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Sudden death due to Vaso-occlusive crisis of Sickle cell anemia: An autopsy diagnosis - A Case Report

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ABSTRACT

Sickle gene is highly prevalent in Central India, and sickle cell anemia has variable clinical presentation and most of the traits are not detected as they remain asymptomatic. Very few numbers of sudden deaths are reported as sickle cell crisis in clinically asymptomatic patients, particularly in autopsy reports due to ignorance of autopsy surgeon in considering this disease as a cause of death despite of its high prevalence in these regions. Deaths with no apparent cause and physical over activity, medical officer must keep in mind the possibility of death due to vaso-occlusive crisis in sickle cell disease. The present case is reported to highlight the significance of considering sickle cell crisis as an etiology for sudden death in cases with no apparent cause, especially in highly prevalent areas. Similarly during autopsy, the role of hematology slides, proper histopathological sampling and toxicological analysis is considered with proper analysis of results.

Key Words: Sickle cell, Vaso-occlusive crisis, Autopsy, Sudden death.

1. INTRODUCTION

Sickle cell disease is an inherited disorder of hemoglobin synthesis due to substitution of thymine for adenine in the glutamic acid DNA codon (GAG---GTG), which results in turn, substitution of valine for glutamic acid at 6th residue position of β globin chain (Taliajerro et al., 1923). Sickle gene is widely recognized specially in the central part of India

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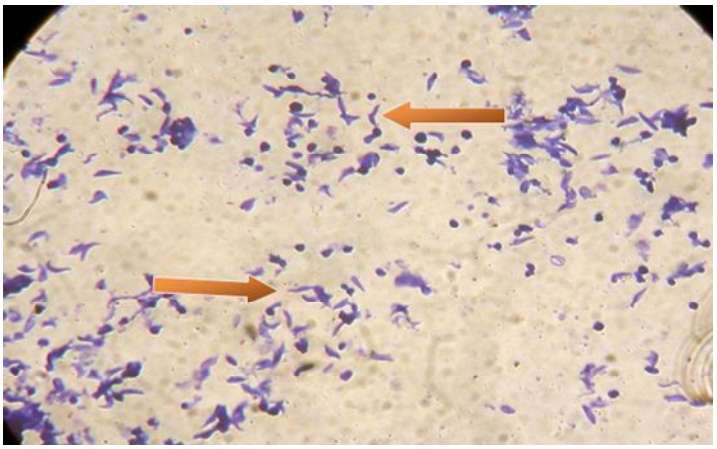

Figure 1
Imprint smear sows sickle RBCs from the cut surface of spleen

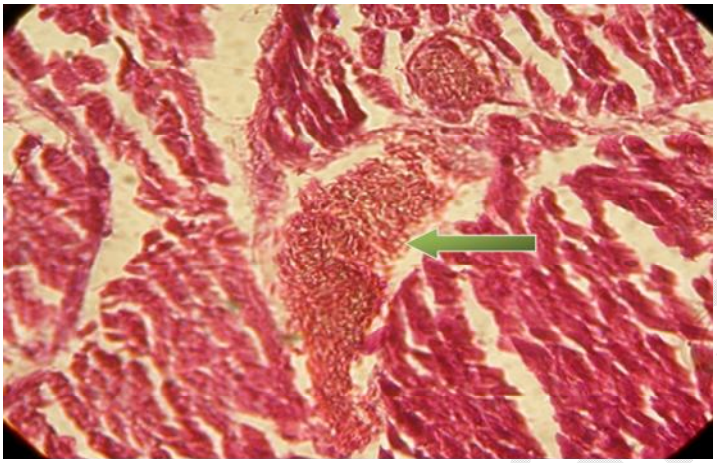

Figure 2
Myocardial vessels stuffed with sickle RBCs (H&E 200X)

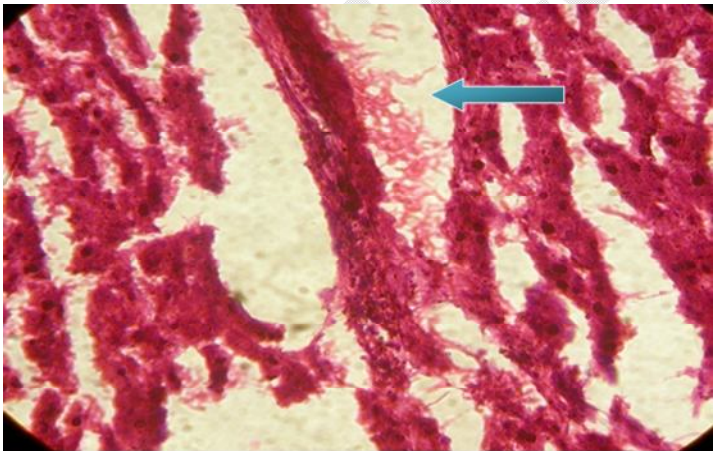

Figure 3
Hepatic vessels filled with sickle RBCs (H&E 200X)

(Negi, 1972). The highest frequency of sickle cell gene in India is reported in Orissa followed by Assam, Madhya Pradesh (Central India), U.P, Tamilnadu and Gujrat (Balgir, 1996).

