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CASE REPORT
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MACULAR INFARCTION IN A PATIENT WITH SICKLE CELL TRAIT

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Abstract

Purpose:
Sickle cell trait affects 8% of African Americans. Once believed to represent a benign carrier state, it has been linked to an increased risk of several of the pathological conditions that arise in sickle cell disease in at-risk individuals with hematologic and vascular comorbidities. Macular infarction is a known complication of sickle cell disease; this article illustrates this unique presentation in a patient with sickle cell trait.

Methods:
Case report.

Patient:
A 74-year-old African American man presented with the complaint of a central scotoma of the right eye.

Results:
Multimodal retinal imaging identified central macular infarction with severe inner retinal atrophy. Laboratory testing confirmed the presence of sickle cell trait. Other pertinent positives included low levels of protein C and protein S, untreated obstructive sleep apnea, and elevated levels of homocysteine in the setting of alcoholic liver cirrhosis and chronic kidney disease.

Conclusion:
Ocular manifestations of sickle cell trait have most frequently been reported in individuals with systemic medical comorbidities that predispose to erythrocyte sickling and vaso-occlusive disease. This case identifies a novel complication of sickle cell trait disorder, macular infarction, in a patient with comorbid associations.

Sickle cell disease results from the inheritance of two abnormal β_1-globin genes. Under conditions of tissue hypoxia, acidosis, hyper viscosity, or dehydration, erythrocytes may undergo sickling leading to vascular occlusion and tissue ischemia. The heterozygous form of the disease, sickle cell trait, has been noted to be a benign carrier state in otherwise healthy individuals. However, ocular complications similar to those observed in sickle cell disease have been reported in patients with medical comorbidities that predispose to erythrocyte sickling and vaso-occlusion.

Case Report

A 74-year-old African American man with a history of idiopathic chronic anterior uveitis presented for follow-up eye care with a six-week complaint of a "gray spot" in the central vision of the right eye. Dilated retinal examination was normal in the left eye but displayed a blunted foveal light reflex in the right eye. Spectral domain optical coherence tomography illustrated an irregular foveal depression associated with paracentral acute middle maculopathy and inner retinal atrophy. The outer retina, including the ellipsoid zone band, was intact (). Fluorescein angiography displayed severe central macular nonperfusion with minimal surrounding retinal vascular leakage in the right eye (). Fluorescein angiography of the left eye was unremarkable. No peripheral retinal abnormalities were noted in either eye including no evidence of retinal vascular nonperfusion. Optical coherence tomography angiography was remarkable for nonperfusion of the superficial and deep retinal capillary plexuses indicative of macular infarction in the right eye () and was within normal limits in the left eye.

