

SICKLE CELL DISEASE A BEHAVIORAL APPROACH TO A SYSTEMIC DISEASE

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Abstract

Sickle cell disease refers to a group of genetic disorders. It is characterized by the presence of sickle hemoglobin, anemia, and acute and chronic tissue injury secondary to blockage of blood flow by abnormally shaped red blood cells. The ocular and visual consequences of this disease are reviewed as well as differential diagnosis and patient management. This case report involves a 10-year-old black female patient who presented with complaints of occasional distance and near blur with poor reading comprehension. The patient was positive for sickle cell disease. After comprehensive optometric and neurological evaluations, the patient was diagnosed with latent hyperopia accommodative insufficiency and inflexibility, and signs of sickle cell retinopathy in both eyes. Overall treatments for sickle cell disease, including medications, photocoagulation and basic optometric care, are discussed along with differential diagnosis.

Key Words

accommodative inflexibility and insufficiency, asthenopia, reading comprehension, retinopathy, sickle cell disease

Introduction

Sickle cell disease is an autosomal recessive disease characterized by crescent-shaped erythrocytes and accelerated hemolysis. Low oxygen tension causes sickling—a distortion of red blood cell (RBC) shape. This sickling crisis may be precipitated by any of the following: trauma, surgery, dehydration, extreme psychological or physical stress, extreme heat or cold. Increased blood viscosity and vascular obstruction occurs secondary to the deformed, sickled RBC. The disruption of blood flow causes vascular occlusions, hemorrhages, infarctions and ischemic necrosis of tissue and organs throughout the body. Patients suffer severe pain from micro vascular occlusions, bone infarcts, leg ulcers and atrophy of the spleen associated with increased susceptibility to bacterial infections, especially streptococcal pneumonia.¹ Approximately 10% of African-Americans suffer from sickle cell disease. The disease is also found in people of Mediterranean, Middle Eastern and Indian decent.²

There are four major types of sickle cell disease, depending on genotype: sickle cell trait, Hb SA (80%); hemoglobin S beta thalassemia, Hb SBeta-thal

(10%); sickle cell anemia, Hb SS (4%); and hemoglobin SC, Hb SC (2%). Other types account for 4%. Sickledex, a hemoglobin electrophoresis test, can identify the presence of sickle cell disease in a patient and differentiate the type of the disease they carry.² SS is the most life-threatening form, while SA has very few systemic complications.³ Sickle cell patients go through a period of pain during sickling crisis. The pain can be broken down into eight stages.⁴ Table 1 summarizes these stages.

Consequences of Sickle Cell on the Eye and Vision

Sickle cell disease effects on the eye can vary. The degree of ocular involvement is not necessarily based on the severity of the systemic disease. Observation of the conjunctival blood vessels during a sickling event will show comma-shaped obstructed vessels. Vasoconstrictors, such as phenylephrine, will enhance the appearance. The presence of comma-shaped capillaries in the conjunctiva is a reliable indicator of sickle cell disease.³

Generally, when hyphema occurs as the result of trauma or introcular surgery, blood cells abnormally enter the anterior chamber. The body is not accustomed to RBCs being inside this avascular chamber. In the sickle cell patient the resulting

Table 1. The Stages of Pain⁴

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| Phase I | The usual state of the patient-no vaso-occlusion |
| Phase II | Pre-pain period- the patient reports no pain, but there are some prodromal signs and symptoms of vaso-occlusion including a loss of luster or a yellowish hue to the eyes. This jaundice is secondary to the break down of RBC due to shortened life spans or sickling |
| Phase III | First sign of pain-often relieved with acetaminophen and/or ibuprofen |
| Phase IV | Accelerating pain-stronger treatment needed, such as acetaminophen with codeine |
| Phase V | Peak pain-often described as "stabbing" or "drilling" pain. Patient is often taken into the emergency room for treatment with phase IV analgesics |
| Phase VI | Decreasing pain compared with phase V |
| Phase VII | Slight dull pain |
| Phase VIII | No pain-patient is back to "normal" |

hypoxia and acidosis in the anterior chamber induces sickling. This causes the blood cells to become trapped in the anterior chamber. These sickled cells obstruct the outflow of aqueous fluid, which causes an increase in intra-ocular pressure, which can induce secondary glaucoma. It can also cause a decrease in blood flow, which causes tissue infarction.^{3,5}

Sickle cell disease also causes a disruption of the uveal tract's blood flow. The iris may display a wedge-shaped sectoral atrophy secondary to closure of radially oriented iris arteries⁵ and/or rubeosis, which may lead to glaucoma. Vessels in the choroid may also become occluded.³

Sickle cell retinopathy is most frequent in Hb SC (33%), second in Hb SBeta-thal (14%), and least frequent in Hb SS (3%). No retinopathy occurs in Hb AS unless there is another condition also present, such as hypertension or diabetes mellitus.⁵ Sickle cell retinopathy can be further divided into nonproliferative and proliferative.

