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Pseudoxanthoma elastic

Pseudoxantoma elástico

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Abstract

The pseudoxanthoma elasticum is a generalized disease of the connective tissue involving the skin, eyes and cardiovascular system triggering the fragmentation and calcification of elastic fibers. Usually occurs after puberty, the manifestations characteristics are small spots, circumscribed, yellowish, located on the neck, axilla and inguinal folds. Angioid streaks in the retina, tendency to hemorrhage and arterial insufficiency are the most common complications. This disease can be inherited as autosomal dominant or recessive. The treatment of ocular manifestations is through the conventional phototherapy laser preventing the occurrence of local hemorrhages. However, new therapeutic approaches are being developed as the long-term use of drugs antiangiogenic, which act by inhibiting the ocular neovascularization. Despite not having yet effectively replaced the original treatment, recent research already show benefits of new technique. The objective of this study is to report on a case of a patient of 37 years, the carrier of the Pseudoxanthoma Elasticum, with angioid streaks and ocular hemorrhage, and the effective treatment with antiangiogenic therapy at the clinic of Ophthalmology in Nova Iguaçu, Rio de Janeiro.

Keywords: *Pxeudoxantoma elastic, angioid streaks; Antiangiogenic therapy; Ocular manifestations; Connective tissue disease; Eye diseases; Case reports*

Resumo

O pseudoxantoma elástico é uma doença generalizada do tecido conjuntivo envolvendo a pele, olhos e sistema cardiovascular desencadeando a fragmentação e calcificação das fibras elásticas. Geralmente ocorre após a puberdade, as manifestações características são manchas pequenas, circunscritas, amareladas, localizadas no pescoço, axila e pregas inguinais. Estrias angioides na retina, tendência à hemorragia e insuficiência arterial são as complicações mais comuns. Esta doença pode ser herdada como autossômica dominante ou recessiva. O tratamento das manifestações oculares convencional é através da fototerapia a laser impedindo a ocorrência de hemorragias locais. Entretanto, novas abordagens terapêuticas estão sendo desenvolvidas como a utilização em longo prazo de drogas antiangiogênicas, as quais atuam inibindo a neovascularização ocular. Apesar de não ter ainda efetivamente substituído o tratamento original, pesquisas recentes já evidenciam benefícios da nova técnica. O objetivo deste estudo é relatar sobre o caso de uma paciente de 37 anos, portadora do pseudoxantoma elástico, com estrias angioides e hemorragia ocular, e o tratamento eficaz com a terapia antiangiogênica no ambulatório de oftalmologia em Nova Iguaçu, Rio de Janeiro.

Descritores: Pxeudoxantoma elástico; Estrias angioides; Terapia antiangiogênica; Manifestações oculares; Doença de tecido conjuntivo; Oftalmopatias; Relatos de casos.

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Introduction

Pseudoxanthoma Elastic is an extremely rare and hereditary disease concentrated in the connective tissue characterized by calcification of the elastic fibers, being responsible for cutaneous, ophthalmological and vascular involvement.[1] Pseudoxanthoma elastic is low in the general population, with an undifferentiated frequency between men and women and a prevalence still uncertain. However, the variation was estimated in 1:25,000 - 1:100,000, being statistically more prevalent in South Africa.[2]

Although it is a hereditary disorder, a large number of patients do not present very evident or characteristic symptoms of the disease. However, non-pruritic plaques, low visual acuity and vascular alterations such as pulse asymmetry or angina pectoris are manifestations that already signal an important development of the disease, since it manifests slowly and gradually.[2]

Diagnosis can be made with the presence of ocular changes associated to skin changes, which may include biopsy of the injured region and the presence of the genetic mutation.[2]

The treatment for pseudoxanthoma is still not curative, only palliative of the several affected areas of the organism.[3]

This study aims to report a case of diagnosed pseudoxanthoma elastic followed and treated at Centro Oftalmológico de Iguaçu, in addition to presenting the ophthalmologic treatment methods and other areas of action of the disease that are currently being used by physicians.