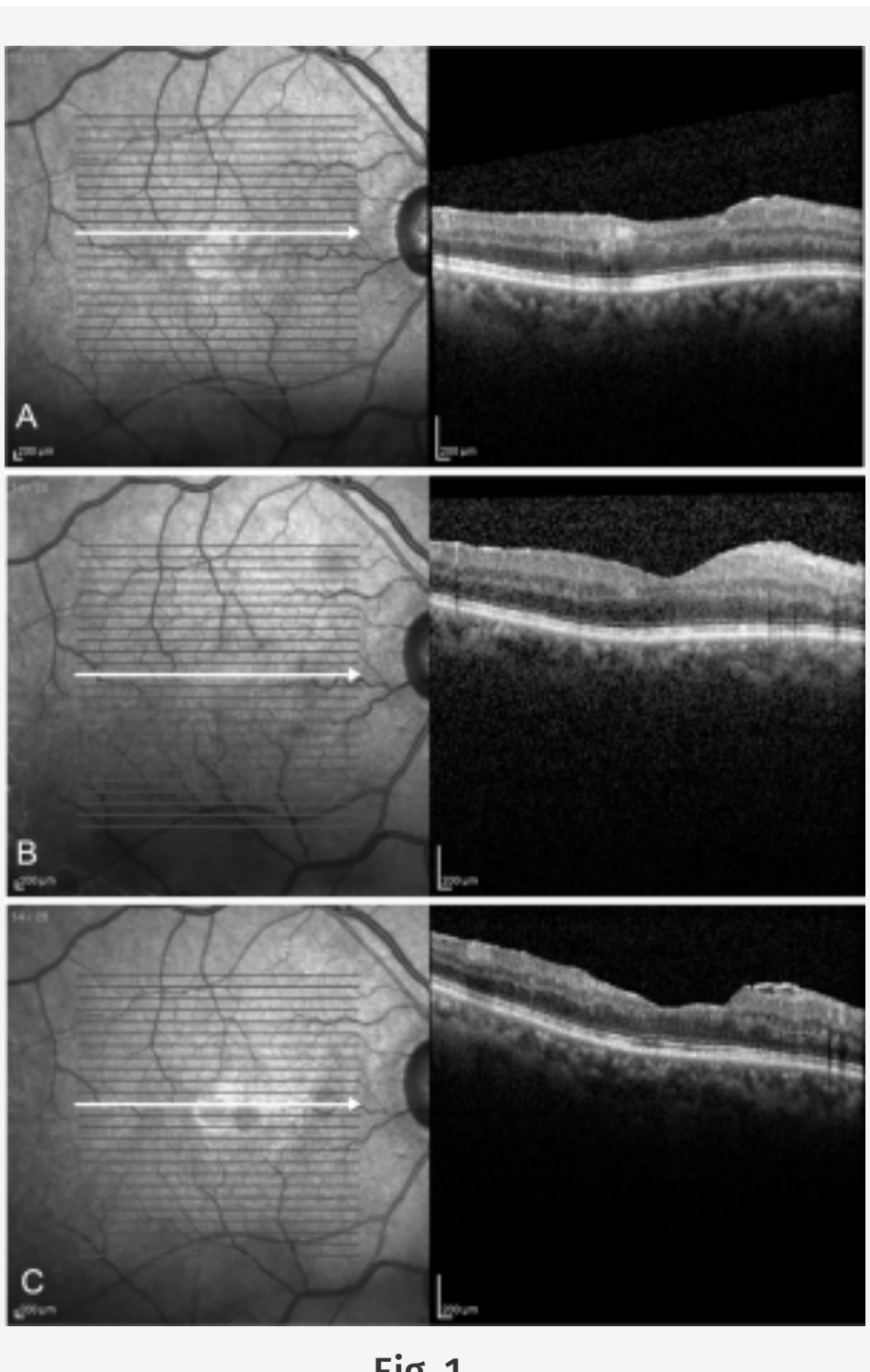

Fig. 1.
Spectral domain OCT B-scans from the right eye. Registered near infrared images show the corresponding level of the B-scan. **A** and **B.** Optical coherence tomography B-scans illustrate small inner nuclear layer infarcts (paracentral acute middle maculopathy) at the level of the superior fovea of the right eye. **C.** Optical coherence tomography B-scans several months later illustrates significant inner and middle retinal thinning of the superior fovea.