The Central India region is a focus of sickle cell disorder with average sickle cell gene frequency being as sickle cell trait found in 9.30% and an SS phenotype (Sickle cell disease) in 0.21% of population of Chhattisgarh (Central India) (Patra et al., 2011). The high prevalence of the gene for sickle cell hemoglobin in the areas of the world where malaria has been common suggests that persons with sickle cell trait have a selective advantage over normal individuals when they contract this disease (Luzzatto, 1979). This disease has variable clinical presentation and most of the Indian patients remain asymptomatic for longer periods due to higher levels of HbF. Sickle cell disease presenting as death in clinically asymptomatic patients with sickle cell disease or sickle cell trait is not uncommon. But, unfortunately less numbers of deaths are reported due to sickle cell crisis because of ignorance of an autopsy surgeon in considering this disease as a cause of death despite of its high prevalence in these regions.

Hence, relatively very few autopsy studies have focused on the cause of death in asymptomatic cases. Therefore, while doing autopsy in cases with no apparent cause and having history of physical over activity, medical officer must keep in mind the possibility of death due to sickle cell crisis. The present case is reported to highlight the significance of considering sickle cell crisis as an etiology for sudden death in cases with no apparent cause, especially in highly prevalent areas. During autopsy, the role of proper histopathological sampling, hematology slides, Hb electrophoresis and toxicological analysis is very important with proper analysis of results and sickle cell crisis is considered to a large extent a diagnosis by exclusion (Charache, 1974).

2. CASE REPORT

In the present case 32 years old male who was apparently healthy, dancing in a wedding procession suddenly collapsed. During shifting to the Hospital died on the way. In the autopsy findings he was average built and no external injuries & abnormal findings were found. All the organs were congested, liver & spleen found enlarged. Stomach contained semi-digested food material. After analyzing internal findings especially considering splenic enlargement all organs were kept for histopathological examination. Similarly viscera were also sent for chemical analysis at Regional Forensic Science laboratory.

Chemical analysis report of viscera did not reveal any poison. Imprint smear from the spleen showed sickling of RBCs. Histopathology report showed congestion and occlusion by sickled RBC's in the blood vessels of heart, lungs, liver, kidneys and spleen (Figures 1-6). So, considering the histopathological findings and exclusion of other possibilities the cause of death was given as "Cardiogenic Shock due to Sickle Cell Crisis".

3. DISCUSSION

Sickle cell anemia is a disease passed down through families as an autosomal recessive inheritance. The red blood cells which are normally shaped like a disc take on a sickle or crescent shape in hypoxic conditions. It manifests in two forms viz. heterozygous (sickle cell trait) or homozygous (sickle cell disease). It results from the point mutation in the genetic code where substitution of thymine for adenine in the glutamic acid DNA codon (GAG---GTG), which results

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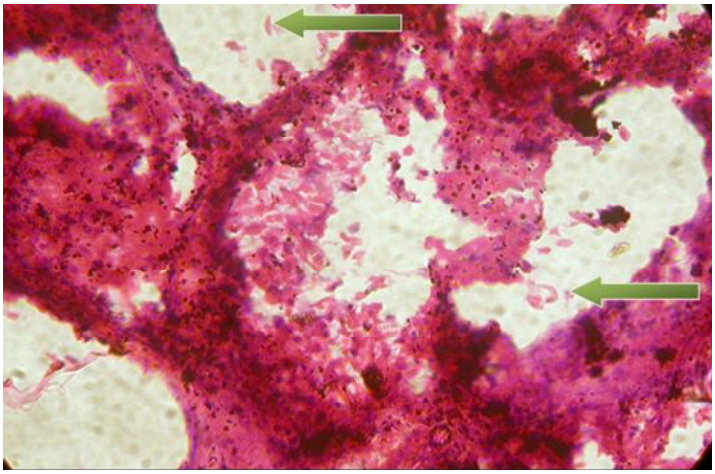

Figure 4
Lung alveoli filled with sickle RBCs (H&E 200X)

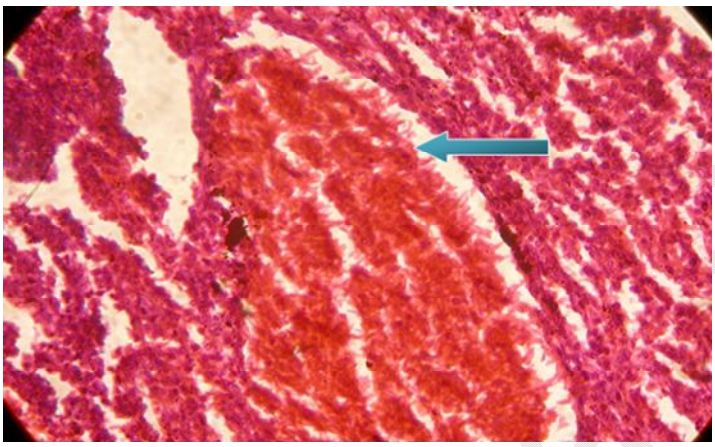

Figure 5
Splenic vessels stuffed with sickle RBCs (H&E 200X)

