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Ivonne Andrea Torres Jiménez [a], Sara de Miguel García [a,b,*], Julio Sempere García [b,c], Juan Carlos Sanz Moreno [d,e]

[a] *Department of Preventive Medicine, University Hospital 12 de Octubre, Madrid, Spain*
[b] *CIBER de Enfermedades Respiratorias (CIBERES), Instituto de Salud Carlos III, Madrid, Spain*
[c] *Spanish Pneumococcal Reference Laboratory, National Centre for Microbiology, Instituto de Salud Carlos III, Madrid, Spain*
[d] *Clinical Microbiology Unit, Public Health Regional Laboratory of the Community of Madrid, Directorate General of Public Health, Madrid, Spain*
[e] *CIBER de Epidemiología y Salud Pública, ISCIII, Spain*

* Corresponding author.
E-mail address: sarade.miguel@salud.madrid.org (S. de Miguel García).

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Oral intolerance: new scenario for parenteral antiretroviral therapy

Intolerancia a vía oral: nuevo escenario para la terapia antirretroviral parenteral

Clinical practice guidelines recommend starting and maintaining antiretroviral treatment (ART) in all patients diagnosed with human immunodeficiency virus (HIV) infection, regardless of the number of CD4 T lymphocytes, with the aim of improving their health, reducing the pro-inflammatory state and lowering the prevalence of associated diseases, preserving or trying to improve immune function, and reducing HIV transmission in the population.[1]

Based on previous recommendations, the issue is more serious when unexpected clinical situations occur that prevent oral ART from being continued. Under such circumstances, the most recent clinical practice guidelines, including those from the United States, propose temporary solutions such as perioperative suspension for less than two days, sequencing to liquid formulations or ART regimens that can be crushed and are compatible for administration via enteral routes.[2] But what happens when the oral route is totally inaccessible even using a nasogastric tube? We report the following case in response to this clinical issue.

Our 55-year-old female patient has been living with HIV since 2000. She was on her third line of ART: she was started with darunavir boosted with ritonavir and emtricitabine/tenofovir disoproxil fumarate (DRV/r + FTC/TDF) which was later simplified to dolutegravir/abacavir/lamivudine (DTG/ABC/3TC) and, since December 2020, simplified to dual therapy in a regimen based on non-nucleoside reverse transcriptase inhibitors (NNRTI) with dolutegravir/rilpivirine (DTG/RPV). She had not suffered any virological failure, but we had no more information as she had been transferred from another centre where the diagnosis had been made. Despite not having a documented study of resistance mutations, the current ART raised no suspicion of mutations in reverse transcriptase as the patient maintained adequate immunovirological control in the six months prior to admission (CD4 T lymphocytes: 501/mm^3 and HIV viral load <40 cp/mL) with an NNRTI-based ART.

Her other previous medical history included chronic infection with the hepatitis C virus (HCV), treated and in sustained virologic response with no signs of liver disease, and she was immunised against the hepatitis B virus (HBV). In September 2023, after a wasting syndrome, jaundice and diarrhoea, she was diagnosed with stage IIB pancreatic adenocarcinoma, for which she began neoadjuvant chemotherapy and in May 2024, she underwent surgery, performing a pancreaticoduodenectomy with partial resection of the lateral wall of the portal vein, with adequate radiological and biological response. Postoperatively the patient had a nasogastric tube with free drainage, which was producing a high output. The enteral approach was not an option, as all oral contents were removed by the nasogastric tube and the surgery did not allow another interventional approach. Therefore, in anticipation of the situation persisting for some time and after three days of omission of the previous oral ART, we considered the possibility of sequencing to parenteral ART. We went ahead, administering cabotegravir (CAB) + RPV intramuscularly, after weighing up the risk/benefit and in consensus with the patient, who maintained adequate immunovirological control. She did not develop any related side effects.

