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# Post-mortem Diagnosis of Vaso-occlusive Sickle Cell Crisis

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**Abstract**

A great deal of controversy continues to surround sickle cell trait and its association with stress-related morbidity and sudden death. Most of the death mechanisms are related to the biological consequences of diffuse microvascular occlusion due to sickling, although a significant number of such sudden deaths remain unexplained even after thorough autopsy. We present a case of unexpected death in a young male with undiagnosed sickle cell trait, who met with a road traffic accident and was diagnosed only after the postmortem. The death was attributed to vaso-occlusive sickle cell crisis secondary to stress and infection.

**Key word:** Sickle cell trait; Sudden death; Vaso-occlusive crisis.

## Introduction

Sudden death in a young male is usually a cause of speculation. The cause of death could be both natural and unnatural. It is traumatizing for the family members and the situation is aggravated if past history is not available [1]. Overall evidence suggests that sickle cell trait (SCT) may be neither a completely benign carrier state nor a true disease entity, but rather a risk factor for certain adverse outcomes that result from the interplay between genetic and environmental influences. Although rare, sudden death is the most serious complication of SCT [2]. We are presenting this case of unexpected sudden death in a young male patient with undiagnosed SCT. The non-specific nature of his complaints and the paucity of clinical signs misguided the clinicians on the potentially lethal outcome.

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*Case presentation*

A 23- year- old male patient was brought for neurosurgical evaluation. He had a history of road traffic accident one and a half months back, for which he was treated else where. On examination, the patient had an in-situ tracheostomy tube. He was conscious, not responding to oral commands with minimal response to deep painful stimuli. There was injury to the face around the mouth and jaw. On auscultation of the chest, bilateral basal crepitations were present. Per abdominal examination revealed no organomegaly. His blood pressure was 100/58mm of Hg, pulse rate was 96/min and oxygen saturation was 92%. The electrocardiogram was normal except for sinus tachycardia. X-ray chest was normal. Only hemoglobin was done which was 9gm%. The electrolytes were normal. Urine was turbid with a trace of albumin, 10-12 pus cells/hpf and 3-4 RBCs /hpf. He was given antibiotics, antacids and IV fluids. A computerized tomography (CT) scan of the head revealed edematous brain with hemorrhagic areas in the left temporal and frontal lobes with a thin bleed in the inter-hemispheric fissure. CT thorax showed collapsed intact lungs. On CT abdomen, liver showed hemorrhagic contusion on posterior surface of the right lobe. He was given oxygen therapy and later given ventilatory support as he became breathless and the oxygen saturation dropped.

The patient's condition deteriorated, had unexpected cardio-respiratory arrest on the next day and could not be resuscitated. A medico-legal autopsy was done.

*Autopsy findings*

Poorly built and poorly nourished body measuring 180cm in length and was weighing 38 kilograms. Body appeared emaciated with sunken eyes, yellow sclera and prominent rib cage. Externally, multiple partially healed wounds were seen. Internal examination revealed an edematous brain with yellow brown areas in the left temporal and both frontal lobes. Lungs showed multiple tiny nodules over the surface and the cut section was grey white to grey brown. The liver was pale yellow in color with brownish black discoloration on the posterior aspect of the right lobe. The provisional diagnoses were that of tuberculosis and immunocompromised state. Random bits from liver, lungs and brain were sent for histopathological examination. On gross examination, the lungs weighed 250gms, cut section there were grey brown to grey white areas of consolidation, bit of liver tissue measured 9x6x2cm, cut section was pale yellow and brain tissue weighed 450gms and cut section showed yellow brown area measuring 4x2cm. (Figs 1A, 1B, 1C)

On histopathology, multiple sections from the lung tissue showed macrophages and blood vessels filled with sickled erythrocytes with areas of consolidation. Sections from the liver showed congested sinusoids filled with sickled erythrocytes Sections from the brain showed edema with blood vessels containing sickled erythrocytes (Figs 2A, 2B, 2C).

