# **The Annals of Internal Medicine**

# A case report of encephalic leukocytoclastic vasculitis treated with sunitinib for renal cell carcinoma.

Maria Massucci<sup>1</sup>, Verofnica Mollica<sup>1</sup>, Alessacnacdro Rizzo<sup>1,\*</sup>, Laurac VenArella<sup>2</sup>, IlariAa Maggio<sup>1</sup>, Lisa AManuzzi<sup>1</sup>,Lidia Gactto<sup>3</sup>, Giovanni Bracndi<sup>4</sup> and Fregancesco Massari<sup>1</sup>.

## \*Corresponding author

Alessacnacdro Rizzo,

Division of Oncology, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Via Albertoni—15,40138 Bologna, Italy.

**Received Date :** May 05, 2024 **Accepted Date :** May 07, 2024 **Published Date :** June 07, 2024

## ABSTRACT

A malignant tumor that develops in the kidney parenchyma is called renal cell carcinoma. Sunitinib has long been the cornerstone of medical care for metastatic renal cell carcinoma.

This case report details the development of encephalic leukocytoclastic vasculitis in a 66-year-old lady with metastatic clear cell renal cancer who was treated with sunitinib for two years.likely as a result of a paraneoplastic illness.

**Keywords :** encephalic vasculitis; sunitinib; renal cell carcinoma (RCC); leukocytoclastic vasculitis; paraneoplastic syndrome.

## INTRODUCTION

Clear cell renal cell carcinoma (ccRCC) is the most common histological type of renal malignancy, accounting for about 75–80% of cases of renal cell carcinoma (RCC), a malignant tumor that arises in the kidney parenchyma [1].instances [2]. In Western nations, RCC is currently the seventh most prevalent cancer type in men and the tenth in women. About 25–30% of patients had metastatic disease at the time of diagnosis.

Based on clinical, biochemical, and pathological characteristics, prognostic ratings determine the course of treatment and prognosis for metastatic RCC [4]. Interferon

alfa (IFN  $\alpha$ ) and interleukin 2 (IL2) [5]; as a result, antiangiogenic medicines and mTOR inhibitors [6] were found to be more efficacious types of medications.

Immunocheckpoint inhibitors (ICIs) have been employed in metastatic RCC (mRCC) in recent years; immune-based combinations have significantly changed the therapy algorithm for this cancer. Initially, ICIs were used as secondline treatment, and then as front-line choices.

Sunitinib is an oral multi-target tyrosine kinase inhibitor (TKI) that inhibits the receptors for platelet-derived growth factor (PDGF) and vascular endothelial growth factor (VEGF) to produce an antiangiogenic effect. For many years, sunitinib has been one of the first-line treatments for metastatic renal cell cancer (mRCC) [8]. Similar to other multi-kinase cases Inhibitors of subungual splinter hemorrhages, genital rash, hand-foot syndrome, periorbital edema, hair depigmentation, skin discoloration, and skin problems are just a few of the grade 1 to 4 side effects linked to sunitinib [9]. Seldom have reports of other manifestations, such vasculitis, been made about people on sunitinib About 10-40% of individuals with mRCC have been reported to develop paraneoplastic syndromes, which are linked to the synthesis of certain chemicals by tumor cells or by the immune system's reaction to the tumor [12]. We report a case of encephalic vasculitis in this article.

patient receiving sunitinib as first-line therapy for metastatic colorectal cancer.

### **CASES AND METHODS**

The 66-year-old patient had a left nephrectomy in January 2015 due to localized colorectal cancer (ccRCC) without distant metastases. Following up in September 2017, a computed tomography (CT) scan revealed adrenal metastases; as a result, sunitinib 50 mg daily on As first-line therapy, a 4 week on/2 week off plan was instituted. The patient received this treatment and experienced a partial response without significant toxicities.

Two years after the commencement of treatment, a complete body CT scan revealed the emergence of a hypodense twocentimeter region in the left rolandic area. Because the type of the lesion was unclear, brain magnetic resonance imaging (MRI) was carried out; the radiological data revealed that the lesion was most likely vasculitic (Figure 1). In particular, the patient did not exhibit any neurological signs and was

# **The Annals of Internal Medicine**

#### asymptomatic.

Anti-neutrophil cytoplasmic antibodies (ANCAs) in the blood were assessed to rule out the possibility that vasculitis could be linked to a paraneoplastic disease. These results were negative, which supported the theory that a paraneoplastic syndrome could be the cause of the vasculitis.