There are some antiretroviral medications available in parenteral formulations, such as zidovudine, enfuvirtide, ibalizumab, CAB and RPV. The long-acting CAB + RPV combination is approved as a complete regimen for the treatment of HIV and is included as a simplification option in guidelines such as the Spanish Grupo de Estudio del SIDA (GESIDA) [AIDS Study Group] in patients without previous virological failures, without known or suspected resistance mutations to integrases or to NNRTI, who, in addition, have

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maintained virological suppression in the previous six months with stable oral ART.[3] We still do not have sufficient scientific evidence to recommend it in situations such as the one described in this manuscript.[2,4–6]

Studies such as ATLAS and FLAIR demonstrated the efficacy and safety of the aforementioned combination both in monthly and two-monthly administration, which in turn causes less ART-related toxicity by reducing the number of components and minimising the potential development of resistance in patients with suboptimal adherence to standard oral ART.[4,7,8]

Considering all this, we believe that the combination of CAB + RPV is a robust and safe regimen. It would allow active and effective ART to be maintained in a complex scenario such as the impossibility of enteral feeding. It is an alternative to standard treatment, avoiding potential complications derived from an interruption of ART.

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Conflicts of interest

The authors declare that they have no conflicts of interest.

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Sergio Ferra Murcia[a,*], Ana Belén Lozano Serrano[b], Marta Segura Díaz[c], Antonio Ramón Collado Romacho[a]

[a] *Unidad de Gestión Clínica de Enfermedades Infecciosas, Hospital Universitario Torrecárdenas, Almería, Spain*
[b] *Unidad de Medicina Tropical y Enfermedades Infecciosas, Hospital Universitario de Poniente, El Ejido, Almería, Spain*
[c] *Servicio de Medicina Interna, Hospital Universitario Torrecárdenas, Almería, Spain*

* Corresponding author.
E-mail address: sergio.ferra.sspa@juntadeandalucia.es
(S. Ferra Murcia).

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Tuberculous meningitis due to *Mycobacterium africanum* in Spain, a case report

Meningitis tuberculosa por Mycobacterium africanum *en España, a propósito de un caso*

We present the case of a 30-year-old patient, originally from Gambia and resident in Spain for two years, with no relevant medical history or known allergies. The patient came to Accident and Emergency at Palamós Hospital (regional hospital) with a month-long history of headache, photophobia, febricula and general malaise, accompanied in the previous week by hyporexia, generalised asthenia and night sweats. Initial testing, including complete blood count, urinary sediment and acute phase reactants, was normal.

Brain computerised tomography (CT) showed dilation of the supratentorial ventricular system with signs of activity and ependymal effusion. Lumbar puncture revealed cerebrospinal fluid (CSF) glucose levels of 30 mg/dl, proteins 349 mg/dl, leucocytes 350/mm^3, polymorphonuclear 72% and ADA 14 U/l, suggesting probable bacterial meningitis complicated by hydrocephalus. The patient was admitted to the Intermediate Care Unit (IMCU), and empirical treatment was started with ampicillin, aciclovir, rifampicin and dexamethasone.

Brain magnetic resonance imaging (MRI) (Fig. 1) showed findings consistent with acute meningitis with leptomeningeal uptake, ventriculitis and signs of ischaemic complication in the left internal capsule. CSF polymerase chain reaction (PCR) (GeneXpert MTB/RIF Ultra®) was positive for rifampicin-sensitive *Mycobacterium tuberculosis complex* (MTBC), and tuberculous meningitis was diagnosed. Tuberculosis treatment was adjusted with rifampicin, isoniazid, streptomycin, linezolid and dexamethasone.

After 72 hours in the IMCU, the patient's state of consciousness deteriorated (Glasgow Coma Scale 8) and he became haemodynamically unstable, requiring intubation and transfer to the Intensive Care Unit (ICU) in a more specialised hospital (Hospital J. Trueta, in Girona), where treatment was adjusted to rifampicin, isoniazid, pyrazinamide, ethionamide and dexamethasone.

In the ICU, the patient developed several complications, including left mydriasis and bradycardia secondary to hydrocephalus, receiving treatment with mannitol and external ventricular drainage (EVD), ventriculitis treated with ganciclovir, tracheobronchitis associated with intubation (due to multi-drug-sensitive *Escherichia coli*) and EVD infection treated with vancomycin and meropenem, eventually becoming haemodynamically stable but neurologically in a coma. Subsequently, the patient developed pneumonia secondary to bronchial aspiration, and treatment was changed to rifampicin, isoniazid, pyrazinamide and levofloxacin,

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