Case report

Female patient, 37 years old, white, single, merchant. Natural of and resident in the city of Rio de Janeiro (RJ) and patient of pxeudoxanthoma elastic in an asymptomatic form, however diagnosed 10 years ago. Since then, she has been regularly followed by physicians of three main specialties: cardiology, ophthalmology and dermatology. She denies other allergies, previous hospitalizations, previous surgeries or other comorbidities. Family history is not worth noting.

On 04/20/2015, the patient went to the ophthalmology office in Nova Iguaçu with urgency. At the appointment, she complained of low visual acuity in the left eye, which began one month before. On examination, there was a slight decrease in the visual acuity in the right eye 20/30, and a great decrease in the visual acuity in the left eye 20/80. Optical biomicroscopy of the anterior segment was normal, and tonometry showed 13/12 in the left eye. Fundoscopy showed angioid striae and hemorrhages in the temporal and juxtapupillary arcade in both eyes (which were not able to be evident in the image exam requested below). The decision was to request an angiofluoresceinography (fluorescence retinography) for a better and more detailed evaluation of the vascular changes observed in the retina. The exam was performed and showed the presence of mild angioid and "peau d'orange" striae in the right eye, in addition to the more exuberant angioid and drusen striae in the left eye.

The patient was then referred to the retina specialist who works at the clinic mentioned above, with the onset of treatment being recommended, and the one chosen was the antiangiogenic therapy with the drug Bevacizumab. The treatment started on 06/10/2014, and the patient already had a worsening of the image, as will be observed. For three consecutive months, intravitreal injections of Bevacizumab were given to the patient, which did not show a significant improvement of the initial condition, and it can be demonstrated in the following images. In the first month, there were multiple angioid striae and hemorrhages still seen in the left eye. In the second month, even more striae were seen, but no improvement in the hemorrhagic area. At the third month of treatment, the exam still showed no regression of the ocular changes.

Unsatisfied with the result that the patient was presenting after three months of treatment with the vitreous injections of Bevacizumab, we discussed with the team and then chose to

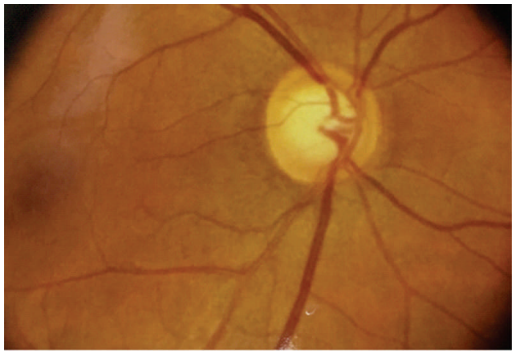

Figure 1: Right eye showing mild angioid and "peau d'orange".striae

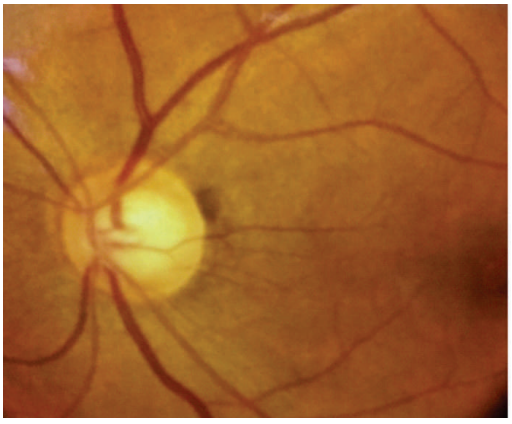

Figure 2: Left eye showing more exuberant and drusen angioid striae.

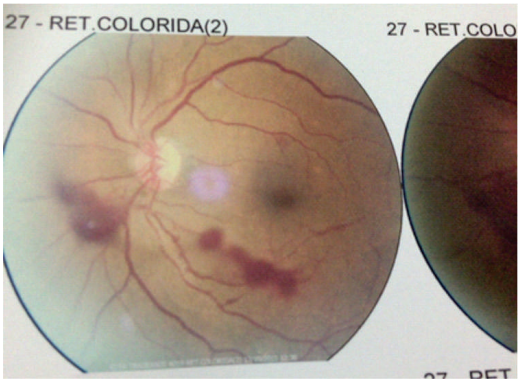

Figure 3: Month 1: presence of multiple angioid striae and haemorrhages in the left eye

Figure 4: Month 2: presence of more calibrated angioid striae and no improvement of the hemorrhagic condition.

