[a] *Department of Endocrinology, Hospital Pedro Hispano, Matosinhos Local Health Unit, Rua Dr. Eduardo Torres, 4464-513 Senhora da Hora, Matosinhos, Portugal*
[b] *Department of Medicine, Hospital Pedro Hispano, Matosinhos Local Health Unit, Rua Dr. Eduardo Torres, 4464-513 Senhora da Hora, Matosinhos, Portugal*
[c] *Department of Radiology, Hospital Pedro Hispano, Matosinhos Local Health Unit, Rua Dr. Eduardo Torres, 4464-513 Senhora da Hora, Matosinhos, Portugal*

* Corresponding author.
E-mail address: franciscosimoesdecarvalho@live.com.pt (F. Simões de Carvalho).

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Eye symptoms in acromegaly, beyond visual field alteration☆

Síntomas oculares en la acromegalia, más allá de la alteración del campo visual

Acromegaly results from chronic growth hormone (GH) hypersecretion which causes an increase in circulating insulin-like growth factor 1 (IGF-1) levels, once the articular cartilage is closed. It develops slowly, with its classic morphological changes having a gradual onset. The excess morbidity and mortality associated with this disease are due to osteoarticular, neurological and cardiovascular impairment. In the eyes, visual field impairment (due to compression of the optic pathway) and, less often, changes in corneal thickness are characteristic.[1] However, other eye symptoms are not common and therefore not included in the usual follow-up of this disease.[2,3]

We report the case of a 46-year-old woman with a history of hypertension being treated with irbesartan 150 mg daily and abnormal baseline blood glucose who visited the accident and emergency department due to painless vision loss in her right eye (RE) for the past 48 hours. She was assessed by ophthalmology and diagnosed with vitreous haemorrhage, which resolved without treatment. Fluorescein angiography showed vascular abnormality with venous stenosis and sheathing in the superior temporal retinal arcade of the RE with prominent vascular loops on the periphery. No neovessels or areas of vascular ischaemia were seen (Fig. 1A and C). Intraocular pressure (IOP) was normal, and there were no abnormalities in the left eye.

In the three months that followed, the patient had recurring episodes of vitreous haemorrhage with partial reabsorption. She was therefore referred for posterior vitrectomy and photocoagulation around the areas of vascular abnormality. Four days after vitrectomy, she presented rebleeding, whereupon the photocoagulation area was enlarged. Diabetic retinopathy, vasculitis and retinal tears were ruled out. Upon enquiry, she stated that her shoe size had increased and that her hands had thickened. As a result, acromegaly was suspected and she was referred to endocrinology.

The patient reported acral enlargement in the last decade, multiple bone pain attributed to osteoarthritis, and an increase in shoe size from 41 to 43. She no longer had menstrual cycles as of age 44. She had physical features consistent with acromegaly and galactorrhoea upon application of pressure. Baseline GH was >40 ng/mL (reference range [RR]: 0.0-5.0 ng/ml), and baseline IGF-1 was 944 ng/mL (RR: 41-209 ng/mL); these findings were confirmed in repeat testing. A 75-g oral glucose tolerance test revealed no GH suppression, with all points >40 ng/mL. IGF binding protein 3 (IGFBP-3) was 10.2 mcg/mL (RR: 3.4-7.6 mcg/mL). Magnetic resonance imaging (MRI) showed a pituitary adenoma measuring 14 mm x 20 mm x 14 mm that displaced the pituitary stalk to the right, compressed the pituitary gland, caused bulging of the diaphragma sellae and extended to the left cavernous sinus (Knosp grade 2) with no compromise of the optic chiasm (Fig. 1E). Colonoscopy revealed a tubular adenoma with high-grade dysplasia, resected with clear margins. Campimetry, echocardiography and thyroid ultrasound were normal. She was referred to neurosurgery for removal of the adenoma, which proceeded without incident. Pathology reported a pituitary adenoma with positivity in immunohistochemistry for GH and incidental positivity for prolactin with a low Ki-67 index.

