International Journal of Research in Medical Sciences
Dhawle MS et al. Int J Res Med Sci. 2017 Jul;5(7):3185-3189
www.msjonline.org
pISSN 2320-6071 | eISSN 2320-6012

DOI: http://dx.doi.org/10.18203/2320-6012.ijrms20173010

Original Research Article

Death due to sickle cell anemia: autopsy diagnosis

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Received: 09 May 2017
Accepted: 05 June 2017

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ABSTRACT

Background: Sickle cell disease (SCD) is well known and is the commonest hereditary hematological disorder which is associated with increased mortality and morbidity. They are group of inherited haemoglobinopathies caused by the occurrence of hemoglobin S (Hbs) in homozygous or heterozygous form or in combinations of Hbs with another hemoglobin such as Hbsc or beta thalassaemia (Hbs-thal). Sickle cell syndromes are remarkable for their clinical heterogenecity including their presentations as sudden and unexpected death due to sickle cell crises. While doing autopsy in cases of deaths with no apparent cause and physical over activity medical officer must keep in mind the possibility of death due to vasoocclusive crisis in sickle cell disease. Aim of the study was to create awareness among the physicians and relatives / public and to minimize future unexpected death from complications or crisis from SCD.
Methods: This is a retrospective study of 10 cases carried in the department of pathology, in tertiary care hospital and covers a period from January 2009 to December 2016. These cases were brought dead to the casualty with a history of sudden death. After post mortem examination, the specimens were sent for histopathological examination.
Results: The record of 10 cases was reviewed. Out of our ten cases 7 were male and 3 were females. The youngest person was 17-year female and oldest was 65 years male. In clinical history 3 cases had complains of chest pain (30%), 3 others had complained of breathlessness (30%), 2 had history of unconsciousness (20%), one case had complained of abdominal pain (10%) and one case had a history of fall and injury (10%). Microscopic examination of each organ was carried out. Organs like lungs, liver, spleen, kidneys, heart and brain showed wide spread congested vessels which were stuffed with RBC.
Conclusions: We present this study to emphasize that sickle cell crisis is one of the cause of sudden unexplained death and highlight the importance of considering sickle cell disease as a cause of death in cases with no apparent cause.

Keywords: Autopsy, Sickle cell disease, Sickle cell crises, Vasoocclusive crisis

INTRODUCTION

Haemoglobinopathies are the commonest inherited disorders worldwide and sickle cell disease shows an important proportion of these. Sickle cell anemia was first described by Herrick. Pauling et al, established that sickle cell disease (SCD) results from a defect in the haemoglobin molecule where there is a glutamine to valine substitution at the sixth residue of the beta globin polypeptide.[1] Homozygosity for the sickle mutation (Hbss) is responsible for the most common and most severe variant of SCD.

It is an autosomal recessive, genetically transmitted hemoglobinipathy which is responsible for a considerable amount of morbidity and mortality.[2] Sickle cell disease is the generic term for the group of haemogobinopathies caused by the occurrence of haemoglobin S (Hbs) in the

homozygous form - sickle cell anemia (Hbss) or heterozygous form - sickle cell trait or in combination of Hbs with another abnormal haemoglobin such as Hbsc or beta- thalassaemia (Hbs B thal).

Sickle cell haemoglobinopathy is prevalent in the tropical and subtropical regions of the world and which may affect any organ or system of the human body.[3] It is an irreversible and untreatable health problem which is seen predominantly among various tribes in the world.

In India Hbs was first detected in the vedeloid tribes in the Nilgiri hills of Tamil Nadu and it was later discovered in other tribes of Orissa and Assam, certain tribes of Marathi.[4,5] Its incidence varies from 5 to 34% and it is restricted to the tribal population.[6]

The clinical features show remarkable heterogenecity. Some have repeated episodes of admissions while others are totally asymptomatic. Severity depends on various factors like climate, socioeconomic conditions, hemoglobin level and percentage of Hb F.[7,8]

Sickle cell disease presenting as death in clinically asymptomatic patients is not uncommon. But unfortunately, less numbers of deaths are reported due to sickle cell anemia because of ignorance of autopsy surgeon in considering this disease as a cause of death despite of its high prevalence.

Hence, while doing autopsy in cases with no apparent cause and history of physical over activity, medical officer must keep in mind the possibility of death due to sickle cell anemia.

