Letter to the Editor

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Received: 24/07/19
Accepted: 26/07/19

Dear Editor:

We would like to respectfully make a series of contributions regarding the original article "Diagnosis and treatment of patients with hereditary hemorrhagic telangiectasia (Osler-Weber-Rendú syndrome) at a university hospital in Colombia" by Dr. Mosquera et al.. Our contributions are on genetic diagnosis, clinical manifestations, medical management and endoscopic management.

Osler-Weber-Rendú syndrome, also known as hereditary hemorrhagic telangiectasia (HHT), is a disease with an autosomal dominant inheritance pattern characterized by telangiectasias and arteriovenous malformations. (1)

To date, the Curaçao criteria remain the parameters to be considered for diagnosis. It has been reported that these criteria are particularly useful in two situations: unaffected older adults, and young adults and children. This is where genetic testing plays an important role even though it is not widely available and is expensive. It should not be underestimated for making an accurate diagnosis. The alterations described related to endoglin (ENG for type 1 HHT) and the activin type A receptor gene (ACVRL1 for type 2 HHT) genes that account for the majority of HHT cases. They generate protein products that influence signaling TGF-β in vascular endothelial cells. The reported data show detection rates with sensitivity of up to 75% for mutations of ENG and ACVRL1 sequences. (1, 2) We also believe that these tests are relevant because of the different degrees of severity associated with different genotype alterations. Patients with HHT type 1 genotype are more serious and have a higher prevalence of pulmonary arteriovenous malformations and more severe episodes of gastrointestinal bleeding than do patients with HHT type 2. However, no significant changes in the severity of epistaxis, age of presentation and mortality rates have been demonstrated. (3)

On the other hand, more detailed descriptions of clinical manifestations and their frequencies seem relevant since they are data that can help a clinician suspect this disease which otherwise might initially be classified as an orphan disease. At least 90% of patients present nosebleeds, and 80% of HHT patients have gastric or small intestine telangiectasias although only 25% to 30% develop overt bleeding which tends to occur in the fifth to sixth decade of life (rarely before 40 years). (1, 4) These data are similar to those found in the study of Dr. Mosquera et al. It is also important to take into account other manifestations. Cardiac manifestations (acute myocardial infarcts and arrhythmia) have low prevalences. Arrhythmia is the most frequent cardiac manifestation. (5)

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There is also evidence that these patients have a higher prevalence of hepatic focal nodular hyperplasia. (6) We point out these clinical data to complement the article since they were not discussed in the patients of the published series.

As part of the review of the available literature, we would also like to complement the article in regard to clinical and endoscopic management. According to reports in the literature, oral or parenteral iron supplements may be sufficient treatment for mild anemia and chronic bleeding of patients with HHT and could even be defined as the first-line. (1) Among the pharmacological treatments described is hormonal therapy (estrogen/progesterone or danacrine preparations). (7) As a second line, antifibrinolytics (aminocaproic acid or tranexamic acid) have been used, (8) and there are also reports of the use of tamoxifen, interferon, thalidomide and sirolimus. (9)

In endoscopic therapy, Nd:YAG (neodymium-doped yttrium aluminum garnet; Nd:Y3Al5O12) lasers and argon plasma coagulation (APC) have been described. The latter is considered to be the most effective method available today. Multiple attempts at local endoscopic therapy are not recommended due to the additive risks of adverse events without additional benefit. (1, 7, 10) There are also data in favor of the use of N-acetylcysteine as an antioxidant. Although prospective controlled studies of its efficacy have yet to be done, it is considered to be a promising management possibility. (11)

We should not put aside recent guidelines which suggest an approach based on five specific measures to optimize care and reduce morbidity and mortality rates: detection of pulmonary arteriovenous malformations (AVM), advice regarding nasal bleeding, evaluation of iron deficiency, antibiotic prophylaxis before dental and surgical procedures, and pregnancy advice. It is known that most pregnancies in women with HHT develop normally. Major complications are rare, but survival is better if HHT is recognized and addressed prior to pregnancy. (10, 12)

The Mayo Clinic currently has the most experience managing HHT-related bleeding with intravenous bevacizumab. In general, it is well tolerated, but a relevant adverse effect is arterial hypertension. It is usually benign course and responds well to medical management. From a cost-benefit perspective that considers transfusions, hospitalization time and iron infusions, in the future biological therapy could become an earlier therapeutic approach. (4) There are reports of the use of pazopanib as an alternative for patients who are refractory to bevacizumab, but more controlled and prospective studies of its efficacy are still needed. (13)

Until 2011, there were no data that favored nutritional measures or lifestyle changes for managing this disease. (1) Despite this, in 2013, Silva et al. suggested that room humidification, nasal lubrication and saline treatments could be beneficial for controllin epistaxis associated with HHT. They also suggested that modifying the intake of foods high in salicylates and those with natural anti-platelet activity (including red wine, spices, chocolate, coffee, certain types of fruit, garlic, ginger, ginseng, and ginkgo biloba) could be beneficial. (14)

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