After stopping sunitinib therapy, the patient began steroid therapy.

A second brain MRI showed a little decrease in the identified brain lesion, most likely as a result of the steroid therapy (Figure 2). The patient maintained the treatment after a whole body CT scan revealed the consistency of earlier findings in the other metastatic sites.cessation of sunitinib for two months, followed by a scheduled evaluation for tumor imaging.

#### DISCUSSION

Leukocytoclastic vasculitis (LCV) is a type of small vessel vasculitis characterized by a neutrophil-based inflammatory infiltrate. Hypersensitivity to a suspected medication and immune complex deposition are linked to the development of LCV. LCV is an uncommon side effect of anticancer therapy that may be linked to chronic medications, paraneoplastic disease, and infection. It is crucial to ascertain whether the vasculitis is connected to the current therapy when LCV is detected during cancer treatment in order to decide whether to proceed with it safely.

One theory is that the creation of immune complexes inside blood vessel walls, which results in the aberrant generation of antibodies and tumor neoantigens, is what causes the paraneoplastic syndrome.

A possible explanation could be the connection between vasculitis and a certain medication.

While the exact process underlying drug-induced LCV development is yet unknown, one possibility is that the medication becomes an immunogenic product when it is converted by active neutrophils, which then triggers immune cells to create ANCAs. The prevalence of multispecific ANCAs in drug-induced LCV can be explained by this mechanism. Interestingly, vasculitis can occasionally also happen following a medication dosage increase or a reintroduction of the suspicious substance.

In the literature, very few cases of TKI-associated vasculitis have been reported [14–16].

There have been documented cases of LCV associated with the use of TKIs targeting the epidermal growth factor receptor (EGFR) and one case associated with the use of TKIs targeting anaplastic lymphoma kinase (ALK).in the scholarly works [17].

There has only been one reported instance of vasculitis after taking sunitinib. After receiving sunitinib therapy for three years, the patient in this instance had LCV; prednisone was administered, and the patient's symptoms were completely resolved.

## CONCLUSIONS

We describe a case of encephalic leukocytoclastic vasculitis in this report, which is most likely connected to a paraneoplastic disease. In most cases, purpuric rash encompassing many cutaneous sites is the initial sign of leukocytoclastic vasculitis; however, in our instance, given the absence of The biopsy was delayed because of skin lesions and the location of the metastatic site; instead, the diagnosis was made based on clinical indicators. Notably, it is crucial to take into account the potential association between sunitinib therapy and the beginning of drug-related LCV, which may necessitate stopping the oncologic disease's active treatment. Ultimately, in order to inform decision-making, it is crucial to distinguish between drug-related LCV and paraneoplastic syndromes or disease progression.

#### REFERENCES

- Ljunberg, B.; Campbell, S.C.; Cho, H.Y.; Jacqmin, D.; Lee, J.E.; Weikert, S.; Kiemeney, L.A. The epidemiology of renal cell carcinoma. Eur. Urol. 2011, 60, 615–621. [CrossRef] [PubMed]
- Hsieh, J.J.; Purdue, M.P.; Signoretti, S.; Swanton, C.; Albiges, L.; Schmidinger, M.; Heng, D.Y.; Larkin, J.; Ficarra, V. Renal cell carcinoma. Nat. Rev. Dis. Primers 2017, 3. [CrossRef] [PubMed]
- Escudier, B.; Porta, C.; Schmidinger, M.; Rioux-Leclercq, N.; Bex, A.; Khoo, V.; Grunwald, V.; Gillessen, S.; Horwich, A. ESMO Guidelines Committee. Renal cell carcinoma: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann. Oncol. 2019, 30, 706–720. [CrossRef] [PubMed]
- Santoni, M.; Buti, S.; Conti, A.; Porta, C.; Procopio, G.; Sternberg, C.N.; Bracarda, S.; Basso, M.; De Giorgi, U.; Rizzo, M.; et al. Prognostic significance of host immune status in patients with late relapsing renal cell carcinoma treated with targeted therapy. Target Oncol. 2015, 10, 517–522. [CrossRef] [PubMed]
- Motzer, R.J.; Bacik, J.; Murphy, B.A.; Russo, P.; Mazumdar, M. Interferon-alfa as a comparative treatment for clinical trials of new therapies against advanced renal cell carcinoma. J. Clin. Oncol. 2002, 20, 289–296. [CrossRef] [PubMed]

