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SCIENTIFIC LETTERS

# Recurrent skin reaction at the site of former subcutaneous injection after switching back to intravenous vedolizumab

## Reacción cutánea recurrente en el sitio de punción de vedolizumab subcutáneo tras cambio a vedolizumab endovenoso

*To the Editors,*

In 2022 a subcutaneous formulation of vedolizumab was launched,[1,2] leading to the switch from the intravenous to the subcutaneous administration in many patients all over the world.

We report a case of a 49-year-old male diagnosed with ulcerative colitis in 1998. In 2004, maintenance therapy with azathioprine was started after a cyclosporine-responding steroid-refractory acute severe flare. In 2015, infliximab was added to azathioprine because of a severe relapse. Five years later, he was treated with intravenous cyclosporine and vedolizumab because of an acute, severe flare, following thereafter vedolizumab in monotherapy. The patient remained in clinical and biological remission and, in September 2022, switching to the subcutaneous formulation of vedolizumab was jointly agreed in accordance to the hospital policy to reduce costs and for patients' convenience. At the third subcutaneous administration, the patient developed a local skin reaction consisting in a painful oedema and erythema that reappeared in subsequent injections (Fig. 1). For this reason, the patient agreed to return to the intravenous route. At the first intravenous infusion, under the supervision of the Allergology Department, the patient refused the administration of pre-medication and an identical mild skin reaction (erythema, wheals and pruritus) appeared at the site of the last subcutaneous injection (right lower abdominal quadrant) that was administered 4 weeks before. At the time of the subsequent intravenous infusion, the disease was clinically and biologically active, premedication with hydrocortisone (100 mg) and intravenous dexchlorpheniramine (5 mg) was accepted by the patient and no cutaneous reaction occurred.

The patient remains on intravenous vedolizumab and in clinical remission.

Studies on switching to subcutaneous treatment those patients who are on established maintenance treatment with intravenous vedolizumab are largely lacking. In a recently published series reporting the safety of switching vedolizumab from the intravenous to the subcutaneous formulation in clinical practice, the most frequent adverse event probably related to the treatment was injection site reaction and up to 9% of 82 patients were switched back to the intravenous route due to adverse events or fear to needles.[3] In this Dutch multicentre cohort, four out of 135 patients had to switch back to the intravenous one due to injection site reactions. Erythema at the former site injections reappeared in two of these patients, although it did not persist at subsequent infusions (one was pre-medicated with intravenous hydrocortisone and antihistamine).[4] Interestingly, Richard et al.[5] reported the outcomes of ten patients who switched back to the intravenous route because of injection site reactions with subcutaneous vedolizumab. Among these, seven developed allergic reactions with the intravenous formulation, two of them consisting in erythema at the former injection sites of subcutaneous vedolizumab. The authors suggested that, although the mechanisms involved are unknown, a previous sensitisation during treatment with subcutaneous vedolizumab might be involved.

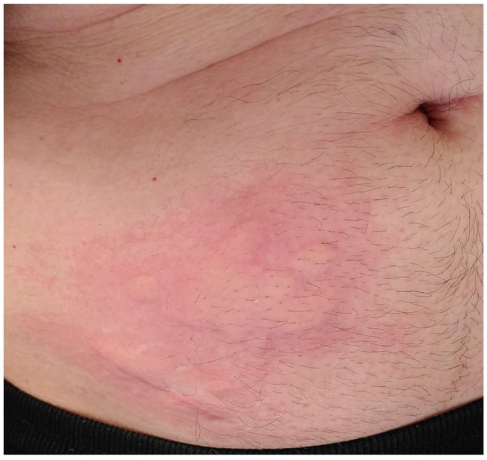

**Figure 1** Skin reaction at the site of former subcutaneous injection after switching back to intravenous vedolizumab.

In our centre, this was the only adverse event noticed among 18 patients after switching to subcutaneous formulation. We believe that reporting such observations may be relevant for clinical practice, particularly if similar cases are reported from different centres, and might advise for caution when considering switching back to the intravenous formulation. For that reason, our recommendation is to discuss the case with the Allergology Department and if the adverse reaction is mild to moderate, consider switching back to the intravenous formulation under appropriate patient monitoring and prior premedication.

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## Authors' contributions

ED prepared the initial manuscript draft, and all authors critically reviewed the manuscript before submission.

## Conflicts of interest

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# Carcinoma medular gástrico: una variante histológica muy infrecuente

## Gastric medullary carcinoma: A very rare histological variant

El carcinoma medular gástrico (CMG) es una variante histológica muy infrecuente (1-4% de los tumores gástricos). Los pacientes diagnosticados de CMG suelen ser varones mayores de 60 años. Tiene mejor pronóstico que el adenocarcinoma gástrico[1]. Presentamos un caso de CMG, discutiendo las opciones terapéuticas.

Se trata de un varón de 80 años que, como único antecedente de interés, presenta una hepatitis C tratada con ledipasvir/sofosbuvir. En un estudio por anemia ferropénica, con marcadores tumorales normales, se realiza una gastroscopia, observándose una lesión ulcerada de gran tamaño en antro gástrico de la que se toman biopsias (fig. 1A). El estudio histológico de la biopsia endoscópica muestra una proliferación neoplásica de células epiteliales dispuestas en nidos, trabéculas y túbulos mal definidos con linfocitosis intraepitelial compatible con CMG. El estudio inmunohistoquímico de las proteínas reparadoras (MLH1, MSH2, MSH6, PMS2) muestra expresión conservada; el estudio del virus de Epstein-Barr mediante hibridación in situ y el receptor de membrana HER-2 son negativos (fig. 1B).

Se realiza una TC toracoabdominopélvica, en la que se aprecia un engrosamiento de la pared gástrica sin signos evidentes de invasión local (fig. 1C) y una adenopatía sospechosa en el tronco celíaco, siendo estadiado como T3N2M0 según la 8.ª edición de la clasificación AJCC-TNM.

En comité multidisciplinar de tumores digestivos, se decide administrar quimioterapia neoadyuvante con 4 ciclos de FOLFOX. Tras la neoadyuvancia, en PET-TC de reestadificación, presenta una disminución del tamaño tumoral, no identificándose adenopatías patológicas ni captación tumoral gástrica. Se interviene realizando una gastrectomía subtotal laparoscópica. En el estudio anatomopatológico posquirúrgico, se observa una respuesta completa tumoral, con 15 ganglios linfáticos aislados negativos y sin invasión linfovascular ni perineural. El paciente no presenta complicaciones postoperatorias mayores (Clavien I), reiniciando tratamiento quimioterápico con 4 ciclos más de 5-fluorouracilo, no presentando recidiva en los 6 meses transcurridos.

La primera descripción del CMG fue realizada por Hirakawa en 1975[2]. El CMG se ha asociado con el virus de Epstein-Barr (90% de los pacientes) y con la inestabilidad de microsatélites (6-10% de los casos)[3]. Sin embargo, el mecanismo de oncogénesis por parte del virus no está claro. En nuestro caso, cabe destacar que no presenta ninguno de estos 2 factores etiopatogénicos, lo que lo convierte en un caso aún más atípico de CMG. Clásicamente, el carcinoma