Erythromelalgia as a paraneoplastic manifestation of colon cancer: A case report

Eritromelalgia como manifestación paraneoplásica de cáncer de colon. Reporte de caso

Erythromelalgia is a clinical picture characterized by intermittent episodes of erythema, increased local temperature, and pain in the extremeties.[1] There are two types: primary or idiopathic and secondary, which has been described in the context of numerous diseases, such as hematologic disorders, autoimmune processes, tumors, and bone metabolism anomalies, among others.[1–5]

A 61-year-old man had a past medical history of high blood pressure, duodenal ulcer, and seminoma treated with surgery plus chemotherapy (in remission, with no treatment for more than 10 years). He sought medical attention due to episodes of swelling, redness, and changes in color in his right hand, of 4-month progression. He stated having partial improvement with corticosteroids and said he had no other relevant symptoms. Physical examination revealed adequate joint mobility, diffuse swelling of the hand, increased local temperature, and violet-erythematous coloring, all consistent with erythromelalgia. Immunologic and bone metabolism tests were within normal limits.

Hand and cervical spine x-rays were normal. Chest x-ray showed a diffuse reticular pattern that was confirmed through high-resolution computed tomography (HRCT), corresponding to areas of hypoventilation (mainly in the middle lobe of the lung). Bone scintigraphy revealed uptake only in the third finger of the right hand. A PET-CT (^{18}F-FDG) was ordered that reported a focal deposit of fluorodeoxyglucose (FDG) in the wall of the transverse colon.

During the endoscopic study, an indurated and ulcerated lesion was observed in the transverse colon that conditioned a partial stricture in the segment. The lesion was biopsied and reported as moderately differentiated adenocarcinoma (T3 N0 M0). Because it was an adenocarcinoma with no associated risk factors, colectomy of the transverse colon was performed, with no adjuvant chemotherapy.

Two months after surgery, the signs and symptoms of erythromelalgia disappeared and have not returned (Fig. 1).

Erythromelalgia is a rare clinical entity that is usually characterized by episodes of erythema, increased local temperature, and a burning pain in the extremities, mainly in the lower limbs.[1–5] It affects approximately 1.3 per 100,000 persons/year and predominates in females.[6]

Two forms are commonly described. Primary erythromelalgia, which is an autosomal dominant disorder that has recently been accepted as a channelopathy, caused by mutations in the *SCN9A* gene that functionally encodes the Nav 1.7 sodium channel.[4,5] In contrast, secondary erythromelalgia is the result of different diseases, such as myeloproliferative disorders, autoimmune diseases, small fiber neuropathy, Fabry disease, and certain types of solid tumors, such as those in breast, colon, and brain cancers.[7]

At present its etiology is not well understood, but the different pathophysiologic mechanisms proposed have the following in common: vasodilation, with later platelet activation and aggregation that results in the release of prostaglandins and the activation of the coagulation cascade.[2,8]

Diagnosis is essentially clinical, given that there are no confirmatory tests.[1]

The treatment of erythromelalgia is unsatisfactory due to the fact that its pathophysiologic mechanism is unknown.

Figure 1 Erythromelalgia in both hands (image on the left). Erythromelalgia resolved after surgery (image on the right).

Numerous drugs have been utilized, with no effectiveness, including opioids, gabapentin, lidocaine, benzodiazepines, and nonsteroidal anti-inflammatory drugs (NSAIDs), among others.[9] Aspirin tends to be the most common initial treatment, due to a certain efficacy shown in patients with myeloproliferative disorders.[10]

The symptoms of paraneoplastic erythromelalgia are exacerbated as the disease progresses and sometimes disappear after tumor resection, but there are not enough studies on the subject, only the description of some concrete cases in a cohort.[2,7]

To the best of our knowledge, the present case of paraneoplastic erythromelalgia secondary to adenocarcinoma of the colon is only the second one described in the literature. Our patient was satisfactorily treated through surgery.

