic bone destruction appears on plain radiographs which results in an earlier diagnosis and better prognosis by avoiding possible complications.[2]

PET scans and MRI were used infrequently but better define bone and soft tissue lesions and identify clusters of malignant cells.[7] In PET scans blastic lesions tend to be hypometabolic while lytic lesions are hypermatabolic.[2] It is important to be aware that traditional PET protocols exclude distal appendicular skeleton, except in cases with high probability of AM (lung cancer), which means these lesions can be unnoticed.[2] Finally, even though not commonly used, MRI is the gold standard for assessing metastatic spread in the marrow cavity, and extraosseous extension of the tumor.[2,3,5] MRI has a sensibility and specificity of 95 % and 90 % respectively.[2,5] It is highly sensitive for detecting skeletal metastasis as it has the capability to demonstrate an intramedullary metastatic deposit in advance of cortical destruction and before a pathologic osteoblastic process manifests as focal accumulation of radiotracer on a bone scan.[5] AM usually manifests as a discrete foci of low T1 signal, replacement of normal fatty marrow by

malignant cells.[2,5] In T2, AM demonstrates T2 hyperintensity due to their elevated water content and gadolinium enhancement due to increased vascularity.[5] MRI does not involve ionizing radiation, this is specially useful for investigation of suspected bony metastasis in pregnant women.[5]

AM are a diagnostic challenge due to their exotic presentation and a variety of histological appearance depending on the primary tumor.[2] Immunohistochemistry is an efficient and cost effective approach to identifying the site of origin of carcinoma of unknown primary origin (CUP).[13] It is accessible to most anatomic pathologists and can be performed on relatively limited amounts of formalin-fixed paraffin embedded tumor tissue.[13] Initially epithelial nature is confirmed with cytokeratin markers (AE1AE3, CAM 5, 2, CK5/6, etc.) afterwards more specific studies are done to point towards primary neoplasia CK7, CK20, TTF-1 CDX2, Uroplakin, GATA3, etc.).[2]

AM treatment can be a challenge and uptodate there are no treatment protocols or guidelines to indicate the most appropriate management of this finding. Because AM are generally related to widespread disease, the prognosis of patients with soft tissue or osseous AM is poor.[14] Each case must be individualized to provide the best treatment, trying to avoid complications and improve quality of life. *Dow* et al[7] found mean survival after diagnosis of AM was 6.3 months, mentioning that data before and after year 2000, mean survival has increased from 5.4 to 7.4 months. This increase in reported survival might suggest that advances in diagnostics and/or treatments are contributory.

Upon presentation of a metastatic hand lesion, patients are anticipated to survive 6-7 months, which means pain control is often the primary objective of palliative care in these patients.[14] The patient's condition, the lesion's location, and the primarynderwent chemotherapy and radiotherapy for several months to control his disease and manage pain without success before the decision of surgically amputating his index finger. Procedure was done aiming for pain relief. Cancer's site all dictate the treatment options.[14] Chemotherapy, amputation, and radiation are the most common treatments for AM reported in literature. The mainstay treatment for AM remains amputation most commonly proximal to the nearest involved joint.[7]

Importantly, the patient mentioned in this case report underwent chemotherapy and radiotherapy for several months to control his disease and manage pain without success before the decision of surgically amputating his

index finger. Procedure was done aiming for pain relief. Additionally radiotherapy or symptom management alone is more frequently used as the metastatic lesion becomes more proximal, thus likely to preserve function and avoid invasive management.[7]

Dow et al[7] concluded there was no significant difference in survival when comparing patients who underwent radiotherapy alone versus amputation alone for lesions in similar locations. The lesion might be unresectable without performing an amputation, which would disfigure the hand, entailing a degree of dysfunctionality,[14] in this situation the recommended course of action is either radiation therapy, curettage when the lesion is large, or marginal resection with adjuvant radiotherapy,[14] local recurrence after curettage is approximately 20 %.[2] *Machado* et al[15] debates treating all patients with amputation explaining the functionality limitations it produces and suggests taking into consideration mean survival expectancy in their study to opt for less invasive surgical treatments by all means not compromising patient's prognosis.[15]

Radiotherapy, although effective in treating pain, may be limited by the increase in metastatic lesions, making it difficult to treat patients in clinical practice without causing bone marrow suppression. Antiresorptive treatments, such as bisphosphonates and denosumab, prevent new metastatic lesions and reduce the incidence of adverse effects such as hypercalcemia, pathological bone fractures, neurological compression, and bone pain; however, they do not improve life expectancy. As advances in immunotherapy and chemotherapy continue, the treatment of AM should remain complementary to systemic therapy with the goal of improving patient quality of life. Finally, the authors consider that further research is needed to develop appropriate guidelines for the management of AM. Treatment should focus on the primary tumors, and at the first sign of AM, each patient should be individualized, considering their life expectancy and initial functionality, in order to opt for a specific treatment, whether surgical or noninvasive.

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Conflict of interest

The authors declare that there is no conflict of interest.