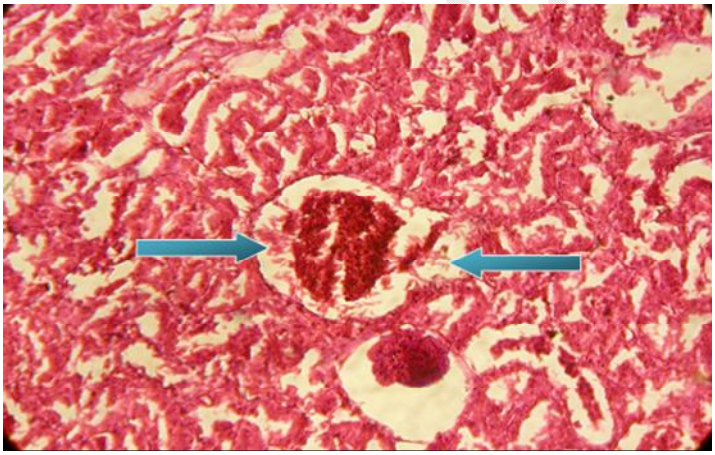

Figure 6
Kidney- congested gomeruli stuffed filled with sickle RBCs (H&E 200X)

in turn, substitution of valine for glutamic acid at 6th residue position of β globin chain (Taliajerro et al., 1923). Acute events in the sickle cell disease include painful vaso-occlusive crisis, infarctive stroke, acute chest syndrome, priapism, aplastic crises, splenic sequestration, haemolytic crises, & infections (Serjeant et al., 1994). The trait patients are mostly asymptomatic and sickle cell crisis can occur in them only if the patient is exposed to extreme hypoxic conditions (Benz, 2005).

Perceived precipitating factors of vaso-occlusive events include skin cooling, emotional stress, physical exertion and pregnancy (Serjeant et al., 1994). Hypoxia due to exertion induces a chain of events in a person with sickle cell anemia that causes sickling, leading to vascular occlusion, potentiating hypoxia and culminating in sudden death (Roberts et al., 2002, Lisa et al., 2009). Similarly infection, fever, anxiety, abrupt changes in the body temperature or hypertonic dyes are precipitating factor for sickle cell crisis (Lisa et al., 2009). In many cases no cause is obvious. But, precipitating factor in this case of sickle cell crisis was physical exertion. The possible risk factors for development of sickle cell vaso-occlusion include hemoglobin S polymerization, sickle cell deformability, sickle blood viscosity, the fraction of dense cells, sickle cell endothelial cell adherence, endothelial cell activation, hemostatic activation and platelets, local and regional environmental factors and physiological factors. Hence, in sickle cell disease related deaths circumstances of death as well as gross and histopathological findings must be considered along with hematological findings. Grossly Cardiomegaly, hepato-splenomegaly, cholelithiasis, evidence of infections and splenic findings suggestive of haemolytic anemia are classical features of the disease. Recurrent infarctions of the spleen due to occlusion of the splenic vasculature by non-deforming sickled RBCs may lead to auto splenectomy.

Tendency for increasing splenic size is associated with higher HbF (Kar et al., 1986). So, evaluation of splenic size and weight is important at autopsy. Histopathological sections of all organs show disseminated intravascular sickling suggestive of vaso-occlusive crisis leading to multiorgan failure and death. The vaso-occlusive crisis which manifests as multiorgan failure and acute chest syndrome is an important cause of death in sickle cell patient (Platt et al., 1994). But, interpretation of histopathological findings should be cautious as death itself involves hypoxia, hypo- perfusion and other processes that could initiate sickling.

4. CONCLUSION

Vaso-occlusive crisis or sickle cell crisis is a common painful complication of sickle cell disease in adolescent and adult. Acute episode of severe pain (crises) are the primary reason that these patients seek medical care in hospital emergency department. Delay or ignorance to this condition is fatal. Clinical profile of sickle cell patients in Central India is less severe as compared to African countries and characterized by late age of presentation, more asymptomatic patients, less frequency of vaso-occlusive crisis and low mortality. Hence, most of the patients remain undiagnosed. This fact is observed in this case presenting as deaths without any significant present or past symptoms of sickle cell disease. So, it is not uncommon to see such a case presenting as death without any significant history. This can lead to many medico legal complications if autopsy surgeon fails to consider this disease as a cause of death. Hence during autopsy, circumstances of death, gross

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findings in the organs, imprint cytology, proper histopathology samples, Hb electrophoresis, molecular studies and toxicological analysis is important.

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