The nonproliferative ocular signs include: venous tortuosity, silver wire arterioles, salmon patch hemorrhages (oval pale retinal hemorrhages), intraretinal hemorrhages, black sunbursts (melanin deposits on the retina due to hemorrhages following small branch retinal artery blockages), macular arteriole occlusions, retinal vein occlusions, angioid streaks, and dark without pressure.^{3,5-7}

Sickle cell retinopathy is one of the most common causes of peripheral proliferative retinopathy and can be broken down into five stages. It is important for the clinician to know that laser coagulation of the neovascular vessels can prevent the end stage retinal detachment.^{3,5} Table 2 summarizes the five stages.

Sickle cell disease may also cause color vision defects. Color vision testing will display more blue/yellow and mixed color defects in patients with sickle cell disease, even in absence of macular or peripheral abnormalities. This is due to the secondary degeneration or loss of cone photoreceptors, which is due to an occlusion of choriocapillaries. It is not associated with retinal vaso-occlusion or neovascularization.⁵

There has been at least one report of sickle cell patients' complaints of asthenopia and diplopia during severe

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| Stage I | Retinal capillaries become plugged by sickle cells |
| Stage II | Peripheral arteriovenous anastomoses |
| Stage III | Neovascularization – "Sea Fans" |
| Stage IV | Vitreous hemorrhage secondary to leakage from fragile neovascular vessels |
| Stage V | Tractional retinal detachments, due to vitreous hemorrhage scars, causing vision loss |

anemia. However, the causes for these symptoms are unknown.⁸

I propose that sickle cell disease, as with other diseases, causes stress on the whole body, including the visual system. Thus, to maximally treat a patient, we must address *all* symptoms. This should involve a thorough evaluation of the visual system, not only an assessment of ocular health.

Case report

A mature 10-year-old black female, accompanied by her mother, was seen at the Nova Southeastern University, College of Optometry's Pediatric/Binocular Vision Clinic for her first eye exam in approximately five years. The patient complained of occasional blurry vision at distance and near. Her ocular history was unremarkable including never wearing compensating lenses; however, family ocular history revealed a brother with a "lazy eye," and a grandmother who developed glaucoma in adulthood. The patient's history revealed that she is positive for sickle cell anemia (Hb SS) and had been hospitalized during sickling crises seven to eight times/year. There was also a family history of diabetes mellitus, hypertension, and sickle cell anemia. The patient experienced a sickling crisis at birth, but otherwise had a normal pre- and peri-natal history. She was a full-term baby who reached all developmental milestones at normal ages. The patient was currently in the fifth grade and was below her grade level in reading, but was average in other subjects. She experienced poor reading comprehension, reversals of letters, and used her finger to keep her place. The patient was taking folic acid tablets daily, and Tylenol with codeine for pain as necessary.

Unaided visual acuity measured 20/200 OD, OS, and OU at distance and near. Confrontation visual fields, pupillary function, EOMs, color vision and stereopsis were normal in both eyes.

Cover test revealed orthophoria at distance and near. The patient did not break fusion, subjectively or objectively, during nearpoint of convergence, even when the target was brought and held to the nose. Her amplitude of accommodation, tested via the pull-out method, was 11.75 OD, OS.

Retinoscopy results were: OD +0.50 - 1.00 x 180, OS +0.50 - 0.75 x 180. Subjective refraction findings, OD and OS were +0.50 SPH, 20/20 (6/6). Cycloplegic retinoscopy findings were: OD +2.00 - 0.50 x 180, OS +2.25 - 0.50 x 180. Binocular evaluation was performed through the phoropter using risley prisms over the subjective dry refraction. At distance, the patient exhibited orthophoria; negative vergence (NV) X/12/6; positive vergence (PV) X/18/6. At 40 cm through the subjective refractive findings, the patient exhibited 3 prism diopters of exophoria ; NV: X/20/12; PV: X/24/16.

Accommodation testing through the phoropter was also performed over the subjective Rx at 40cm. NRA: +2.75, PRA: -2.25. Accommodative amplitude with minus lens to blur was significantly decreased: 4.50D OD, OS. Accommodative facility was tested with +/- 2.00 flippers, out of the phoropter and over the subjective Rx and was 7 cpm OD and OS; 6 cpm OU. Patient displayed more difficulty with the plus lenses throughout the test. Monocular Method Estimate retinoscopy indicated: +0.50 OD, OS.