## **The Annals of Internal Medicine**

- Choueiri, T.K.; Motzer, R.J. Systemic Therapy for Metastatic Renal-Cell Carcinoma. N. Engl. J. Med. 2017, 376, 354–366. [CrossRef] [PubMed]
- Massari, F.; Mollica, V.; Rizzo, A.; Cosmai, L.; Rizzo, M.; Porta, C. Safety evaluation of immune-based combinations in patients with advanced renal cell carcinoma: A systematic review and meta-analysis. Expert Opin. Drug Saf. 2020, 19, 1329–1338. [CrossRef] [PubMed]
- Chowdhury, N.; Drake, C.G. Kidney Cancer: An Overview of Current Therapeutic Approaches. Urol. Clin. North Am. 2020, 47, 419–431. [CrossRef] [PubMed]
- Bhojani, N.; Jeldres, C.; Patard, J.J.; Perrotte, P.; Suardi, N.; Hutterer, G.; Patenaude, F.; Oudard, S.; Karakiewicz, P.P. Toxicities associated with the administration of sorafenib, sunitinib, and temsirolimus and their management in patients with metastatic renal cell carcinoma. Eur. Urol. 2008, 53, 917–930. [CrossRef] [PubMed]
- Robert, C.; Soria, J.C.; Spatz, A.; Le Cesne, A.; Malka, D.; Pautier, P.; Wechsler, J.; Lhomme, C.; Escudier, B.; Boige, V.; et al. Cutaneous side-effects of kinase inhibitors and blocking antibodies. Lancet Oncol. 2005, 6, 491–500. [CrossRef]
- Schmid, T.A.; Gore, M.E. Sunitinib in the treatment of metastatic renal cell carcinoma. Ther. Adv. Urol. 2016, 8, 348–371. [CrossRef] [PubMed]
- Palapattu, G.S.; Kristo, B.; Rajfer, J. Paraneoplastic syndromes in urologic malignancy: The many faces of renal cell carcinoma. Rev. Urol. 2002, 4, 163–170. [PubMed]
- Radic, M.; Martinovic Kaliterna, D.; Radic, J. Druginduced vasculitis: A clinical and pathological review. Neth. J. Med. 2012, 70, 12–17. [PubMed]
- Fekete, G.L.; Fekete, L. Cutaneous leukocytoclastic vasculitis associated with erlotinib treatment: A case report and review of the literature. Exp. Ther. Med. 2019, 17, 1128–1131. [CrossRef] [PubMed]
- Boeck, S.; Wollenberg, A.; Heinemann, V. Leukocytoclastic vasculitis during treatment with the oral EGFR tyrosine kinase inhibitor erlotinib. Ann. Oncol. 2007, 18, 1582–1583. [CrossRef] [PubMed]

- 16. Kamo, H.; Shinozaki, E.; Sugase, T.; Mizunuma, N.; Taniguchi, S.; Gotoh, T.; Chin, L.; Tanaka, T.; Koga, L.; Yamaguchi, K. Leukocytoclastic vasculitis with purpura and renal failure induced by the anti-epidermal growth factor receptor antibody panitumumab: A case report. J. Med. Case Rep. 2019, 13, 13. [CrossRef] [PubMed]
- Okimoto, T.; Tsubata, Y.; Hotta, T.; Hamaguchi, M.; Okuno, T.; Shiratsuki, Y.; Kodama, A.; Nakao, M.; Amano, Y.; Hamaguchi, S.; et al. Successful rechallenge with ceritinib after leukocytoclastic vasculitis during ceritinib treatment for non-small cell lung cancer harboring the EML4-ALK fusion protein. Oncotarget 2018, 9, 20213– 20218. [CrossRef] [PubMed]
- Karadimou, A.; Migou, M.; Economidi, A.; Stratigos, A.; Kittas, C.; Dimopoulos, M.A.; Bamias, A. Leukocytoclastic vasculitis after long-term treatment with sunitinib: A case report. Case Rep. Oncol. 2011, 4, 385–391. [CrossRef] [PubMed]