**Fig 1A: Lung with grey brown to grey white areas of consolidation**

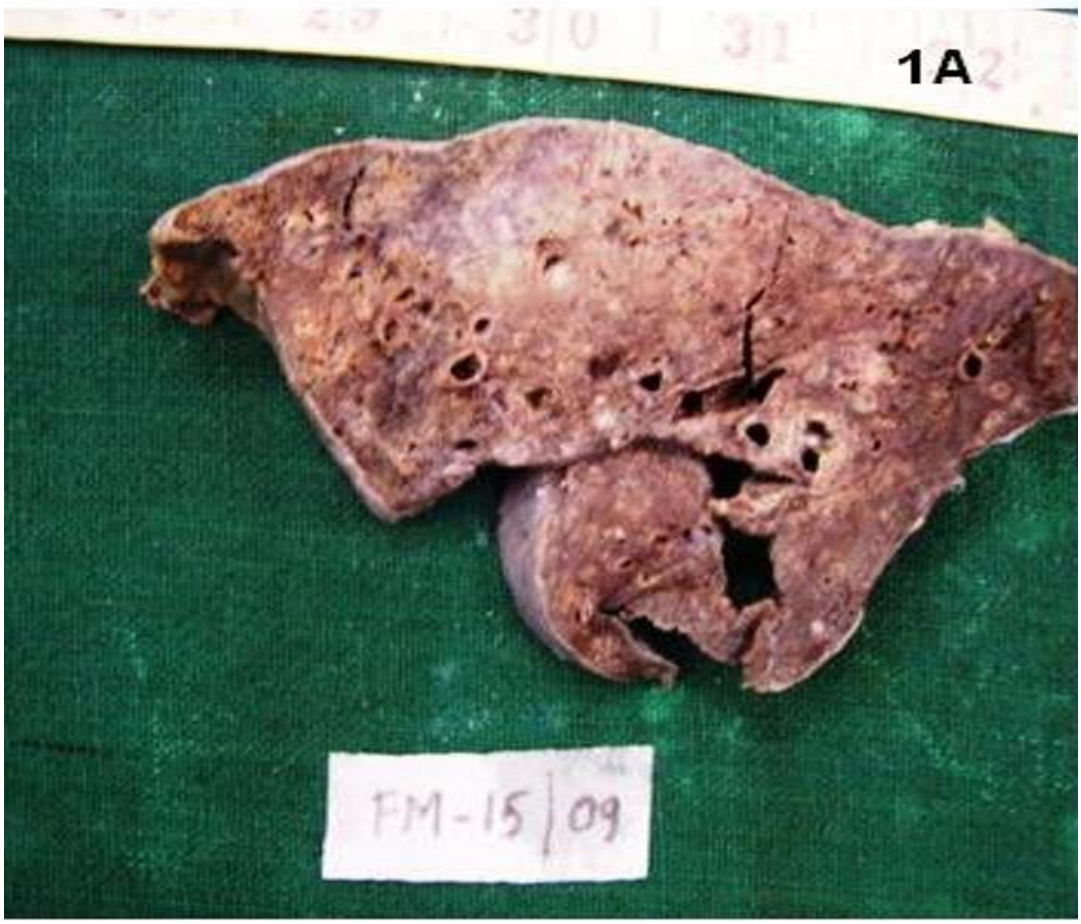


**Fig 1B: Liver appears pale yellow**


**Fig 1C: Cut section of brain with yellow brown area**

**Fig 2A: Photomicrograph showing sickled RBCs in the lung (H&E, x200)**

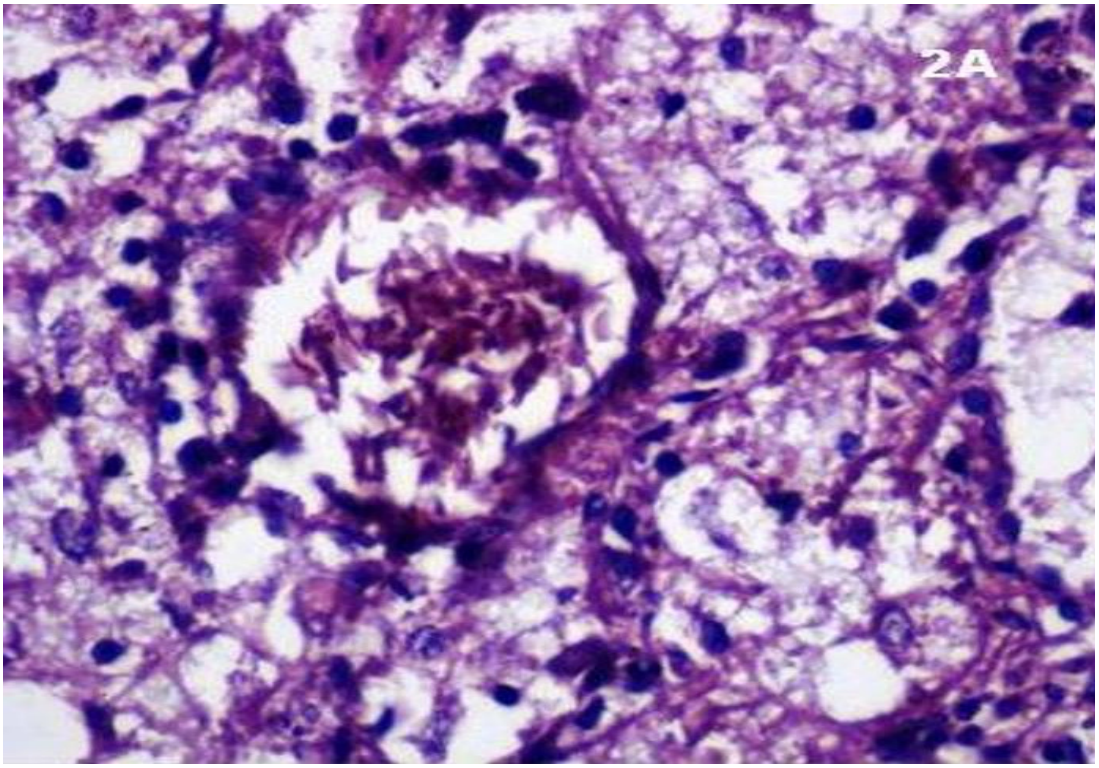



