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Decoding The Unexpected: Autopsy Review of Sickle Cell Fatalities

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Abstract

Sickle cell disease (SCD) is a common inherited hemoglobinopathy characterized by structural abnormalities of haemoglobin, resulting in recurrent vaso-occlusive crises and progressive multi-organ failure. This retrospective autopsy-based study was conducted in the Department of Pathology, at tertiary care teaching institute in Maharashtra, over a two-year period from January 2023 to December 2024. A total of 25 autopsy cases diagnosed with sickle cell disease were analysed. Of these, 16 cases were males and 09 were females, with an age range of 11 to 51 years. Histopathological examination revealed marked vascular congestion and the presence of sickled red blood cells in all major organs, including the liver, spleen, lungs, kidneys, heart, and brain. The most common cause of death was sickle cell crisis leading to multi-organ failure. This study underscores the importance of considering sickle cell disease as a significant differential diagnosis in cases of unexplained sudden death.

Keywords: Sickle Cell Disease, Sickle-Shaped, Morphological Alterations

Introduction- Sickle cell disease (SCD) is a group of inherited hemoglobinopathies characterized by the presence of haemoglobin S (HbS). The disorder occurs either in the homozygous state as sickle cell anaemia (HbSS) or in compound heterozygous forms, resulting from the inheritance of HbS with another abnormal haemoglobin, such as haemoglobin C (HbSC) or β-thalassemia (HbS/β-thalassemia). In sickle cell anaemia, a single point mutation in the β-globin gene leads to the substitution of glutamic acid by valine at the sixth position of the β-globin chain, resulting in the synthesis of structurally abnormal haemoglobin S (HbS). This molecular alteration promotes polymerization of deoxygenated HbS, leading to erythrocyte sickling, vaso-occlusion, and the diverse systemic manifestations associated with the disease.[1] Hemoglobinopathies are the most common inherited disorders globally, and sickle cell disease accounts for a substantial proportion of these.[2,3]

Sickle cell disease (SCD) was first described in 1910 by James B. Herrick, a Chicago-based cardiologist, during his observations of West Indian dental students who presented with pulmonary symptoms. Herrick coined the term "sickle-shaped" to describe the characteristic morphology of red blood cells observed in these patients. In India, sickle haemoglobin was first reported in 1952

by Lehmann and Cutbush among the Veddoid tribal population of the Nilgiri Hills in Tamil Nadu. Subsequently, the presence of sickle haemoglobin was documented in several other tribal populations across India, including tribes from Odisha, Assam, and parts of Maharashtra.[4]

Sickle haemoglobin shows a high prevalence among tribal communities of central, southern, and western India, with wide regional variation in frequency, ranging from 10% to 23% [5,6]. An increased prevalence of sickle cell disease has also been reported among non-tribal communities residing in these regions. Among Indian states, Maharashtra, Madhya Pradesh, and Tamil Nadu exhibit a comparatively higher burden of the disease. Central India represents a major focus of sickle cell disorder, with particularly high prevalence reported from the Vidarbha region of Maharashtra. Studies from this region have documented a wide variation in prevalence, ranging from 4% to 40%, with an average sickle cell gene frequency of approximately 4.3%.[7]

Autopsies were conducted at post-mortem centre in a tertiary care teaching institute were included in this study.[8-11]

The clinical manifestations of sickle cell disease demonstrate marked heterogeneity. While some individuals remain largely asymptomatic, others experience recurrent episodes requiring repeated hospital admissions. The severity of the disease is influenced by multiple factors, including climatic conditions, socioeconomic status, baseline haemoglobin levels, and the proportion of fetal haemoglobin (HbF).[12,13]

Sickle cell disease may occasionally manifest as sudden, unexpected death in clinically asymptomatic individuals. However, due to limited awareness among autopsy surgeons regarding the potential of sickle cell anaemia as a cause of death, the condition is often underreported despite its high prevalence in certain populations. Hence, it is imperative that medical officers consider sickle cell anaemia as a possible underlying cause while performing autopsies in cases with no apparent cause of death, particularly when there is a history of recent physical exertion.

