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annual-theme/year-of-health-and-care-workers-2021/vaccine-equity-declaration) promoted by the World Health Organization. This initiative calls governments, pharmaceutical companies, regulatory agencies, and world leaders to join forces to accelerate the equitable distribution of vaccines around the world, especially among healthcare workers. We ask all health organizations (professional associations, scientific societies, academic and research institutions, etc.), as well as physicians and other health professionals, to also adhere to this declaration.

In the face of a health threat such as the one that we are currently living, no one is safe until we are all safe. Hence, in this exceptional situation, preserving everyone's health is the only legitimate goal."

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Bradycardia due to remdesivir: Report of two cases☆

Bradicardia por remdesivir: estudio de dos casos

Dear Editor:

The current 2019 coronavirus disease (COVID-19) pandemic is posing a global scientific and health challenge in the generation of quality evidence. Very few treatments have proven to be effective, although several options have been proposed.[1] Remdesivir, a nucleotide analog with *in vitro* activity against the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) by inhibiting its ribonucleic acid (RNA) replication, is one of the most widely used and approved treatments for COVID-19 according to its summary of product characteristics. Because data obtained in clinical trials seem to indicate that hospitalized patients requiring low-flow oxygen therapy achieve the best results with this treatment, these are the types of patients in whom this drug's use is contemplated in the document prepared by the Spanish Health Ministry.[2] The aim of antiviral treatment with remdesivir is to prevent an increase in the severity of the disease, promote the patients' clinical recovery, and, thus, indirectly reduce the length of the hospital stay of COVID-19 patients. According to the drug's summary of product characteristics,[3] it is indicated for adults and teenagers with pneumonia secondary to a SARS-CoV-2 infection requiring supplemental oxygen therapy. The dose of remdesivir administered to patients ≥12 years and weighing at least 40 kg is 200 mg as a loading dose on the first day and 100 mg daily as of the second day, both administered through an intravenous infusion. The treatment's total duration should be at least 5 days and no more than 10 days. The most frequent adverse effects reported are transaminase level elevation, nausea, headache, and skin rash.[3]

In this paper we present two cases of symptomatic sinus bradycardia secondary to the administration of remdesivir in two patients with SARS-CoV-2 pneumonia.

The first patient is a 47-yearold overweight man with no pathological history who was admitted to the hospitalization ward due to presenting with bilateral pneumonia secondary to a SARS-CoV-2 infection. Because his oxygen saturation was 93%, oxygen therapy at a flow of 2 L/min was started, together with intravenous treatment with dexamethasone 6 mg/day, bemiparin 3500 IU/day, paracetamol 1 g/8 h, and inhaled drugs. Because he did not improve with this therapy, treatment with remdesivir was started while maintaining dexamethasone. After receiving the third dose of remdesivir, he developed symptomatic bradycardia with presyncope symptoms, with sinus bradycardia (heart rate of 45 beats/min) being diagnosed. After discontinuing dexamethasone and remdesivir, treatment with intravenous boluses of methylprednisolone 250 mg/day was administered for three days owing to the potential heart involvement of the SARS-CoV-2 infection. Since he continued to exhibit signs of asymptomatic bradycardia (heart rate of 49–50 beats/min), a Holter monitor study was carried out, detecting sinus rhythm readings. The bradycardia gradually resolved within the 72 h following the drug's withdrawal. He was eventually discharged nine days after his initial admission with an improved and stable condition.

The second patient is a 74-year-old hypertensive man who was diagnosed with a non-operable squamous cell lung cancer in May 2020 and treated with chemoradiotherapy with curative intent. On admission, the patient presented with respiratory failure secondary to moderate pneumonia caused by a SARS-CoV-2 infection, owing to which treatment with ceftriaxone 2 g/day, azithromycin 500 mg/day, bemiparin 5000 IU/day, as well as chronic ambulatory medication (losartan 50 mg/day and tamsulosin 0.4 mg/day) was started. As he did not improve, three boluses of intravenous methylprednisolone 125 mg/day and remdesivir at the standard dose were added to his treatment regimen. After receiving the third dose of remdesivir, he developed sinus bradycardia (heart rate of 45 beats/min), owing to which remdesivir and azithromycin were discontinued. The bradycardia resolved within the following 24 h and, once his clinical condition had improved, he was discharged from the hospital two days later.

We conducted a search in PubMed using terms "adverse drug reaction" and "remdesivir", identifying hypotension secondary to the drug's infusion as a potential adverse reaction described in the available literature,[4] in addition to atrial fibrillation.[5] However, no cases of bradycardia similar to those reported in this paper have been reported to date. Remdesivir is a drug with few data available on its use and for which the mechanism of action and safety profile have not yet been described in detail.

After applying the modified Karch and Lasagna causality algorithm used by the Spanish Pharmacovigilance System for Medicines for Human Use (SEFV-H, *Sistema Español de Farmacovigilancia de Medicamentos de Uso Humano*), both adverse drug reactions (ADRs) were classified as possible (4 points) and reported through a yellow card notice to the SEFV-H.

The pharmacist's role is crucial in ensuring patient safety, and the notification of adverse effects is a key aspect of pharmacovigilance, particularly when using therapies for which there is limited experience in terms of their management.

Knowing both the efficacy and safety profile of the therapies used in the treatment of COVID-19 is an additional challenge for healthcare professionals in relation to which we must always maintain a critical and cautious attitude owing to the avalanche of information to which we are being subjected.

