

CASE REPORT

Retinal alterations in patients with sickle cell disease: a case series

Alterações retinianas em pacientes com doença falciforme: uma série de casos

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ABSTRACT: This study intends to evaluate the main fundoscopic findings in patients with sickle cell hemoglobinopathy by the observation of the most common retinal alterations. Retrospective and descriptive examination was carried out using fundoscopies and retinographies of 34 patients accompanied by a specialized ophthalmology service and by blood centers in the State of Alagoas. The most commonly found type of hemoglobinopathy was SS, followed by SC and S-thal hemoglobinopathies. From the total of patients evaluated, 58.8% were male. 29.41% presented retinal alterations. As for the genotype, 42.86% of the patients with genotype SC had retinal changes. A small number of retinal changes were observed in the analyzed sample, and all patients with signs of sickle cell retinopathy presented hemoglobinopathy of type SS or SC. The SS genotype was the most prevalent of the patients, but the SC genotype was the riskier for the development of retinal alterations.

Keywords: Retina; Fundus oculi; Anemia, sickle cell; Ophthalmology.

RESUMO: O presente estudo tem por objetivo avaliar os principais achados fundoscópicos em pacientes portadores de hemoglobinopatia falciforme, observando quais as alterações retinianas mais comuns nesse grupo. Realizou-se um estudo retrospectivo e descritivo através de fundoscopias e retinografias de 34 pacientes acompanhados por serviço de oftalmologia especializado e pelo Hemocentro do Estado de Alagoas. O tipo de hemoglobinopatia mais encontrado foi o SS, seguido pelas hemoglobinopatias SC e S-thal. Do total de pacientes avaliados, 58,8% eram do sexo masculino. 29,41% dos pacientes apresentaram alterações retinianas. Quanto ao genótipo, 42,86% dos pacientes com genótipo SC tinham alterações retinianas. Foi observado um reduzido número de alterações retinianas na amostra estudada, e todos os pacientes com sinais de retinopatia falciforme apresentavam hemoglobinopatia do tipo SS ou SC. O genótipo SS foi o mais prevalente dentre os pacientes, mas o genótipo SC foi o de maior risco para o desenvolvimento de alterações na retina.

Palavras-chave: Retina; Fundo de olho; Anemia falciforme; Oftalmologia.

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INTRODUCTION

Sickle cell diseases represent a group of inherited diseases, more prevalent in people of Black African heritage, characterized by abnormal hemoglobin formation^{1,2,3,4,5}. According to the *Programa Nacional de Triagem Neonatal* (PNTN) of the Brazilian Ministry of Health, 3,500 children are born in Brazil per year with sickle cell disease (SCD) and 200,000 with sickle cell trait; besides, it is estimated that 7,200,000 people have sickle cell trait (HbAS) and between 25,000 and 30,000 people have SCD⁶.

A mutation occurs in the hemoglobin beta-globin gene, which results in abnormal hemoglobin (HbS)^{1,2}. Such mutation causes the replacement of one amino acid (glutamic acid) with another (valine), at position 6 of the hemoglobin beta chain². Due to that, these molecules undergo a variation in shape (sickling) in specific situations of pH change, such as when the oxygen tension falls^{7,8}.

Four of the most common genotypes are the homozygous (SS), the heterozygous, also known as sickle cell trait (AS), the one associated with hemoglobin C (SC) and the one associated with thalassemia (S-Thal)^{9,10}. SS patients experience a more severe systemic condition than those of the SC type. However, ocular occlusive effects are more prevalent in SC type, due to a moderate anemia and a higher blood viscosity^{9,10}.

The pathogenesis of sickle cell retinopathy accounts for intravascular sickling, hemolysis, hemostasis, and thrombosis⁷. Peripheral capillary hypo perfusion can progress to capillary rearrangement/dilation, anastomosis, and neovascularization of the retina, usually in the transition area between the perfused retina towards the non-perfused one⁷. Initially, the neo vessels are flat (“sea fan”), but they can evolve associated with fibroglial proliferation towards the vitreous, or yet they can bleed leading to a vitreous hemorrhage (HV)⁷. Traction on the retina can cause up to its detachment^{7,11}.

In this sense, sickle cell retinopathy can be classified as proliferative and nonproliferative⁷. The main effects of the non-proliferative form are pre-retinal hemorrhages of the “salmon patch” type and retinal hyper pigmentations known as “black sunburst”^{7,10}.

Nevertheless, when the retinopathy reveals the presence of neovascularization it is classified as proliferative and can be categorized into 5 stages^{9,7,10}:

- I - Arteriolar occlusions in the retina perimeter;
- II - Arteriovenous anastomoses in the retina perimeter;
- III - Fibrous and neovascular proliferation;
- IV - Vitreous hemorrhages;
- V - Retinal detachment.

Thus, this study intends to describe the main fundoscopic ophthalmic variations in patients at the

hematological service in the State of Alagoas.

METHODS

A retrospective and descriptive investigation was conducted on 34 patients treated at the Hospital de Olhos Santa Luzia in Maceió-AL Ophthalmology Service and at the Hemocentro de Alagoas (HEMOAL). They were all previously diagnosed as having hemoglobinopathies (hemoglobin electrophoresis in alkaline pH) and were treated by the aforementioned Hematology service. In order to conduct this description, the patients’ medical records were analyzed from the period of 2018 to 2019.

The Research Ethics Committee of Centro Universitário Tiradentes (UNIT-AL) has approved this investigation.

The research protocol included complete identification (age, sex), type of hemoglobinopathy, and complete eye examination. Retinographies were performed according to clinical indication.

Patients who had therapeutic indications had their respective procedures performed after evaluation.