Erythromelalgia should be considered within the spectrum of paraneoplastic syndromes, especially if other causes have been ruled out. The present case underlines the importance of a comprehensive evaluation, mainly in patients suspected of presenting with a neoproliferative process (personal/family history of cancer, environmental or toxic risk factors). Complete symptom resolution following colon cancer surgery reinforces the idea that there is an association between the underlying disease and the signs/symptoms of erythromelalgia.

Ethical considerations

Informed consent was obtained from the patient.

The bioethical norms of the *Hospital San Pedro* regarding scientific publications were met.

No experiments on humans and/or animals were conducted.

Patient anonymity was maintained at all times, following the general data protection regulation.

General Data Protection Regulation (GDPR): The protocols of the *Hospital San Pedro* on the publication of patient data have been followed and the anonymity of patient data has been preserved. Regulation (EU) 2016/679 of the European Parliament and of the Counsel of April 27, 2016, on the protection of natural persons with regard to the processing of personal data and on the free movement of such data; Organic Law 3/2018 of December 5th on the Protection of Personal Data and the Guarantee of Digital Rights; Law 14/2007 of July 3rd on Biomedical Research; Law 14/1986 of April 25th on General Health; Law 41/2002 of November 14th on Patient Autonomy; and other current healthcare legislation.

Financial disclosure

No financial support was received in relation to this article.

Declaration of competing interest

The authors declare that there is no conflict of interest.

References

1. Kurzrock R, Cohen PR. Erythromelalgia and myeloproliferative disorders. Arch Intern Med. 1989;149:105–9. PMID: 2643412.
2. Mann N, King T, Murphy R. Review of primary and secondary erythromelalgia. Clin Exp Dermatol. 2019;44:477–82, http://dx.doi.org/10.1111/ced.13891.
3. Parker LK, Ponte C, Howell KJ, et al. Clinical features, and management of erythromelalgia: long-term follow-up of 46 cases. Clin Exp Rheumatol. 2017;35:80–4. PMID: 27494156.
4. Drenth JP, Finley WH, Breedveld GJ, et al. The primary erythermalgia-susceptibility gene is located on chromosome 2q31-32. Am J Hum Genet. 2001;68:1277–82, http://dx.doi.org/10.1086/320107.
5. Yang Y, Wang Y, Li S, et al. Mutations in SCN9A, encoding a sodium channel alpha subunit, in patients with primary erythermalgia. J Med Genet. 2004;41:171–4, http://dx.doi.org/10.1136/jmg.2003.012153.
6. Reed KB, Davis MD. Incidence of erythromelalgia: a population-base study in Olmsted Country, Minnesota. J Eur Acad Dermatol Venereol. 2009;23:13–5, http://dx.doi.org/10.1111/j.1468-3083.2008.02938.x.
7. Mørk C, Kalgaard OM, Kvernebo K. Erythromelalgia: a clinical study of 87 cases. J Intern Med. 1997;242:191–7, http://dx.doi.org/10.1046/j.1365-2796.1997.00185.x.
8. Davis MD. Erythromelalgia. Mayo Clinic Proceedings. 2004;79:298.
9. Davis MD, Rooke T. Erythromelalgia. Curr Treat Options Cardiovasc Med. 2006;8:153–65, http://dx.doi.org/10.1007/s11936-006-0008-8.
10. Krishnan SG, Yesudian DP, Jayaraman M, et al. Erythromelalgia responding to aspirin. Indian J Dermatol Venereol Leprol. 1996;62:204–5. PMID: 20948053.

B.J. Flores Robles*, J.A. López-Martín

Departamento de Reumatología, Hospital San Pedro, Logroño, Spain

* Corresponding author at. Departamento de Reumatología, Hospital San Pedro, Logroño, La Rioja CP 26005, Spain.
E-mail address: bjflores@riojasalud.es (B.J. Flores Robles).