Despite substantial advancements in the treatment of sickle cell disease (SCD), overall survival remains compromised by significant morbidity and mortality. Autopsy findings in such cases often reveal a broad spectrum of morphological alterations, some of which may not be directly attributable to the cause of death. This limitation is compounded by the scarcity of autopsy-based studies and a general reluctance among the public to consent for clinical post-mortem examinations. Moreover, once a patient's genotype has been established, relatives often perceive little value in further pathological evaluation.

The present study seeks to delineate the autopsy findings encountered in incidentally detected cases of sickle cell anaemia, emphasizing the major morphological changes, their pathological significance, and the frequency of lesions that may have contributed to death. The objective is to evaluate the spectrum of pathological changes observed in our centre and to enhance awareness among clinicians and the general public, thereby aiming to reduce unexpected deaths arising from sickle cell–related complications or crises. In this context, analysis of histopathological findings were observed in various organs of 25 cases of sickle cell anaemia.

Material and Methods: - This retrospective study was conducted in the Department of Pathology at a tertiary care teaching institute over a two-year period, from January 2023 to December 2024. A total of 25 cases of sickle cell anaemia were included in the study. Autopsies were performed, and viscera were received for detailed

histopathological examination. The organs examined included the lungs, heart, liver, kidneys, spleen, and brain.

Relevant clinical data such as age, gender, ethnic background, and clinical presentation were retrieved from hospital records, while additional circumstantial information was obtained from police panchnamas. The study focused on both gross and microscopic (histopathological) findings in the collected specimens. During the same study period, a total of 1100 autopsies were conducted at our institution.

Results

During the two-year study period (January 2023–December 2024), a total of 1100 autopsies were conducted, among which 25 cases demonstrated the presence of sickled red blood cells on histopathological examination of various organs. The peak age of mortality was observed in the second and third decades of life, with a mean age of 26 years. The male-to-female ratio was 2:1, which likely reflects a bias in case selection, as all cases were of Medicolegal nature.

Parameter	Findings	Remarks
Total autopsies performed	1,100	
Sickle cell disease–positive cases	25 cases (2.27%)	Diagnosis confirmed by presence of sickled red blood cells on histopathological examination
Age range (years)	11 – 36	Younger age group
Predominant age group	2nd–3rd decades	Majority of cases occurred between 20–30 years
Sex distribution	Male: 16 (64%)Female: 9 (36%)	Male to female ratio = 1.7 : 1
Nature of cases	100% medico legal	Autopsy based study; reflects inherent selection bias

Cause of Death / Clinical Presentation

Cause of Death / Clinical Presentation	Number of Cases (n)	Percentage (%)
Sudden and unexpected death	6	24%
Death associated with fever	4	16%
Gastrointestinal symptoms (acute gastroenteritis, diarrhoea, vomiting)	4	16%
Respiratory symptoms (breathlessness, chest pain, anxiety, respiratory failure)	6	24%
Death during treatment of pre-existing illness	5	20%
Total	25	100%

Diagnostic Category	Cases Number
Sickle cell occlusive crisis with multiorgan dysfunction	23 (90.0%)
SCD with associated pathology (CAD / IHD / Meningoencephalitis)	2(10.0%)

Discussion

Sudden death is defined as an unexpected death occurring in a relatively healthy patient who suddenly dies either at home or in the hospital, with or without vaso-occlusive crises.[14] The diagnosis of multiorgan failure was assigned if two or more vital organs were involved at the time of death. These organs included the lungs and at least one other vital organ such as the brain, kidney, or liver. Thromboembolism did not include stroke but was defined as the finding of thrombi in the lungs at autopsy.[15]

In our study, the most common mode of death is due to sudden death and death due to respiratory failure followed by fever and acute chest syndromes.