RESULTS

34 patients were examined, and only 29 of them had any genotype data in medical records. Three types of hemoglobinopathies were found: 21 patients exhibited type SS, 7 patients exhibited type SC, and 1 patient exhibited type S-Thal (Table 1). The age range varied from 7 to 50 years, with an average of 19.5 years (standard deviation of 11.88612), and 20 patients were male (58.8%) (Table 2).

Few ophthalmic changes were found in the studied group. (Figures 1 and 2) Regarding the 34 patients, 10 had retinal alterations, and only one patient had very increased vascular tortuosity and peripheral vessel occlusion. Five patients manifested mild tortuosity and 3 patients presented high tortuosity (Table 3). The patient with type S-Thal manifested retinography without any alterations (Table 3).

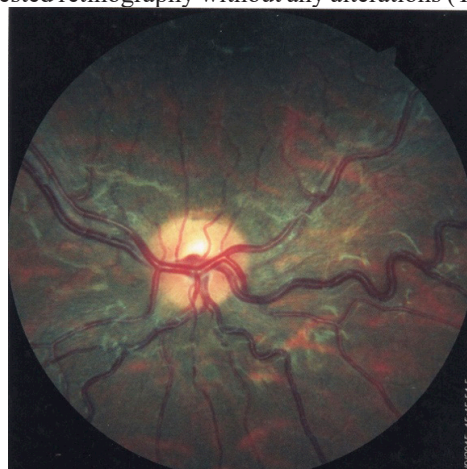


Figure 1- Retinography of a patient with sickle cell disease, SS genotype, showing mild tortuosity in the retinal vessels



Figure 2 - Retinography of a SC patient manifesting mild tortuosity of retinal vessels, regardless of any thickening

Table 1: Incidence of hemoglobinopathies genotypes

Incidence of hemoglobinopathies		
Types	N° of Patients	%
SS	21	72,41
SC	7	24,14
AS	0	0
S-THAL	1	3,45
Total	29	100

Table 2: Epidemiological characteristics of patients with sickle cell hemoglobinopathy

Epidemiological characteristics of affected patients			
Age range	Sex		Total cases
	Male	Female	
0-10	5	2	7
11-20	7	10	17
21-30	4	-	4
31-40	2	1	3
41-50	2	1	3
Total	20	14	34

Table 3: Correlation between retinal pathology and hemoglobinopathy type

Correlation between retinal pathology and hemoglobinopathy type			
Types	Total cases	Retinal pathology	
		Present (%)	Absent (%)
SS	21	6 (28,57)	15 (71,43)
SC	7	3 (42,86)	4 (57,14)
AS	0	- -	- -
S-THAL	1	0 (0)	1 (100)
Total	29	9	20

DISCUSSION

This investigation pondered through a descriptive case series and a sensible amount of qualitative statistics, the evaluation of patients with hemoglobinopathies treated at the Hemocentro de Alagoas (HEMOAL), a reference hospital regarding the treatment of hematological diseases in the State. In the collected sample, most of the patients had hemoglobinopathies of the SS type (70.97%), which is consistent with the results of other previously published papers^{7,9,12,13} (Table 1). The S-Thal type (3.45%) completed the total sample along with the SC type (24.14%), which according to the literature has a higher prevalence of proliferative sickle cell retinopathy^{7,12,14}, as confirmed in this study (42, 86% in SC type versus 28.57% in SS type) (Table 3).

In Brazil, it is estimated the prevalence of 700 to 1,000 new annual cases of sickle cell disease and more than 2 million carriers of the HbS gene. The object of this study - sickle cell retinopathy - develops in up to 42% of sickle cell individuals in the second decade of life¹⁵. However, there are no studies with sufficient samples to assess the incidence of sickle cell retinopathy among the Brazilian population.

The vessel wall thickening was detected in only one case in a patient with the SC genotype (Figure 3). The tortuosity increase of the retinal vessels, on the other hand, accounts for all the other pathological fundus conclusions in the analyzed sample.

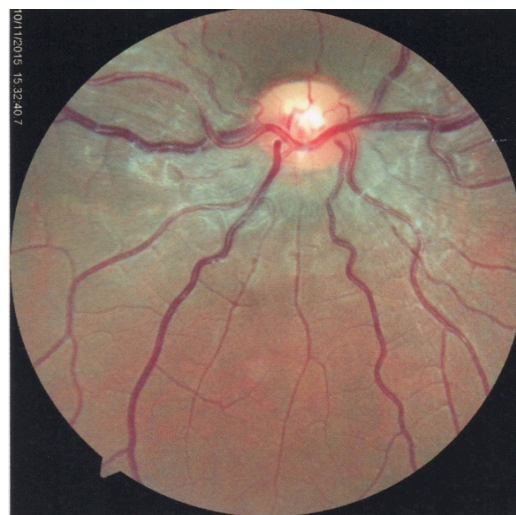


Figure 3 - Retinography exhibiting the wall thickening of the retinal vessels associated with the SC genotype

Due to originally benign ophthalmic variations, patients have not been needed specific treatment and are being followed up with a specialized ophthalmology service and the State Blood Center.

CONCLUSION

From a quantitative and a qualitative perspective, a small number of retinal variations were observed in the studied sample - the authors attribute this to a small sample caused by the lack of access and following-up of some patients. All patients with signs of sickle cell retinopathy presented SS or SC hemoglobinopathy.

It was perceived that the SS genotype was the most prevalent among the patients, although the SC genotype,

according to the literature, revealed the highest risks for the development of retinal variations, largely proliferative, over patients with sickle cell anemia.

As a descriptive case series study provided with some amount of qualitative statistics, it is concluded that even with a larger sample, it would not be possible to establish the correlation between the sickle cell genotype and ocular fundus variations. For that, it would be necessary to carry out genetic clinical trials with animals in order to identify such a correlation.

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