**Fig 2B: Photomicrograph of liver with sickled RBCs within sinusoids (H&E, x200)**

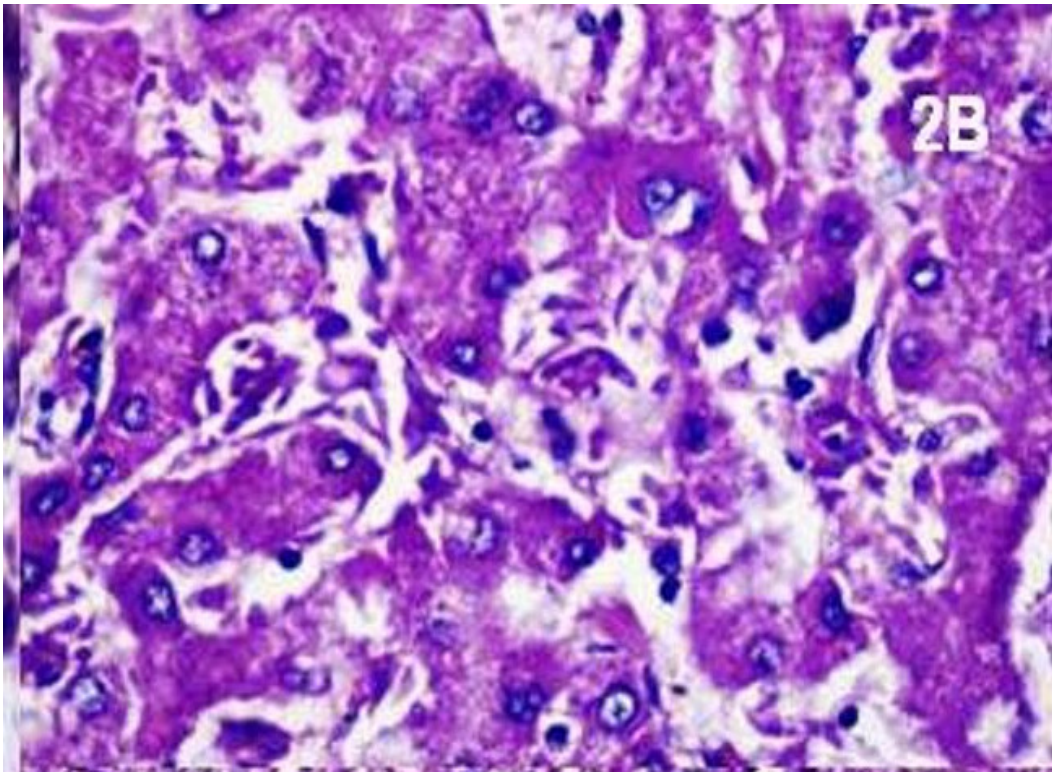
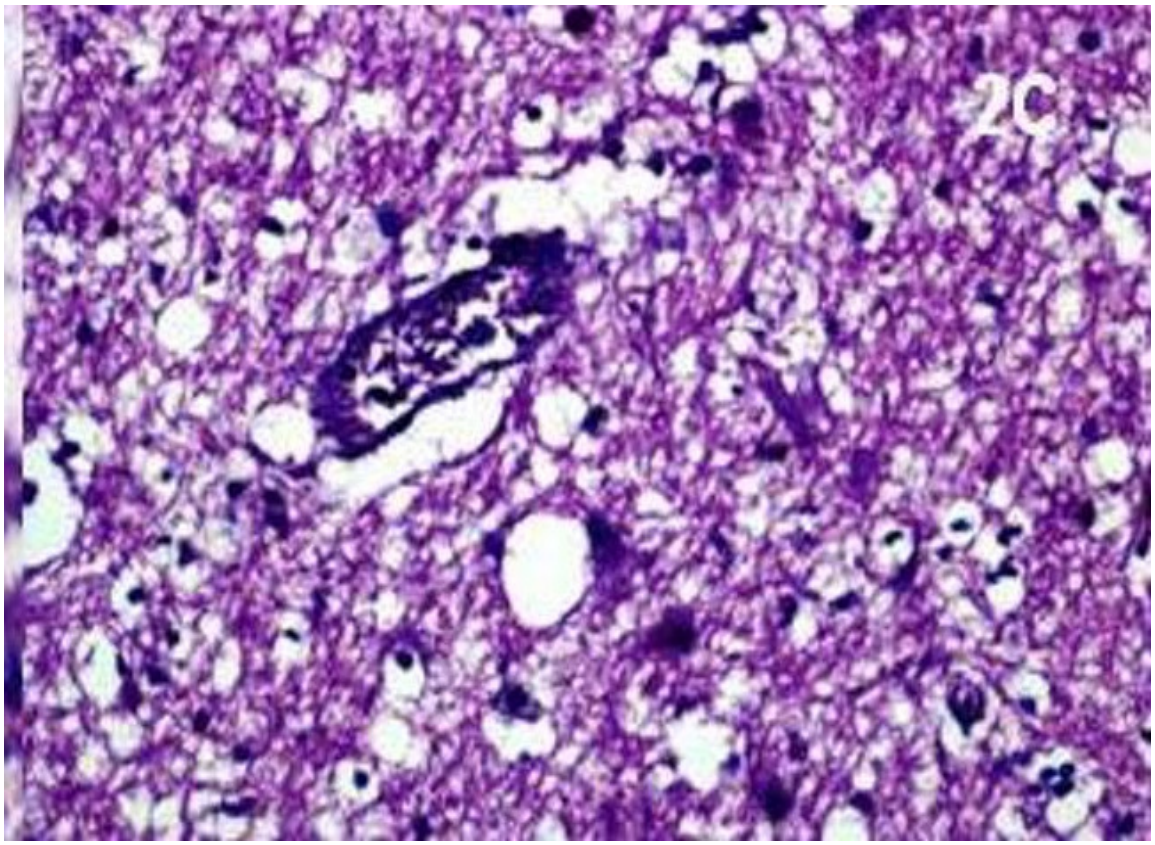