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Refractory juvenile dermatomyositis: Response to tofacitinib

Dermatomiositis juvenil refractaria: respuesta al tofacitinib

Dear Editor:

Juvenile dermatomyositis (JDM) is a chronic systemic autoimmune disease, mainly manifested as muscle weakness and rash, which can also be accompanied by calcifications and even involves lung, heart and other organs. Hence, it is necessary to adopt timely and effective therapy to stop the progression of the disease damage. Glucocorticoids and disease modifying anti-rheumatic drugs (DMARDs) are a main therapy. However, patients with JDM who are unresponsive to corticosteroids or other immunosuppressive medications face poor outcome and suffer from various sequelae of the disease.[1,2] Therefore, it is important to find new treatments for refractory JDM. Recently, multiple centers have tried biologics including rituximab, abatacept, tofacitinib and tocilizumab for refractory dermatomyositis. Though some trials fail to reach its primary end point, janus-Kinase (JAK) inhibitor tofacitinib for refractory dermatomyositis patients showed an overall good efficacy.

In JDM, type I interferon participates in the pathophysiological process by inducing the expression of proinflammatory cytokines. In addition, STAT3 can be transferred to mitochondria and might involve in regulating the release of mitochondrial calcium pool. This is of potential significance to calcification in patients with dermatomyositis. Herein, JAK inhibitors may be a meaningful treatment for JDM with calcification.[3,4] We did like to report a successful case of treating extensive calcifications in refractory JDM with tofacitinib.

Our patient was a 2.1-year-old child whose clinical manifestation is severe proximal muscle weakness, with the score on the childhood myositis assessment scale (CMAS) score of 26/52 and Gottron's papules over his hands' small and large joints. His both legs were covered with lumps. The results of laboratory tests showed the following abnormal values: high lactate dehydrogenase (LDH = 387 U/L, reference range 155–345 U/L) and erythrocyte sedimentation rate (ESR = 43 mm/h, reference range 0–15 mm/h). Antinuclear antibodies were positive with a titer of 1:100. The myositis-specific autoantibodies screening demonstrated positive anti-NXP2 and X-ray of thighs demonstrated extensive deep calcium deposits. Biopsy for the subcutaneous mass on the left leg showed calcified nodules, and biopsy for the muscle showed inflammatory musculopathy, which are consistent with muscle damage changes.

According to the Bohan and Peter criteria, the patient was diagnosed with cutaneous calcinosis with JDM. He started to be treated with oral prednisolone 2 mg/kg/day, intravenous immunoglobulin 2 g/kg), subcutaneous methotrexate, oral cyclosporine (5 mg/kg/day). As a result, the laboratory tests significantly improved thanks to the treatment. CMAS score was from 26/52 to 36/52 and the skin lesions slightly improved, but this cannot prevent the progression of calcifications (Fig. 1A).

So he began to be treated with tofacitinib at 4 because of muscle weakness without complete remission and progression in calcifications. He accepted dose escalation until the optimal tolerated treatment doses applicable to his weight and renal function (5 mg/day). Six months later, the skin lesions saw complete remission and CMAS score was from 36/52 to 40/52, and physician global VAS score from 8 to 4. Inflammation of calcifications were fully resolved. 17 months later, CMAS score was from 40/52 to 48/52, physician global VAS score from 4 to 2 and calcifications became either stable or regressive. There were no new lumps underneath the skin (Fig. 1B). During the treatment with tofacitinib, there was no hospitalization due to infectious diseases. The number of white

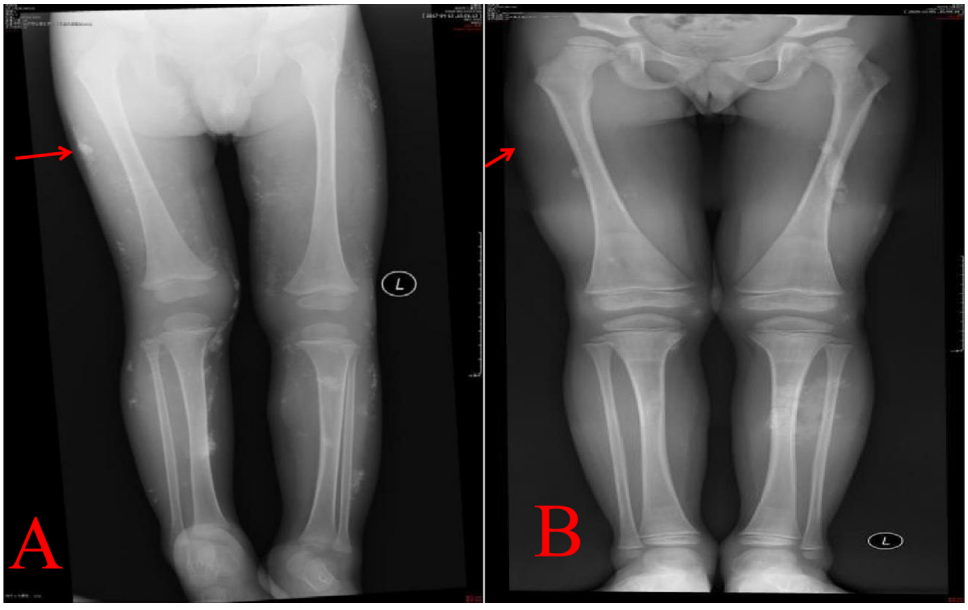

Fig. 1. (A) X-ray findings of calcification on the patient's two legs before being treated with tofacitinib, there were a lot of calcifications on both legs. (B) X-ray findings of calcification on the patient's two legs, after 17 months' treatment with tofacitinib, calcifications regressed. In (A), the white dot image in the figure is calcification as shown by the red arrow. In (B), the calcification as shown by the red arrow has disappeared.