Following surgery, the patient's quality of life improved; her bone pain resolved and her acral enlargement subsided. Her IGF-1 levels dropped; six month after surgery, they were 278 ng/mL. While awaiting hormonal re-evaluation, which was delayed by the COVID-19 pandemic, she started lanreotide 60 mg every 28 days, with normalisation of her IGF-1 levels. Her hypertension and elevated baseline blood glucose resolved without any need for drug treatment. Since her operation, she has not presented any visual abnormalities or evidence of vitreous haemorrhage. Follow-up fluorescein angiography showed persistent vascular malformations in the superior temporal area with no areas of ischaemia or neovessels in the RE (Fig. 1B and D).

Acromegaly of pituitary origin may be associated with visual field abnormalities due to compression of the optic chiasm in 18%-25% of patients.[2] Impairment starts at the periphery of the superior temporal fields and progresses to bitemporal hemianopia; in long-standing cases, it may even cause amaurosis. Evidence of other eye symptoms is limited.[1–3]

Elevated intravitreous IGF-1 levels have been implicated in the pathophysiology of proliferative diabetic retinopathy.[4] In addition, improvement in diabetic retinopathy has been reported in patients with diabetes who experienced pituitary apoplexy or underwent pituitary ade-

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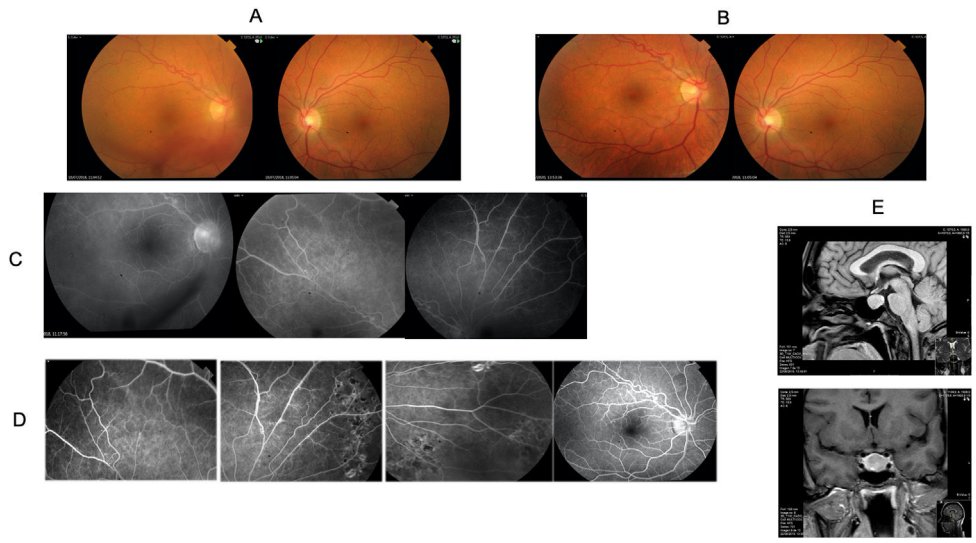

Figure 1 Retinographies, fluorescein angiography and pituitary magnetic resonance imaging. A) Initial retinography showing vitreous haemorrhage. B) Follow-up retinography. C) Initial fluorescein angiography: superior temporal retinal arcade of the RE with vascular abnormality (venous stenosis and prominent vascular loops) on the periphery. No neovessels and no areas of vascular ischaemia. D) Follow-up fluorescein angiography showing laser scars and no neovessels. E) Pituitary magnetic resonance imaging: a pituitary adenoma measuring 14 mm x 20 mm x 14 mm that displaced the pituitary stalk to the right, compressed the pituitary gland, caused bulging of the diaphragma sellae and extended to the left cavernous sinus (Knosp grade 2). No compromise of the optic chiasm.

noma resection, due to the angiogenic effects of GH and IGF-1. By contrast, vascular endothelial growth factor (VEGF) levels, which are elevated in retinal proliferative diseases, are normal in acromegaly.[5] Fuchtbauer et al.[6] reported that patients with acromegaly had higher numbers of vascular branching points in the retina with no morphological abnormality of those vessels and no greater tortuosity. However, there are conflicting data with respect to the prevalence of retinopathy and proliferative diabetic retinopathy in patients with acromegaly and diabetes.[7–9]

An increase in IOP has been reported in patients with acromegaly, even those under clinical chemistry monitoring.[1] In fact, they had significantly higher levels of central corneal thickness (CCT) but lower retinal nerve fibre layer (RNFL) thickness. Acromegaly duration was correlated with IOP and CCT levels.[1] Other studies have reported increased macular and peripapillary choroid thickness as well as increased RNFL thickness in patients with acromegaly.[10]

Acromegaly is an uncommon disease with high rates of associated morbidity and mortality if it is not detected and treated in time; therefore, early diagnosis is key.