This study reviews the autopsy findings that are seen in incidentally detected sickle cell anemia cases in terms of showing major morphological changes; importance and frequency of those lesions that possibly lead to death.

This is to evaluate the pathological autopsy findings in our centre and to create awareness among the physicians and relatives / public and to minimize future unexpected death from complications or crisis from SCD.

Keeping this perspective in mind here we report our analysis in terms of pathological changes seen in various organs in 10 cases of sickle cell anemia in whom the diagnosis was not previously known.

METHODS

This is a retrospective study of 10 cases carried in the department of pathology, in tertiary care hospital and covers a period from January 2009 to December 2016. These cases were brought dead to the casualty with a history of sudden death. After post mortem examination, the specimens were sent for histopathological examination. We received gross specimen of lungs, heart, liver, kidney, spleen and brain for histopathological examination in all autopsy cases. The data of clinical history, gross and microscopical examination of all cases were analyzed.

Study is based mainly on

- Histopathological findings
- The data on the case paper provided by autopsy surgeon
- Data obtained from Police Panchnama.

RESULTS

Out of our ten cases 7 were males and 3 were females. The youngest person was 17-year female and oldest was 65 years male.

No previous details regarding haemoglobinopathy were available except in 2 cases. In clinical history 3 cases had complains of chest pain, 3 others had complains of breathlessness, 2 had history of unconsciousness, one case had complain of abdominal pain and one case had a history of fall and injury.

Figure 1: Gross photograph of spleen enlargement and congestion.

Figure 2: Gross photograph of lung pieces-brownish discoloration.

On gross in 4 cases splenomegaly was seen with congestion (Figure 1). One case showed hepatomegaly and one case had cardiomegaly. In one case, lung showed changes of tuberculosis and in other case lung showed changes of CVC and pneumonia; while rest of the cases of lungs showed congestion (Figure 2).

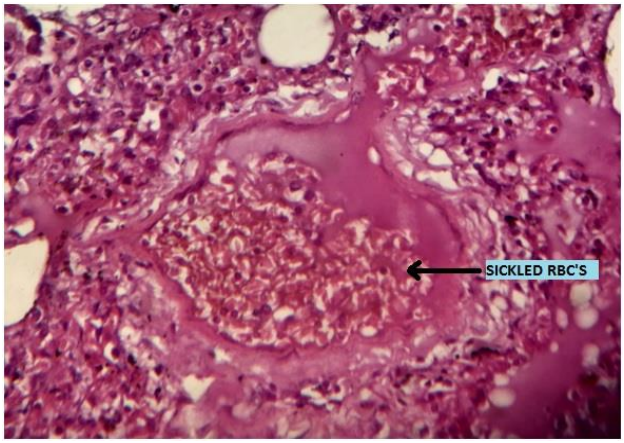

Figure 3: H and E 40X microphotograph of lung congestion with sickled RBCs.

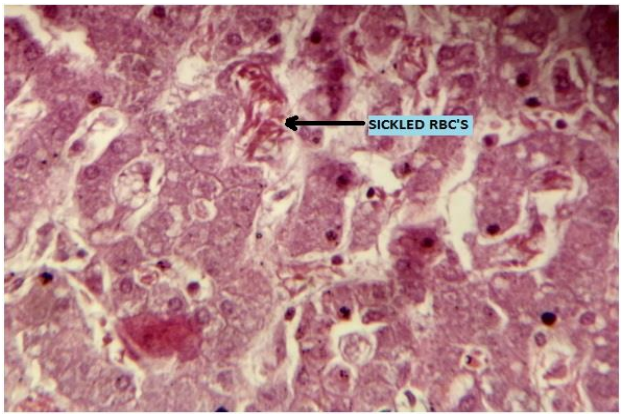

Figure 4: H and E 40X microphotograph of liver sickled RBCs.

