



# The Royal College of Pathologists

## ***Guidelines on Autopsy Practice***

### **Scenario 2: Autopsy for sickle cell disease and sickle trait**

#### **The role of the autopsy**

- To determine the pathologies that led to death and the contribution of sickle cell diseases – mainly homozygous HbSS and HbSC disease.
- A significant proportion of deaths occurs peri-operatively, and requires careful examination to determine what took place.

#### **Pathologies and causes of death encountered at autopsy**

The main causes of death in HbSS and HbSC sickle disease include:

- acute chest syndrome (ACS)
- pulmonary vascular thrombosis and cor pulmonale
- sudden cardiac failure from fibrosis in adults
- multi-organ failure following sickle pain crisis
- bacterial infections: pneumonia, meningitis, bacteraemia, osteomyelitis
- acute splenic sequestration
- chronic renal failure
- cerebrovascular accident – haemorrhage and infarction
- pregnancy-related – with multi-organ failure and pulmonary disease
- hyperhaemolysis (post-transfusion) syndrome in adults
- aplastic crisis (in children)
- seizures induced by pethidine
- respiratory depression from fentanyl-patches and other opiates.

In patients with HbAS (sickle trait), unexplained death from acute cardio-respiratory arrest is approximately 28 times more frequent than among normal HbAA persons; this usually occurs after severe exertion.

#### **Specific health and safety aspects**

None.

## **Clinical information relevant to the autopsy**

- All the present relevant and past medical history details, particularly the mode of death, recent operation records, drug and pain-relief therapy, current radiology.
- Laboratory results such as blood cultures must be gathered.
- Discussion with the sickle physicians is always helpful to understand the complex pathophysiological processes taking place.

## **The autopsy procedure**

- Standard full autopsy, with careful attention to the coronary, pulmonary and cerebral arteries.
- Include vertebral bone marrow sampling.
- If agreement is obtained (and stress its importance), remove one femur and split it longitudinally; this enables examination of marrow hyperplasia and sampling of old and recent sites of bone infarction. It can be replaced to strut the leg during reconstruction.

## **Recommended blocks for histological examination – best practice**

Histological studies are essential to diagnose and to understand the pathogenesis of sickle-related death. Gross observation and pathological guesswork only will fail to provide the correct cause of death within the sickle cell complex of disorders, will not satisfy the clinicians or help them with clinical governance issues, and will certainly not satisfy the relatives of the deceased. The following represents recommended best practice.

- Heart – if cardiac malfunction is the likely significant event, take at least three blocks of the left ventricle and one of the right ventricle. Ideally, also take the right atrio-ventricular septal block for fixation and serial slicing to examine the AV node and the bundle of His area.
- Lungs: multiple samples (at least one per lobe) to identify the ACS, pneumonia, small pulmonary arterial thrombosis.
- Vertebra; femoral bone and marrow (proximal, mid- and distal).
- Both kidneys.
- Spleen.
- Liver.
- Skeletal muscle (particularly if a crush injury is suspected).
- Any recent operation sites.
- Brain if a stroke was clinically suspected or is pathologically evident.

Fix the samples ideally in buffered formalin, to reduce artefactual post-mortem sickling of red cells.

## **Other samples required**

- Urine, blood, meninges and lung cultures for sepsis.
- Peripheral blood, urine and vitreous humour if opiates were administered during the final medical management. (NB Fentanyl is not detected by routine screening for drugs of abuse; it must be specified.)
- Spun blood for serology, e.g. B19 virus infection; for mast cell tryptase analysis if acute anaphylaxis is suspected.

- Whole blood if the red cell sickle status had not been evaluated pre-autopsy but is suspected clinically or morbid anatomically.

### **The clinicopathological summary**

- Determine whether sickle cell disease is the underlying factor in the cause of death sequence, played a contributory role or was irrelevant to the cause of death.
- Consider whether drug overdose caused fatal respiratory depression or seizures.
- Lay out the pathological sequence logically; the clinicians and relatives are going to study the autopsy report closely.
- Consult a more experienced pathologist to review the case and histology, etc. if the pathology and cause of death are not clear.

### **Specimen cause of death opinions/statements**

- 1a. Acute cardio-respiratory failure
- 1b. Acute chest syndrome following painful crisis
- 1c. Sickle cell disease
  
- 1a. Anaemia
- 1b. Hyperhaemolysis syndrome
- 1c. Sickle cell disease
  
- 1a. Septicaemia
- 1b. Cholecystitis (laparoscopic cholecystectomy on xx/xx/xx [insert date])
- 1c. Sickle cell disease
  
- 1a. Acute cardio-respiratory failure
- 1b. Exertion and sickle cell trait (HbAS)

### **References**

1. Kark JA, Posey DM, Schumacher HR, Riehle CJ *et al.* Sickle cell trait as a risk factor for sudden death in physical training. *NEJM* 1987, 317:781–787.
2. Okpala I (editor). *Practical Management of Haemoglobinopathies*. Blackwell Publishing, 2004 (includes chapter by Lucas SB. ‘The morbid anatomy of sickle cell disease and sickle cell trait’).
3. Manci EA, Culberson DE, Yang YM, Gardner TM, Powell R, Haynes J Jr *et al.* Causes of death in sickle cell disease: an autopsy study. *Br J Haematol* 2003,123:359–365.
4. Stuart MJ, Nagel RL. Sickle cell disease (seminar). *Lancet* 2004,364:1343–1360.

### **The RCPATH Working Party on the Autopsy**

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