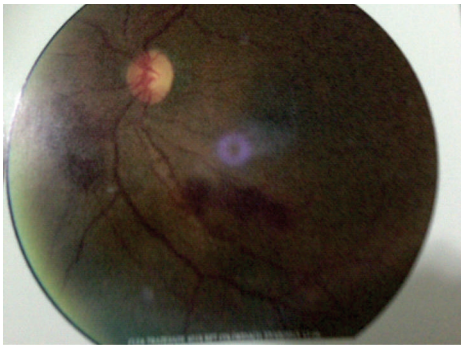

Figure 5: Month 3: maintenance of angioid striae and hemorrhage

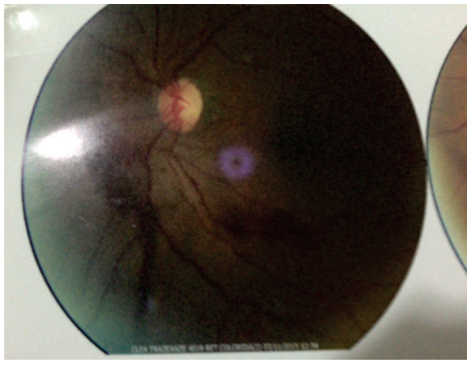

Figure 6: Month 4: mild decrease in the size of the striae and involution of the hemorrhagic condition.

continue with the antiangiogenic therapy as it was the current most promising treatment, but changing the drug used in the treatment, with Ranibizumab being then used. The patient had so far three intravitreal injections of Ranibizumab and showed a significant improvement of the initially presented clinical condition, with improvement of visual acuity - before it was 20/80 and now it is 20/40 - and imaging, as can be seen below, which demonstrates the importance of the early treatment with the right drug.

In the fourth month of treatment, after changing therapeutic drug, promising changes have already begun to be observed. A regression in the caliber of the preexisting angioid striae and mainly the control of the hemorrhagic foci. Were observed During the following month, the size of the striae reduced significantly, and the hemorrhage became even more devastating. In the last application, the changes observed continued to progress satisfactorily, and the course of the ocular disease seems to have been controlled.

The patient is still under ophthalmologic follow-up at Centro Oftalmológico de Iguaçu, and has not yet taken the next intravitreal injection, and improvement is expected to be even more significant than what has been achieved so far.

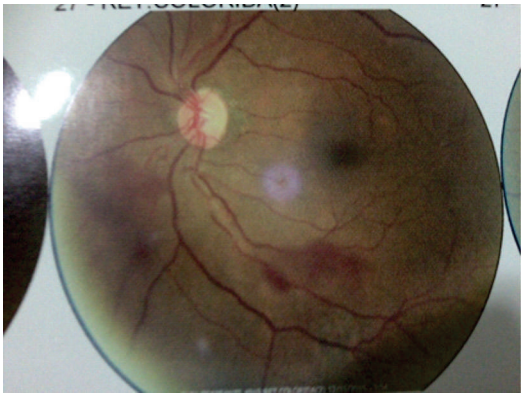

Figure 7: Month 5: improvement of angioid striae already present, and important involution of the hemorrhagic foci.

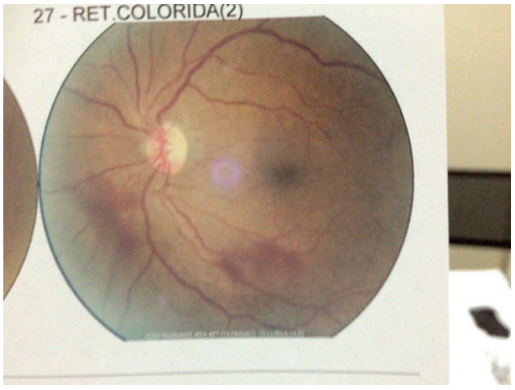

Figure 8: Month 6: significant recovery of ocular changes and restraint of the appearance of new striae, approaching a normal retinography.