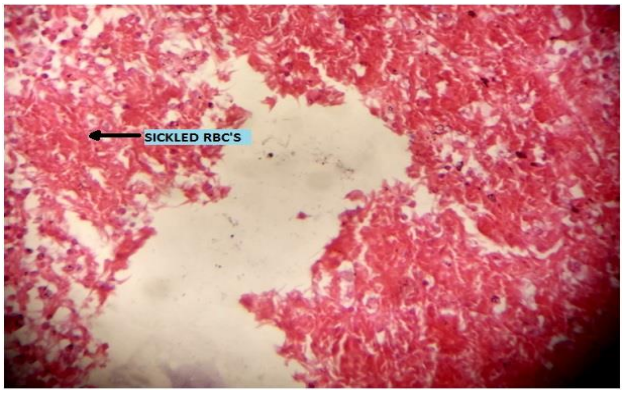

Figure 5: H and E 40X microphotograph of spleen-congested sinusoids and sickled RBCs.

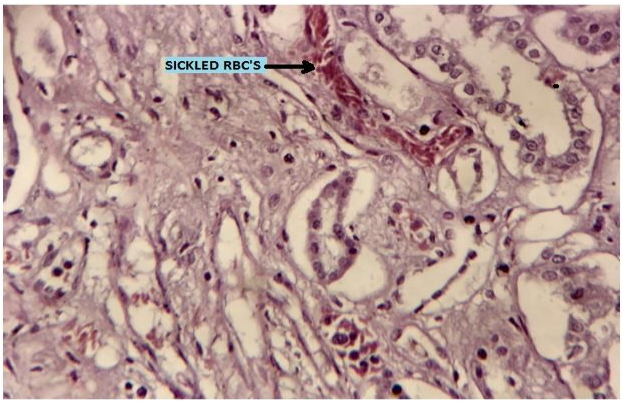

Figure 6: H and E 40X microphotograph of kidney-congested glomeruli with sickled RBCs.

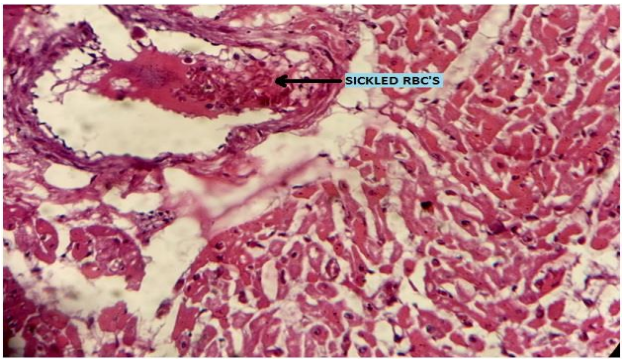

Figure 7: H and E 40X microphotograph of heart myocardial fibers and vessels containing sickled RBCs.

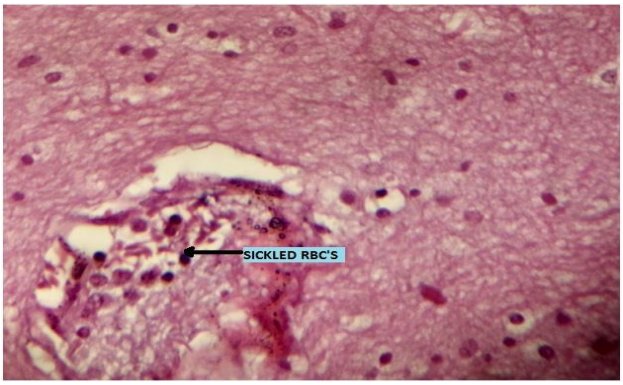

Figure 8: H and E 40X microphotograph of cerebrum-sickled RBCs in the vessels.

Most of the organs like lungs, spleen, liver and kidney showed congestion. Microscopic examination of each organ was carried out. Organs like lungs, liver, spleen, kidneys, heart and brain showed widespread congested vessels which were stuffed with RBC. Figure 3 – 8 show sickled RBC in lungs, liver, spleen, kidney, heart and brain. Table 1 shows the presentations and morphological features of these different cases.

Table 1: Presentations and morphological features of these different cases.

