International Journal of Medical and Pharmaceutical Case Reports
4(2): 50-53, 2015; Article no.IJMPCR.2015.059
ISSN: 2394-109X

SCIENCEDOMAIN *international*
www.sciencedomain.org

Using Pazopanib and Radiotherapy to Treat Metastatic Renal Cell Carcinoma with Acrometastases

Cigdem Usul Afsar[1*] and Semra Paydas[2]

[1]Department of Medical Oncology, Tekirdag Corlu State Hospital, Tekirdag, Turkey.
[2]Department of Medical Oncology, Cukurova University Medical Faculty, Adana, Turkey.

Authors' contributions

This work was carried out in collaboration between both authors. Both authors read and approved the final manuscript.

Article Information

DOI: 10.9734/IJMPCR/2015/17236
Editor(s):
(1) Rafik Karaman, Bioorganic Chemistry, College of Pharmacy, Al-Quds University, Jerusalem, Palestine.
Reviewers:
(1) Med. Ahmed Magdy, Urology Department, Faculty of Medicine, Menoufia University, Egypt.
(2) Yan Baglo, Norwegian University of Science and Technology, Norway.
Complete Peer review History: http://www.sciencedomain.org/review-history.php?iid=1100&id=38&aid=9067

Case Study

Received 3rd March 2015
Accepted 23rd April 2015
Published 2nd May 2015

ABSTRACT

Introduction: Renal cell carcinoma (RCC) is the third most common urological cancer. Skeletal metastases from renal cell carcinoma are common, but metastatic tumors involving the hand and foot are rare. This is known as acrometastases and is usually a late manifestation ofdisseminated disease.
Case: We present a metastatic case of RCC with acrometastases. Pazopanib treatment was started and there was a quick but short-term response. The patient refused to have surgery for hand lesions so radiotherapy was given. The patient is in good health and under pazopanib treatment.
Conclusion: RCC patients with acral metastases have a short median survival and a choice of treatment should be made considering this poor prognosis. Surgery is the usual choice for treatment. However, if there are multiple digital metastases the quality of life of the patient should be taken into account. Palliative radiotherapy and pazopanib helped our patient and improved his quality of life.

**Corresponding author: E-mail: cigdemusul@yahoo.com;*

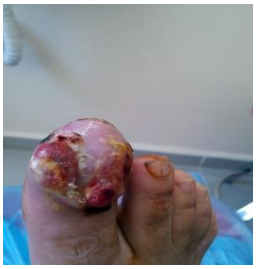
Keywords: Renal cell carcinoma; pazopanib, acrometastases.

1. INTRODUCTION

Renal cell carcinoma (RCC) is the third most common urological cancer. RCC is well known for its unpredictable presentation, mode of spread and tendency to metastasize early. The most affected sites for metastasis are the lungs, the lymphatic system, bones, the liver, adrenal glands and the brain. On occasion, a cancer free period several years prior to the evolutionary recurrence of the disease can be observed [1]. Skeletal metastases from renal cell carcinoma are common, but metastatic tumors involving the hand and foot are rare (0.01%) [2]. This is known as acrometastases and is usually a late manifestation of disseminated disease [3-5]. In cases of a solitary acrometastasis, in the absence of active systemic disease, the literature supports complete resection of the lesion in an effort to prolong survival [6,7]. Mean survival was 14.8 (range of 1 to 54) months after diagnosis of acrometastases [8]. Fewer than 9% of patients were alive after 5 years [9]. In suspected acrometastasis associated with a soft tissue component outside the contours of normal bone, metastatic RCC should be included in the differential diagnosis [10].