After the patient's acromegaly was diagnosed and treated, she presented no vitreous haemorrhage relapse and, although she had previously undergone photocoagulation, her clinical chemistry monitoring for acromegaly might have helped to maintain her clinical stability. It is important to bear in mind the possible association between eye diseases and systemic diseases, between which causality may or may not be present. Although we could not demonstrate a direct causal relationship between vitreous haemorrhage and acromegaly, since co-occurrence of pre-existing vascular malformation could not be ruled out entirely, we recommend broadening ophthalmological assessment beyond campimetry in patients with acromegaly to include examination of retinal vascularisation.

References

1. Sen E, Tutuncu Y, Ozturk F, Aksakal FN, Elgin U, Balikoglu-Yilmaz M, et al. Comparing acromegalic patients to healthy controls with respect to intraocular pressure, central corneal thickness, and optic disc topography findings. Indian J Ophthalmol. 2014;62(8):841–5.
2. Clemente D, Ramírez V, Lucas Morante T. Capítulo 17. Hipersecreción de hormona del crecimiento: Acromegalia y Gigantismo. En: Manual Endocrinología de la Sociedad Española Endocrinología y Nutrición [Internet], [consultado 16 Jun 2021]. Disponible en: www.seen.es.
3. Giustina A, Barkan A, Beckers A, Biermasz N, Biller BMK, Boguszewski C, et al. A Consensus on the Diagnosis and Treatment of Acromegaly Comorbidities: An Update. J Clin Endocrinol Metab. 2020;105(4):937–46.
4. Frystyk J. The growth hormone hypothesis - 2005 revision. Horm Metab Res Horm Stoffwechselforschung Horm Metab. 2005;37 Suppl 1:44–8.
5. Nagai Y, Ando H, Nohara E, Yamashita H, Takamura T, Kobayashi K. Plasma levels of vascular endothelial growth factor in patients with acromegaly. Horm Metab Res Horm Stoffwechselforschung Horm Metab. 2000;32(8):326–9.
6. Füchtbauer L, Olsson DS, Coopmans EC, Bengtsson BÅ, Norrman LL, Neggers SJCMM, et al. Increased number of retinal vessels in acromegaly. Eur J Endocrinol. 2020;182(3):293–302.
7. Malhotra C. Proliferative diabetic retinopathy in acromegaly. Oman J Ophthalmol. 2010;3(2):96–7.
8. Azzoug S, Chentli F. Diabetic retinopathy in acromegaly. Indian J Endocrinol Metab. 2014;18(3):407–9.

9. Wu TE, Chen HS. Increased prevalence of proliferative retinopathy in patients with acromegaly. J Chin Med Assoc. 2018;81(3):230–5.
10. Yazgan S, Arpaci D, Celik HU, Isik I. Evaluation of macular and peripapillary choroidal thickness, macular volume and retinal nerve fiber layer in acromegaly patients. Int Ophthalmol. 2018;38(2):617–25.

Cristina Tejera Pérez[a,*], Nuria Olivier Pascual[b], Ana María Sánchez Bao[a], Maria Rosa Arroyo Castillo[b]

[a] *Servicio Endocrinología y Nutrición, Complejo Hospitalario Universitario de Ferrol, CHUF, Ferrol, La Coruña, Spain*
[b] *Servicio Oftalmología, Complejo Hospitalario Universitario de Ferrol, CHUF, Ferrol, La Coruña, Spain*

* Corresponding author.
E-mail address: cristina.tejera.perez@sergas.es
(C. Tejera Pérez).