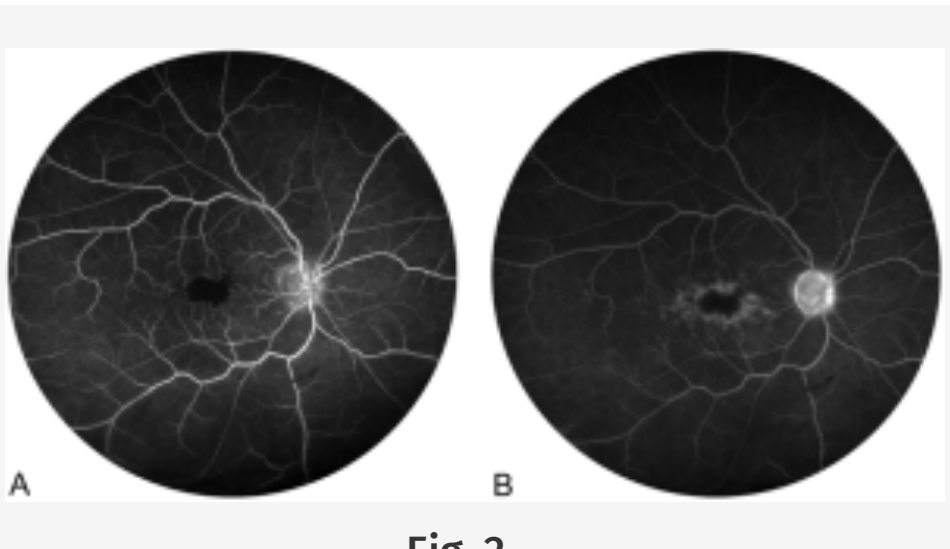

Fig. 2.
Fluorescein angiogram of the patient's right eye. **A.** Venous and (**B**) recirculation phases illustrate severe macular ischemia with enlargement of the foveal avascular zone and late perifoveal leakage. The periphery is grossly normal.

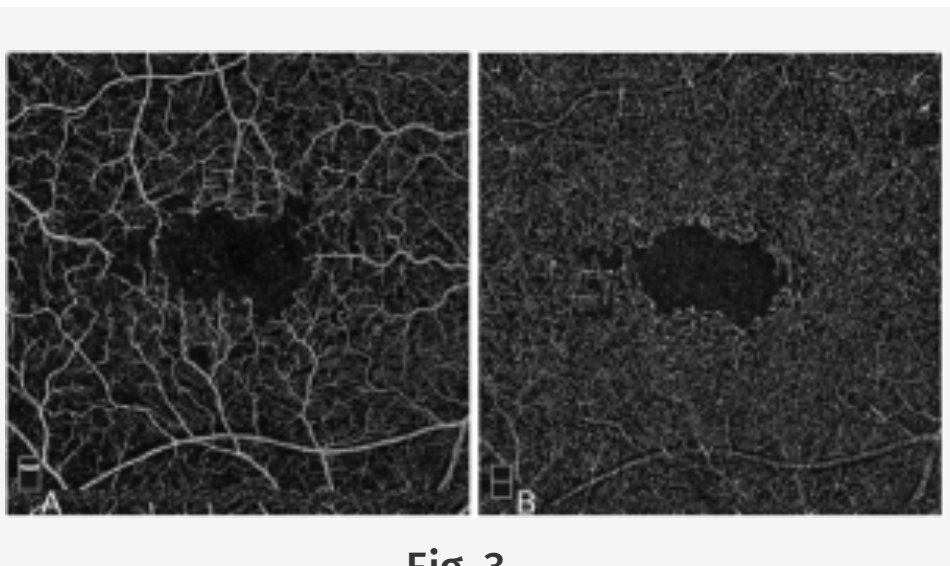

Fig. 3.
En face OCT angiogram with segmentation of the superficial (**A**) and deep retinal capillary plexus (**B**) illustrates severe flow deficit of the central macula with enlargement of the foveal avascular zone.

Further investigation of the patient's medical record was notable for numerous medical comorbidities, including poorly controlled hypertension, hyperlipidemia, Stage 3 chronic kidney disease, untreated obstructive sleep apnea, and cirrhosis of the liver secondary to active, chronic alcoholism. Two years before this episode, the patient was diagnosed with an infarction of the medullary cavity of the distal femur. The patient denied a history of recreational drug use.

Laboratory workup, including hemoglobin electrophoresis, disclosed a new diagnosis of sickle cell trait with 38.9% hemoglobin S and 61.1% hemoglobin A. Additional testing found that the patient exhibited slightly low levels of protein C (66%, reference 70–180) and protein S (40%, reference 70–150) and elevated levels of homocysteine (22.2, reference 5.0–13.9). The patient was also noted to have chronic idiopathic thrombocytopenia; however, the erythrocyte and leukocyte levels were normal. Other laboratory testing including erythrocyte sedimentation rate, antinuclear antibody, lupus anticoagulant, rheumatoid factor, antineutrophil cytoplasmic antibody, antithrombin III activity, cardiolipin antibodies, Factor II and V, rapid plasma reagin, angiotensin-converting enzyme, and toxoplasmosis antibody were all negative. Recent blood glucose was within normal limits, and there was no evidence on examination or imaging studies of diabetic retinopathy. A recent computed tomography scan of the chest was negative for sarcoidosis. Carotid ultrasound was negative for clinically significant stenosis or flow abnormalities. Previous electrocardiograms were normal. There were no signs or symptoms of structural heart disease. QuantiFERON gold testing was inconclusive likely due to a previously diagnosed but presumed inactive ***Mycobacterium kansasii*** pulmonary infection.