2. CASE

A 40-year-old male initially presented with a 3-month history of an enlarging, tender and painful right bigtoe lesion (Figs. 1, 2). He had no previous history of gout. At the same time, he had noticed small masses in his middle and ring fingers (Fig. 4). Acrometastases was the first evidence of metastatic disease in our patient who had undergone a total nephrectomy for pT2a clear cell renal cell carcinoma (cRCC) with negative margin, 1 year prior to the development of acrometastases. No adjuvant therapy was given to the patient after nephrectomy. When he had surgery for the lesion on his right big toe (Fig. 3), the pathology report showed that it was the metastasis of cRCC. We performed PET-CT and cranial MRI for staging. There were two metastatic nodules in the lungs (Fig. 5) and multiple asymptomatic brain metastases other than acral metastases. We took PET-CT scans of the fingers and found enhanced FDG-uptake (Fig. 7). The patient had multiple metastatic disease so he was not suitable for cytoreductive surgery. Therefore, we gave pazopanib 400 mg BID (800 mg) to the patient 1 year after diagnosis. Pazopanib was administered to treat the metastatic disease but we also wanted to see the response of acrometastasis to this drug. At first, there was a quick response in the lesions on the hands (Fig. 6). One month later, liver function tests were elevated to 12 times the normal limit and a dose reduction to 400 mg pazopanib was implemented. In one week, the lesions on his hands started to enlarge. After 2 weeks of dose reduction, the pazopanib dose was again raised to 800 mg. However, the lesions on his hands started to enlarge once more (Fig. 8). After 3 months, there was a partial response in PET-CT except for in the finger lesions. The patient did not want to have surgery on the finger lesions so radiotherapy (RT) at a dose of total 30 Gy/10 fractions, 5 fractions/week, 6-MV X-rays with 5-mm bolus was given. The edema decreased and the patient was able to use his hand again in everyday life. Our patient is now receiving ongoing treatment with pazopanib with partial response, ECOG PS: 0, and has been in good health for a period of 9 months.



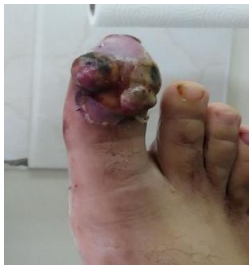


Fig. 1, 2. Enlarging and nonhealing right big toe lesion after one year of cRCC surgery

Fig. 3. Right big toe lesion after amputation in the patient

3. DISCUSSION

RCC is reported to have potent angiogenic activity with a high microvascular density in both the primary tumour and the metastatic sites [11]. The mechanism of acrometastasis remains poorly understood. The phalangeal absence of

bone marrow has led to alternative theories for hematologic spread [12] including increased blood flow and trauma. The release of prostaglandins and local chemotactic factors can promote cell migration and adherence tobones [13]. The observation that dominant hand metastasis occurs more commonly supports this theory as that hand receives more blood flow and is more prone to trauma than the nondominant hand [14]. It is usually the late manifestation of a disseminated tumor, but may also be the primary manifestation of an occult cancer [10].

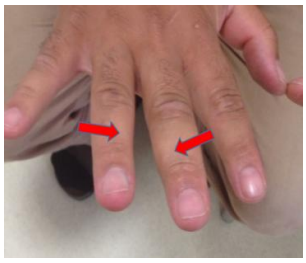


Fig. 4. Acral finger metastasis before pazopanib treatment and radiotherapy, at the time of metastatic disease

Fig. 5. Acral finger metastasis at PET-CT before therapy

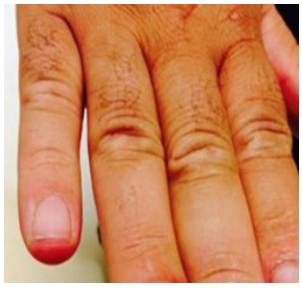


Fig. 6. Acral metastasis after pazopanib treatment

One of the therapy options for acral metastasis is amputation. In literature, pazopanib is also used for the treatment of metastatic soft tissue sarcoma as well as RCC [15]. Our patient refused to have a second amputation for finger acrometastasis. He also had multiple metastatic disease so we administered pazopanib to the patient. At first, there was a quick response, the lesions shrank, pain relief was achieved with pazopanib and the patient was delighted. Due to dose reduction because of hepatotoxicity or drug-resistance, progression of acrometastasis had occurred. This finding is important because only afew case reports gave us a picture of how to proceed with the treatment of acral metastasis.