Case no.	Age	Sex	Presentation	H/o haemogobinopathy	Gross examination	Histological examination
1	25	M	Chest pain	Not known	Lungs - firm / brownish	Lungs congested and packed with sickled RBC.
2	21	M	Chest pain	Not known	Splenomegaly spleen - congested	Spleen severely congested and packed with sickled RBC.
3	42	F	Fall and injury	k/c/o sickle cell anemia	Spleen, liver, kidneys congested	Changes of hemosiderosis in liver, spleen and kidney. Packed with sickle RBC.
4	48	M	Chest pain	Not known	Cardiomegaly LVW thickness 2 cm RVW thickness 0.7 cm. Whitish area of 1x1 cm at apex.	Heart, kidney shows sickled RBC.
5	35	M	Abdominal pain	Not known	Liver congested	Liver congested and packed with sickled RBC.
6	28	M	Giddiness followed by unconsciousness	Not known	Spleen and kidneys congested	Spleen, kidney, cerebrum, coronary arteries shows sickled RBC.
7	17	F	Joint pain and breathlessness	k/c/o sickle cell anemia	Lungs - patchy consolidation Spleen / liver enlarged kidney congested	Lungs, liver, kidney, spleen, myocardium and cerebrum shows sickled RBC.
8	29	M	H/o sudden unconsciousness	Not known	Pleural adhesions, both lungs consolidated, splenomegaly, spleen, liver, lungs, kidney congested	Spleen- shows sickled RBC with congestion. Coronary shows sickled RBC. Liver shows fatty change.
9	18	F	Breathlessness	Not known	Lungs - thick plura, firm congested Kidney- congested	Lungs- CVC with pneumonia with sickled RBC. Kidney- show sickled RBC.
10	65	M	Breathlessness	Not known	Spleen - enlarged lungs - firm, small whitish lesion liver - congested.	Liver, Kidney, spleen shows sickled RBC. Lung – Tuberculosis.

DISCUSSION

SCD has an autosomal recessive inheritance. It manifests in 2 forms viz heterozygous (Sickle cell trait) or homozygous (Sickle cell disease). It results from the point mutation where glutamate is replaced by valine at the sixth residue position of the beta globin chain.[9] The clinical course of sickle cell disease is punctuated by acute painful episodes referred to as 'Crisis' which are the hallmark of the disease. These acute events include painful vasoocclusive crises, infarctive stroke, acute chest syndrome, aplastic crisis, hemolytic crisis, splenic sequestration, priapism and infections.[10] The trait patients are mostly asymptomatic and sickle cell crisis can occur in them only if patient is exposed to extreme hypoxic conditions.[10] Vasoocclusive crisis occurs when the micro circulation is obstructed by sickled RBCS. This results ischemia and infarction of the adjacent organs like the

lung, liver, kidney, spleen and cerebrum. Various factors precipitating vasoocclusive crisis are cold weather, infection, dehydration, acidosis, alcohol intoxication, emotional stress, pregnancy etc. In all our cases, the vessels of organs like lungs, liver, spleen, kidney, heart and brain were clogged with sickled RBC.

While acute sequestration crisis is the most common disorder that result in spleen enlargement due to sudden accumulation of large quantities of blood, which leads to severe anemia, shock and death. These findings were seen in four cases. One of our cases showed changes of pneumonia.

There are various studies regarding the cause of death in sickle cell disease. In one study 33% death occurred in relatively healthy patients without chronic organ failure, but died during classical sickle cell crisis and 78% died during acute painful episode or acute chest syndrome.[11]

Platt et al studied 3764 patients of SCD and studied 209 adult patients who died of SCD. Peak incidence of death among children with sickle cell anemia occurred between 1-3 years of age. 18% of death in adults was due to chronic organ failure and 33% of death occurred in relatively healthy patients who died during a sickle cell crisis. 78% died either due to painful episode or acute chest syndrome.[12]

In most of the studies, death in SCD is due to acute chest syndrome, sickle cell crisis, chronic organ damage, painful and splenic sequestration crisis. Sickle cell crisis is the second most common cause of death. Failure of early intervention in patient with SCD contributed to sudden death of this group of patients. This is because the disease was not known until after autopsy.

CONCLUSION

Sickle cell disease is a commonest hereditary disorder which is associated with increased morbidity and mortality. The goal is to create awareness among physicians and relatives on need of autopsy so as to minimize future unexpected deaths. Aggressive screening should be done at all possible levels for sickle cell disease. The education regarding the precipitating factors like dehydration, physical stress is given to the individuals. Our direct aim is to produce new generation with healthy RBC. We present this study to emphasize that sickle cell crisis is one of the cause of sudden unexplained death and highlight the role of autopsy in such cases.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Dhawle MS, Tangde AR, Rathod SG, Bindu RS Death due to sickle cell anemia: autopsy diagnosis. Int J Res Med Sci 2017;5:3185-9.