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Letter to the Editor

Management of aplastic anemia during the phase of defervescence of the COVID-19 pandemic[☆]



Abordaje de la aplasia medular en la fase de defervescencia de la pandemia por COVID-19

Dear Editor,

Medullary aplasia (MA) is a disease characterised by the failure of the haematopoietic function and the resulting pancytopenias. It is normally a medical emergency. Here is a brief presentation of the principal therapeutic approaches.^{1,2}

Calcineurin inhibitors (CNI). Its use could confer protection against the development of the most severe forms of COVID-19. This seems to be due to its potential inhibitory effect on viral replication and, above all, to the modulation of the host's excessive immune response to infection.³ Therefore, the use of cyclosporine A (CsA) or tacrolimus would be suitable for patients who require it.

Eltrombopag (EPAG). This is approved by the FDA and the EMA for patients refractory to immunosuppressive treatment (second line), and by the FDA for patients with MA without previous treatments (first line) who are not candidates for transplantation. No adverse effects of EPAG have been reported on the progression of the SARS-CoV-2 infection, so it should be considered a safe drug in the current epidemiological context.

Antithymocyte globulin (ATG). Increased infectious morbidity is a well-known adverse effect of the use of ATG. However, there are no specific data regarding SARS-CoV-2. Therefore, although it is logical that its administration was limited during the maximum effervescence of COVID-19, at the present time it seems reasonable to use it, provided that the expected risk/benefit ratio is favourable.

Triple therapy (ATG/CsA/EPAG). The use of this combination of drugs has resulted in the best results in MA, in the shortest time.^{4,5} Today, it is more important than ever to be able to free patients from their transfusion needs and hospital dependency. Therefore, the use of triple therapy in the different lines, whenever possible, should be a priority.

Bone marrow transplant (BMT). HLA-identical sibling BMT is the first-line treatment of choice for patients under 40 years of age with very severe, severe, and less severe MA with transfusion requirements or infections.¹ BMT should be offered immediately to newly diagnosed patients and to those who may have been on a waiting list for the past few months. In other words, the sooner the candidate patients are transplanted, taking advantage of this

phase of improvement in the epidemiological situation of the SARS-CoV-2 pandemic, the better for their cure options. Regarding the indication of BMT (from HLA-identical siblings or from alternative donors) in second or subsequent therapeutic lines, the reasoning would be similar. If the indication is BMT, the procedure should be carried out as soon as possible. There is no need for the transplantation methodology (source of progenitors, conditioning, prophylaxis against GVHD, duration of immunosuppression, etc.) to vary from other situations.

Hospital care for patients with MA, once in the outpatient phase, should be limited to essential actions and be supplemented with telemedicine, whenever possible. The initial management of febrile neutropenia should, however, be performed in the hospital setting.^{6,7}

Patients must, of course, comply with the rules applicable to the general population regarding social distancing, the use of masks, hand hygiene, and so on. These practices should be observed until, in one way or another, group immunity against SARS-CoV-2 is achieved, although this does not seem likely to occur in the short term.

Like everyone else, MA patients can catch COVID-19. Therefore, a high index of suspicion should be maintained against this possibility when compatible symptoms are presented (fever, cough, fatigue, etc.).⁸

MA is a medical emergency and, as such, its treatment should be started as soon as possible after its diagnosis. This is particularly important in cases involving infections, profound neutropenia, and/or increased transfusion requirements. Therefore, the treatment of patients with MA must be prioritised in our current epidemiological situation. And this should be applicable to both newly diagnosed MA patients and those who may have received temporary suboptimal management over the past months. The attitude to follow in the near future will be marked by the course of the pandemic.