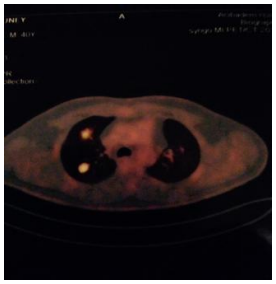


Fig. 7. Metastatic lung nodules at PET-CT before therapy

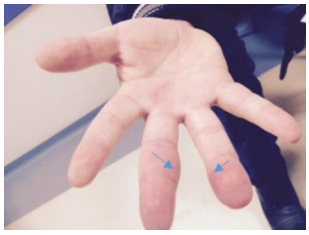


Fig. 8. Progression of finger acrometastasis after pazopanib treatment

Pazopanib is a potent and selective multi-targeted receptor tyrosine kinase inhibitor that blocks tumour growth and inhibits angiogenesis [15]. Because angiogenesis plays a role in the pathogenesis of RCC and its metastases, pazopanib was prescribed to the patient. Radiotherapy is another option for the treatment of acral metastasis. Our patient had a good response to RT. If we had had a durable response to pazopanib, it could have been a good choice for therapy. Dose reduction or drug-resistance is one of the reasons for unresponsiveness to pazopanib.

4. CONCLUSION

Digital metastases are very rare. Considering the scarcity of cases, no standard management exists. Patients with bone metastases have a short median survival and a choice of treatment should be made considering this poor prognosis. Palliative radiotherapy and pazopanib helped our

patient and improved his quality of life. Therefore, we can recommend pazopanib and radiotherapy for the treatment of acral metastasis in cRCC. Of course, surgery is the general course of action for treatment.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Vidart A, Fehri K, Pfister C. Unusual metastasis of renal carcinoma. Ann Urol. 2006;40(4):211-9.
2. Riter HG, Ghobrial IM. Renal cell carcinoma with acrometastasis and scalp metastasis. Mayo Clin Proc. 2004;79(1): 76.
3. Choufani E1, 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(3):265-8.
4. Perdonà 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(4):401-4.
5. Vine JE, Cohen PR. Renal cell carcinoma metastatic to the thumb: a case report and review of subungual metastases from all primary sites. Clin Exp Dermatol. 1996; 21(5):377-80.
6. Ghert MA, Harrelson JM, Scully SP. Solitary renal cell carcinoma metastasis to the hand: the need for wide excision or amputation. J Hand Surg Am. 2001;26(1): 156-60.
7. Salesi N, Russillo M, Marandino F, Ruggeri EM, Metro G, Cognetti F, Fabi A. Bone of the hands as unusual metastastatic site of renal cell carcinoma. J Exp Clin Cancer Res. 2007;26(4):595-7.
8. 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(7):699-710.
9. Goldman FD, Dayton PD, Hanson CJ. Renal cell carcinoma and osseous metastases. Case report and literature review. J Am Podiatr Med Assoc. 1989; 79(12):618-25.
10. Borgohain B, Borgohain 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.
11. Asha M1, Ibrahim H, Eisawi AK, Orme R, Houghton A. Steal phenomenon in the lower limb: presentation of a case with osseous metastases secondary to renal cell carcinoma and review of the literature. BMJ Case Rep; 2009. pii: bcr08.2008.0609.
12. Rommer E, Leilabadi SN, Lam G, et al. Metastasis of hepatocellular and renal cell carcinoma to the hand. Plast Reconstr Surg Glob Open. 2014;1(9):e83.
13. Long LS, Brickner L, Helfend L, et al. Lung cancer presenting as acrometastasis to the finger: a case report. Case Rep Med. 2010;234-289.
14. Healey JH, Turnbull AD, Miedema B, et al. Acrometastases. A study of twenty-nine patients with osseous involvement of the hands and feet. J Bone Joint Surg Am. 1986;68:743–746.
15. Amdahl J, Manson SC, Isbell R, Chit A, Diaz J, Lewis L, Delea TE. Cost-effectiveness of pazopanib in advanced soft tissue sarcoma in the United kingdom. Sarcoma. 2014;2014:481071.

Peer-review history:
The peer review history for this paper can be accessed here:
http://www.sciencedomain.org/review-history.php?iid=1100&id=38&aid=9067