Tensions by applanation were 10 mmHG OD, OS. Biomicroscopy revealed unremarkable anterior segment ocular health. Dilated examination of the posterior segment displayed tortuous vessels OU. A hemorrhage with surrounding areas of infarction was found on the inferior temporal retinal OD. In addition, areas of vitreous fibrosis not connected with the underlying retina were detected in the superior retina OS. Our diagnoses were:

Retinopathy secondary to sickle cell disease (non proliferative)

Accommodative insufficiency

Accommodative inflexibility

Latent hyperopia

In view of the degree of latent hyperopia found in the cycloplegic retinoscopy and the patient complaints, I prescribed the following bifocal correction for full time wear: OD and OS: +0.50 SPH, ADD +0.75D OU. A future appointment was made at this time.

The patient returned in one month for a progress evaluation. She and her mother reported an improvement in reading comprehension and a decrease in blurriness and asthenopia. Visual acuities with the prescribed spectacles were: 20/20 O.D., O.S., O.U. distance and near. I educated the patient's mother of the effects sickle cell disease can have on the eyes and visual system, informed her of the child's retinal condition, and stressed the importance of a full optometric evaluation annually, to monitor the patient's visual system. I also began the process to inform the child's general medical care provider of my findings.

I recommended a complete vision training evaluation in view of the latent hyperopia and previous accommodative findings. However, the patient's mother felt the spectacles had alleviated the symptoms and were a significant help in the child's academic achievements and refused further intervention at this time.

Management

Systemic treatment of sickle cell disease is primarily preventative. Folate acid supplements are usually taken daily because dietary folate may not meet the increased amount required for RBC production. Hemoglobin, hematocrit and reticulocyte counts should be determined periodically.^{2,9}

Treatment for pain during sickling events is primarily analgesic including narcotics and NSAIDs, intracellular hydration and hypotonic oral or intravenous fluid, bed rest and treatment of underlying infection.²

There are a number of new treatment trials being performed in the U.S. today. Oral hydroxyurea (Hydrea) has been shown to decrease pain events, hospital admissions, and the need for blood transfusions. In addition, bone marrow transplantations have converted 27 patients in

the U.S. from SS (sickle cell anemia) to SA (sickle cell trait).²

The most successful treatment of proliferative sickle cell retinopathy is local scattered photocoagulation to areas of neovascularization. It has been suggested that 360-degree peripheral circumferential photocoagulation should be used in unreliable patients to avoid new sea fans.¹⁰ It has been shown that when feeder vessels are treated there is a higher risk of choroidal neovascularization and retinal detachments. Fluorescein angiography determines the effectiveness of the therapy. In cases of persistent hemorrhaging, it may be necessary to perform a vitrectomy.³

Other ocular and visual conditions should be individually treated. In the case of my patient, who suffered from uncorrected hyperopia and accommodative dysfunctions, bifocal spectacles worn full-time relieved her symptoms.

Differential Diagnosis

There are many conditions that also produce proliferative retinopathy. Some of those conditions are: sarcoidosis, diabetes mellitus, branch retinal vein occlusion, embolic retinopathy, Eales' disease, retinopathy of prematurity, familial exudative vitreoretinopathy, chronic myelogenous leukemia, radiation retinopathy, pars planitis, carotid-cavernous fistula, ocular ischemic syndrome, and collagen vascular disease.³

A thorough work-up is necessary to distinguish sickle cell retinopathy. It includes the following: an extensive medical and family history, dilated fundus evaluation, sickledex hemoglobin electrophoresis, and fluorescein angiography.¹

Conclusions

Sickle cell disease is a relatively common disorder in African Americans. It affects all the organ systems, and often patients who suffer from the disorder frequently seek assistance from their doctors and/or emergency rooms only when a serious medical crisis occurs.⁷ I propose that most of these patients are unaware of the effects the disease can have on their eyes and visual system until serious complications occur. My patient is a case in point: she had not been advised by her medical care providers to seek regular eye and vision care, had not had an optometric or ophthalmologic examination in five years, and was living with previously un-

detected retinitis and a functional vision problem. Her reason for seeking care at our clinic was to deal with blurred vision, asthenopia and a reading problem. Consequently, in the interest of adequate care of patients with sickle cell disease, optometrists should educate these patients of the disease's potential eye and vision consequences, arrange for periodic regular optometric care, and provide appropriate treatment including referrals to other health care practitioners.

Acknowledgment

The graphic for the cover and title page of this article is published, with permission, from the Sickle Cell Information Center Website at www.SCInfo.org, The Sickle Cell Information Center, P.O. Box 109, Grady Memorial Hospital, 80 Jesse Hill Jr Drive SE, Atlanta, GA 30303.

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Date accepted for publication:

January 3, 2003