**Fig 2C: Photomicrograph of brain showing edema with blood vessel containing sickled RBCs (H&E, x100)**




## Discussion

Sickle cell disorder (SCD) is remarkable for its clinical heterogeneity. Some patients have repeated episodes of admissions while others are totally asymptomatic. Although everyone with SCD shares the same gene mutation, there are five recognized haplotypes based on its origin. They are Bantu, Arab-India, Senegal, Benin, Cameroon and Central African Republic. The Central African patients have the worst prognosis while those from Senegal have the least form of the disease[3]. From the little history available, he had a virtually asymptomatic childhood & was apparently never diagnosed as having sickle cell disease. CT scan did not reveal any gall stones & there was no evidence of joint swellings, deformities or leg ulcers suggesting chronic disease.

There is a dearth of data on SCD in India as compared to that in Africa and America. Leg ulcers and priapism are said to be uncommon, while splenomegaly is common in Indian SCD. This is unlike most African or American patients who have non functional small spleens due to repeated infarcts [1,3 ]. There was no splenomegaly in the present case.

The strongest factor in SCT patients implicating intravascular sickling with tissue injury and even death is hypoxia. The decreased arterial $PO_2$ levels initiated events that lead to acidosis, excess lactate and intravascular sickling [4].

The patient had a very short history of illness following road traffic accident. He had evidence of breathlessness, anxiety and urinary tract infection. The patient's CT scan and autopsy suggested focal areas of infarction in the brain, lung and liver.

Acute chest syndrome is a severe and catastrophic complication of SCD and is characterized by chest pain, tachypnoea, fever, cough and arterial oxygen desaturation.

It can be severe with reported deaths of 4.3% in adults and is presumed to occur due to in situ sickling within the lung, producing pain and temporary pulmonary dysfunction [5,6]. The most frequent findings are rales. Infiltrates may be seen in the chest x ray, even though quite often it may be normal. Although there was no history of fever, chest pain or cough in the present case, he had rales and complained of breathlessness. Under these circumstances, a diagnosis of acute chest syndrome cannot be ruled out. Moreover he did not respond to the oxygen or ventilatory support. In addition to this, exchange transfusions must have been advocated in the treatment of acute chest syndrome[6], which was not done in the present case.

The patient's urine was turbid with pus cells indicating urinary tract infection. Provocative factors for sickle cell crisis include infection, fever, excessive exercise, anxiety, abrupt changes in temperature and hypoxia. Except for fever and excessive exercise all the precipitating factors were present in our patient. We believe all these factors precipitated sickle cell crisis and may have contributed to regional hypoxemias in the lung or even acute chest syndrome. During his present illness he was given fluids, analgesics, steroids and oxygen therapy but it could not prevent the cascade of events which resulted in sudden unexpected death. Exchange transfusions, which have been reported to improve survival, unfortunately could not be done due to lack of diagnosis.

## Conclusion

Sudden death may occur in susceptible persons with SCT when poor physical conditioning, dehydration, heat stresses, anxiety or hypoxic states precipitate sickling of the abnormal erythrocytes. SCT may be overlooked as an etiological factor in sudden death. The initial set of investigations did not include a peripheral blood examination possibly because a hematological disorder was not suspected. This ultimately proved to be critical as a complete hemogram would have helped to recognize the impending disaster. Early recognition of this potentially fatal condition is crucial, as intensive supportive therapy would have prevented the catastrophic event.

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