Discussion

As observed and described before, the patient reported presents exclusive clinical manifestations of ocular origin, being emphasized in this topic this specialty of treatment. The patient in question was treated with antiangiogenic therapy instead of the traditional laser photocoagulation, first using Bevacizumab and from the third session on using Ranibizumab, with satisfactory development in both cases, but presenting better results with the second drug.

For three decades, treatment with laser photocoagulation was the treatment of choice for choroidal neovascularization, especially in those with extrafoveal location.[4] Georgalas et al.[2] found that 73% of patients deteriorated vision after photocoagulation to the point of becoming legally blind. Clarkson et al.[5] observed the same visual results, but in all patients studied. In spite of this, photocoagulation showed recurrence rates of 77%, generally occurring in the first three months.[6]

Antiangiogenic therapy has been studied since 2014, and lesion stabilization, choroidal neovascularization, and even improvement of the patient's visual acuity are expected if the treatment is initiated in the early diagnosis period.[7] This treatment is based on intravitreal injections with agents that inhibit endothelial and vascular growth factor, these agents being mainly Ranibizumab and Bevacizumab.[8] Comparing the two drugs, Ranibizumab has subconjunctival hemorrhage, mild ocular pain and scintillating scotomas as the most common side effects, and less than 1% of patients can develop them. After 2 years of injection, endophthalmitis, and systemic events were not significant, but it is a drug with a higher cost.[9] On the other hand, Bevacizumab is more likely to develop systemic effects, but it is still more widely used because of its low cost.[2,8]

In a case report study by Savastano et al.[10] it was possible to observe development in the treatment of ocular manifestations of the pseudoxanthoma elastic. In this case, a 54-year-old patient with a history of heart disease had visual loss in the right eye. Ophthalmologic exam revealed neovascularization and decreased visual acuity, and normal left eye, being diagnosed with angioid striae associated to pseudoxanthoma elastic. Treatment with intravitreal Bevacizumab once a month was discontinued due to lack of efficacy. After 9 months, the patient reported the same symptomatology in the left eye, and an ophthalmologic exam revealed the same diagnosis. Treatment in the left eye started with one a dose (one intravitreal Ranibizumab injection per month for a period of three months) followed by treatment. After 21 injections, the right eye showed deterioration of the retinal layer. The left eye had a small foveal scar, with other areas preserved. Finally, the visual acuity remained stable in the left eye, but deteriorated in the right eye. Therefore, the sight function was maintained, and the patient tolerated the treatment well over a period of 6 years, which in turn had pseudoxanthoma elastic and high cardiovascular risk. When compared to the administration of both drugs, the early use of Ranibizumab preserved moderate visual function, a result that was different in the right eye. As justification, we can observe the progression of the disease that was already in different stages in the eyes, suggesting that in order to achieve the best results antiangiogenic therapy should be started as soon as possible.

Another case report study by Savastano et al.[10] showed another 51-year-old patient using Ranibizumab as the treatment of choice for 5 years with complete stabilization of the disease by having 12 injections during the first year. Over the next 4 years, he received two additional injections only in cases of mild recurrence; in the left eye the vision remained stable. The patient was treated with a regimen other than Ranibizumab, and showed the efficacy of a regimen with longer interval time between doses.

Conclusion

Taking into account what was stated, we can conclude that although the diagnosis is difficult it should be made as soon as possible in order to avoid the irreversibility of the clinical consequences as shown above.

According to the articles studied, the treatment of ocular manifestations still needs to be better elucidated, since there is still a great difficulty in the choice of treatment, as there is no unanimity in which conduct is performed and that it is in fact effective in the long term. The greater difficulty in defining the treatment encompasses the very recent findings on antiangiogenic therapy, thus waiting for agreement on therapy to be defined from the results of future studies, since no comparative study could be found for treatment techniques.

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