involvement, mainly in the right eye, with abundant exudation and intraretinal edema (Fig. 1A).

Due to suspected acute hypertensive retinopathy caused by hypertensive crisis, arterial pressure (AP) was taken, 230/150 mmHg with similar values on several readings. The diagnostic of malign arterial hypertension in a patient without known antecedents caused the patient to be referred to internal medicine for urgent medical treatment and secondary hypertension study. Renal magnetic resonance revealed a lesion which depended on the left suprarenal gland, with well-defined edges, solid and necrotic-cystic areas which produce a mass-like effect (Fig. 2). 24-h urine analysis for noradrenaline and normetanephrine was positive, with the remaining supplementary tests being negative. With the diagnosis of left pheochromocytoma, surgical resection was decided with laparoscopic adrenalectomy. 3 months later, AP readings returned to normal, VA was 20/20 in both eyes and the exudation, hemorrhages and partial papillary edema progressively disappeared (Fig. 1C). Macular OCT revealed a near complete recovery of the normal foveal profile with progressive subretinal liquid reabsorption (Fig. 1B). In addition, headaches and excessive sweating also disappeared.

Malign hypertension can involve hypertensive encephalopathy expressions such as intense headaches, vomit, visual alterations, convulsions or even coma. Pheochromocytoma should be considered in differential diagnostics in the presence of said symptoms. In the present case, ophthalmological involvement pointed to a suspicion of hypertension and therefore we consider ocular fundus as a necessary exploration in cases of severe or prolonged cephalalia.

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**VEGF-A and VEGF-Ax: Bad protein and good protein**

**VEGF-A y VEGF-Ax: proteína mala y proteína buena**

Dear Editor,

The vascular endothelial growth factor (VEGF) is crucial for the development of blood vessels and endothelial cell proliferation, with VEGF-A being its main conductor in playing an essential role in physiological processes. However, a cruel irony underlies VEGF-A: on the one hand this molecule is key in the development of organs as well as in human growth and maintenance but on the other hand it promotes the growth of solid tumors and metastasis as well as a range of anomalous vasoproliferative processes which compromise visual function. Since VEGF was discovered 25 years ago, researchers have focused on finding a way in which blocking VEGF could slow down or halt the growth of tumors which require blood supply to survive and develop. In 2003, the first phase 3 clinical trials with a VEGF
inhibitor—bevacizumab—demonstrated that the inclusion of this agent in standard treatment for metastatic colorectal cancer increased general survival an average of 4 months. To date, it is estimated that over 30 VEGF inhibitors have been identified and tested in over 2000 clinical trials. Blocking VEGF-A, which was introduced in ophthalmology less than a decade ago, has become the basis for treating intraocular neovascular destructive processes. At present it is considered that the design of new VEGF inhibitors has run its course. There are only 2 ways to improve VEGF inhibition therapy: one is to find predictive biomarkers with the ability to indicate the positive or negative response of patients, and finding the best way to utilize VEGF inhibitors in combination with other therapies. It is important to identify which patients have greater probabilities of responding in order to avoid prescribing a drug which we know that will not work. Recently, a VEGF-A variant has been discovered which could point the path for the development of new forms of therapy. The new protein is generated when the termination codon is ignored in the protein synthesis (programmed translational read-through), thus producing a slightly altered VEGF-A (with 22 additional amino acids) which has been named VEGF-Ax (x for extended). Paradoxically, this minute alteration in the molecule produces a change which is totally the opposite of its original effect, i.e., it halts vascularization. Even though this new molecule has been discovered in animals, it could be that in the near future a VEGF-Ax injection would be highly relevant in treatments for humans. However, what is the significance of this when anti-VEGF-A is being utilized with good results? VEGF-Ax is useful as a biomarker to assist in the decision of which therapy to be applied. Not only conventional anti-VEGF-A is unable to diminish neovascularization, but it also blocks the antiangiogenic effects of VEGF-Ax. Accordingly, in the processes in which VEGF-Ax increases, antiangiogenics should be avoided in therapy because we are injecting a drug with potential side effects without therapeutic possibilities.

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