According to Kar BC et al too noted attacks of pain, fever, and anaemia [16] were the predominant presenting features. Extensive study by Kate SL et al anaemia, intermittent Jaundice, severe Joint pain, and recurrent infection were the common symptoms.[17]

Sickle cell anaemia is the structural disorder of haemoglobin. Sickle gene frequency is between 5% to 40% distributed in three different geographic zone, mainly in tribal population of central and southern part of India. [18] In our study, male predominance and peak age group of death (21-30 Years) is similar to the mean age of death reported between 32 to 45 years in other study series.[19]

In many cases, precipitated factor for vaso-occlusive crisis is not known and patients are collapsed on duty, or with complain of dyspnoea and chest pain of short duration, which is a sign of vaso-occlusion followed by death. Few cases are brought dead and history was not available. Knowledge of disease was only after autopsy. Second most common cause of death in our study is infection which is comparable to the study by Perronne V et al.[20]The most common route of infection was respiratory tract (13%), followed by gastrointestinal tract (12%) and genitourinary which is similar to various studies. [21]

The clinical course of sickle cell disease (SCD) is characterized by acute painful episodes**,** traditionally referred to as crisis, which form the hallmark of the disease**.** These crises lead to a wide spectrum of clinical manifestations that have been extensively documented in medical literature. The disease usually becomes evident during childhood or adolescence**.** Patients commonly present with haemolytic anaemia**,** jaundice**,** and recurrent vaso-occlusive crises**.** Other frequent complications include hand-foot syndrome**,** acute chest syndrome**,** and splenic sequestration crises**.** Additionally, affected individuals are prone to recurrent infections such as pneumonia**,** osteomyelitis**,** and dactylitis due to impaired splenic function and reduced immunity**.**

Failure of early diagnosis and timely intervention in patients with sickle cell disease (SCD) has contributed to sudden and unexpected deaths in this group. In several instances, the disease was diagnosed only during post-mortem histopathological examination, underscoring the crucial need for early detection in childhood through timely clinical evaluation and family screening. Preventive strategies should include genetic counseling, discouragement of consanguineous marriages, and implementation of premarital screening programs to identify affected individuals and carriers. To reduce mortality, aggressive screening programs should be implemented at all possible levels to identify affected individuals early. Furthermore, education and awareness about precipitating factors such as dehydration, infection, and physical stress must be emphasized, and exposure to such triggers should be avoided whenever possible.

In diagnosed cases, prophylactic and supportive treatments play a vital role in enhancing the quality of

life and preventing complications. Ultimately, the goal should be to reduce preventable deaths and ensure that future generations are safeguarded from the fatal consequences of this inheritable yet manageable disease.

Conclusion-

Sickle Cell Disease (SCD) is the most common hereditary blood disorder causing high morbidity and mortality. This study highlights the role of autopsy in identifying SCD as a cause of sudden unexplained deaths and in improving awareness among physicians and families. Community education and premarital counseling are key to preventing future cases and reducing disease burden.

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Legend Figures

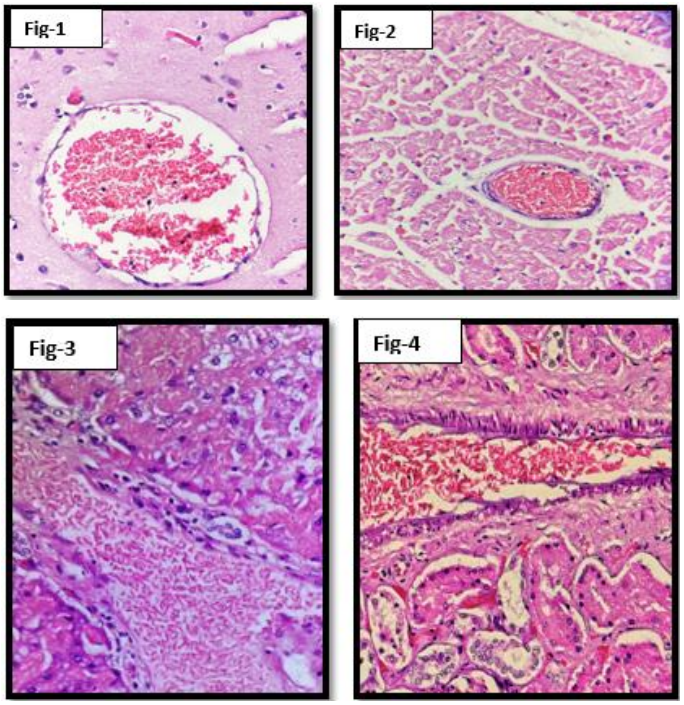

Figure 1 - 4: from brain, heart, liver, kidney shows dilated blood vessels which are packed with sickle cell RBCs.