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Adrenal schwannoma: A case report[☆]



Schwannoma suprarrenal: descripción de un caso

Dear Editor:

A schwannoma is a benign, encapsulated tumor originating in the Schwann cells of the peripheral sympathetic nervous system, the cranial nerves of the head and neck, and the upper or lower limbs. Its occurrence in an adrenal gland is unusual.¹ Most of these tumors are benign, with malignant ones being more common in cases of Von Recklinghausen's disease. They are more prevalent among women than men (1.2:1), and the mean age of onset is 49 years. Most are discovered as incidental findings, and their symptoms seem to be related to the size of the tumor, such as abdominal pain caused by the mass effect. Hormonal test findings tend to be normal. Computed tomography (CT) images tend to show a well-defined, encapsulated, homogeneous mass and magnetic resonance imaging (MRI) reveals a heterogeneous mass, with either cystic degeneration or hemorrhagic areas with a hypointense T1 signal and a hyperintense T2 signal, which, therefore, lead to a differential diagnosis of pheochromocytoma or adrenal carcinoma.²

We hereby present the case of a 55-year-old woman with hypertransaminasemia secondary to alcohol consumption. A requested MRI revealed a heterogeneous, left adrenal mass with a diameter of 3.5 × 3 cm, with some irregular areas of hyperintense T2 signal and others of hypointense cystic degeneration/central necrosis. The lesion contained no adipose or hemorrhagic material, and exhibited no signs of invasion of the adjacent structures or adenopathies. A differential diagnosis of either pheochromocytoma or adrenal carcinoma was proposed as the main option.

The patient was referred to the Endocrinology Department for further examination. She reported a three-year history of arterial hypertension, with a worse control of her blood pressure levels over the previous year (mean 160/100 mmHg), owing to which she is currently under treatment with two antihypertensive drugs. A hormonal study was requested to determine the concentrations of renin mass, aldosterone, urinary free cortisol, plasma cortisol after administering 1 mg of dexamethasone, urinary metanephrines, dehydroepiandrosterone sulphate, total testosterone, androstenedione, and 17-hydroxyprogesterone, all of which fell within normal limits.

The patient was subsequently referred to the Surgery Department to undergo a left adrenalectomy and reach a definitive pathological diagnosis. This procedure was performed laparoscopically in March 2017, with the pathological study of the samples obtained yielding a diagnosis of a schwannoma limited to the adrenal gland. The macroscopic description was reported as an adrenal gland measuring 8.5 × 4 × 3 cm, with a 3.5 × 3.2-cm nodule delimited by a capsule. The nodule corresponded to a solid

mass with whitish-grayish cystic areas. The microscopic description reported a tumor in the adrenal medulla that was displacing its cortex and was comprised by a proliferation of spindle cells with a fascicular pattern, elongated nuclei, and an ill-defined cytoplasm, with areas of increased cellularity, nuclear “pseudo-palisading”, myxoid areas with poor cellular representation, and blood vessels with thick and hyalinized walls. Areas of ischemia, cystic degeneration, and polymorphous nuclei without mitosis were also observed. The mitotic index was less than 1 mitosis/10 high power fields (HPFs), and the Ki-67 index was 5%. In addition, an immunohistochemistry study revealed a positive result for the S-100 protein and a negative one for actin, caldesmon, desmin, AE1-AE3, and inhibin.

After the procedure, the patient was re-examined in the Endocrinology Department with the aid of a Holter blood pressure device, which revealed mean blood pressure levels of 107/74 mmHg and, therefore, a need for decreasing her antihypertensive medication. A physical examination revealed no “café au lait” spots, but several axillary freckles were detected in a region where, according to the patient, several, small, pedunculated, benign tumors had previously been removed. The corresponding pathology report could not be retrieved from her medical history.

To conclude, schwannomas are solid, encapsulated tumors, frequently presenting with areas of bleeding, necrosis, and cysts, which are generally located in the cranial and cervical cutaneous nerves, with their presence in the retroperitoneum and adrenal glands being rare. Because CT or MRI images rarely allow their preoperative differentiation from pheochromocytomas or adrenal carcinomas,^{3,4} preoperative hormonal testing is advised to rule out an increase in metanephrine levels requiring prior treatment with alpha-blockers. Only a single case of a schwannoma associated with increased levels of urinary catecholamines in the laboratory tests has been described. Pathological studies often reveal hemorrhagic and cystic areas within the tumors. In addition, despite not being pathognomonic, positivity for the S-100⁵ protein in the immunohistochemistry studies is a fundamental finding. The clinical evolution of this condition is generally benign, except in cases associated with Von Recklinghausen's fibromatosis, where malignancy is more frequent.

The patient was also examined in the Ophthalmology Department to have an optic glioma ruled out owing to the suspected diagnosis of type 1 neurofibromatosis, although she did not fulfill the criteria for genetic testing.

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