The patient was followed during the next three months. His visual acuity declined from 20/70 to counting fingers, although he reported no subjective change in the central scotoma. Sequential optical coherence tomography scanning showed progressive atrophy of the inner and middle retina of the central macula in the right eye and remained within normal limits in the left eye ().

Discussion and Conclusions

Macular infarction is associated with a spectrum of etiologies including thrombotic and embolic events (e.g., branch retinal artery occlusion), retinal vasculitis (e.g., Behçet disease and systemic lupus erythematosus), medication toxicity (e.g., aminoglycoside and dapsone), and hyperviscosity syndromes. A well-known and important cause of macular infarction is sickle cell disease, which occurs when rigid, sickled erythrocytes occlude the thin capillaries supplying the inner and middle retina in the central macular region.

Although sickle cell disease patients may develop findings of proliferative and nonproliferative retinopathy, including macular infarction, there is insufficient evidence to establish increased rates of intraocular complications in sickle cell trait patients who are otherwise healthy. One study of 124 healthy individuals with sickle cell trait failed to detect any evidence of retinopathy. However, numerous case reports have documented retinal complications in sickle cell trait patients with comorbid conditions predisposing to hypercoagulable or sickling complications in the retina. These include reports of chorioretinal infarction in the setting of severe dehydration and fever, cilioretinal artery occlusion associated with elevated rheumatoid factor, and proliferative retinopathy associated with coexisting systemic illnesses, such as sarcoidosis, tuberculosis, syphilis, diabetes mellitus, or uncontrolled hypertension. Current evidence also suggests that diabetic retinopathy is more severe in individuals with sickle cell trait, although some evidence exists to the contrary.

In this article, we report a novel case of macular infarction in sickle cell trait. The central macula is perfused by narrow end arterioles and terminal capillaries that skirt the foveal avascular zone. The baseline degree of erythrocyte sickling in sickle cell trait is unlikely sufficient to cause occlusion of these vessels in a healthy patient. However, our patient's numerous comorbidities likely produced local hypoxia, hyper viscosity, and acidosis sufficient to trigger a local sickling event affecting the parafoveal region.

Cirrhosis patients suffer from an underproduction of the three major anticoagulant proteins, protein C, protein S, and antithrombin leading to a hypercoagulable state; our patient exhibited significantly decreased levels of two of these factors. In addition, Stage 3 chronic kidney disease may predispose to metabolic acidosis because of impaired ammonia excretion and decreased renal bicarbonate reabsorption. Alcoholism is also a known cause of metabolic acidosis due to the development of lactic acidosis and ketoacidosis. Untreated obstructive sleep apnea produces a respiratory acidosis as a result of retention of carbon dioxide. Finally, the patient's untreated hypertension increased the risk of vaso-occlusive disease because of chronic endothelial damage. Similar to other reported patients, it is not possible to attribute a single comorbid condition to the macular infarction, but it may be the case that several played a role. Interestingly, the patient also had a history of bilateral medullary bone infarcts of the femurs indicating previous vaso-occlusive events. A comprehensive evaluation revealed no other known causes of macular infarction that could account for the patient's findings.

This case report describes isolated macular infarction in a patient with sickle cell trait and associated systemic comorbidities that predisposed to erythrocyte sickling, vaso-occlusive disease, and a hypercoagulable state. An estimated 300 million people worldwide, including 8% of African Americans, are affected by sickle cell trait. It is important to assess for both sickle cell trait and sickle cell disease in patients with macular infarction. Hemoglobin electrophoresis is the preferred method of diagnosis as opposed to other less specific laboratory tests, such as a SICKLEDEX. This report emphasizes the importance of tight management of systemic medical conditions in sickle cell trait patients.

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