



The Royal College of Pathologists

Guidelines on Autopsy Practice

Scenario 6: Deaths associated with epilepsy

The role of the autopsy

- To establish that epilepsy has caused or contributed to:
 - death as a result of status epilepticus
 - death as a result of an accident during a seizure
 - death as a result of aspiration during a seizure
 - death as a result of epilepsy treatment
 - sudden and unexpected death associated with epilepsy (SUDEP – see definition below).
- To exclude other causes of death which might mimic SUDEP, e.g. sudden cardiac death.
- To identify the cause of the epilepsy if present, e.g. neuropathological lesion, acute intoxication.
- To provide accurate data for the inquiries into the incidence of and remedial factors around epilepsy-associated deaths.

Pathology encountered at the autopsy

- External evidence of a seizure, e.g. incontinence, tongue-biting.
- Injuries, bruises, burns, etc.
- Brain swelling, focal brain abnormalities, e.g. tumours or contusions.
- Cardiomegaly or other cardiac abnormalities that might be associated with sudden death.

- Pulmonary oedema, aspirated gastric contents.

Specific health and safety aspects

None, unless epilepsy complicates HIV or HCV infections.

Clinical information relevant to the autopsy

- Details of type, duration and frequency of seizures and any recent deterioration in seizure control.
- Details of antiepileptic drug regimes and compliance.
- Cause of epilepsy and MRI/EEG data to target brain tissue sampling.
- Details of circumstances surrounding death – police photographs, evidence of incontinence/vomiting, position of body, circumstances that might have caused injury, number of tablets in bottles and dates of prescribing/doses, eye-witness accounts.
- Any other relevant medical information, especially history of cardiac disease, abnormal ECGs, history of diabetes, proneness to vasovagal attacks, history of alcoholism, learning difficulties, etc.

The autopsy procedure

1. Documentation of external injuries, evidence of incontinence and tongue-biting, petechial haemorrhages in skin/conjunctiva to suggest asphyxia, evidence of disorders, e.g. neuro-fibromatosis, Sturge-Weber syndrome or tuberous sclerosis, which may be complicated by epilepsy.
2. Full autopsy.
3. Sampling for toxicology and biochemistry (see below).

Specific significant organ systems

- Brain: swelling, contusions, developmental abnormalities, tumours, etc. as causes of epilepsy; evidence of mesial temporal (Ammon's horn) sclerosis and cerebellar atrophy as consequences of epilepsy and its treatment.

- Heart: cardiomegaly, evidence of coronary artery disease or other cardiac causes of sudden death.
- Lungs: evidence of pulmonary oedema and/or aspiration.
- Bladder: if empty, may suggest a seizure.

Organ retention and brain histopathology

It is not possible or necessary for specialist neuropathologists to perform all the authorized autopsies on patients with epilepsy, but it is best practice for a specialist to be involved in the interpretation of the neuropathology.

- The case should be made for whole brain retention and fixation for 2–3 weeks, and referral to a neuropathology centre.
- If that is not permitted, the next best process is to fix brain coronal slices for several days, accurately document the gross appearances of the brain (ideally with photography) and then sample for histopathology. The slices may be referred to the neuropathology centre.
- If even that is not permitted, it is essential that smaller samples be selected, fixed and trimmed for histopathology, and a neuropathologist can provide an evaluation.

In pressing the case for whole brain retention, the importance of such optimal examination in SUDEP cases (see below) must be emphasised.

The scheme for brain slice sampling and small sample selection is presented in Love (2001, 2004).

In summary:

- Brain coronal slices, 1.5 cm thick:
 - a) just in front of the midbrain
 - b) just behind the midbrain. These will include the cerebral samples indicated below.
- Brain sites for histology sampling:
 - a) cingulate gyrus
 - b) hippocampus and parahippocampal gyrus R+L
 - c) middle frontal gyrus

- d) superior and middle temporal gyri
- e) caudate nucleus
- f) putamen and globus pallidus
- g) cerebellar vermis
- h) cerebellar hemisphere including dentate nucleus
- i) any macroscopic abnormality.

Recommended other blocks for histological examination – best practice

- Heart: 3 LV and 1 RV blocks to exclude ischaemic damage or myocarditis.
- Lung: confirm/exclude oedema/aspiration.
- Any other macroscopically-abnormal organs.

Other samples required – best practice

- Blood, urine and gastric contents for anti-epileptic drug, drugs of abuse and alcohol estimations.
- Vitreous humour for biochemistry, if history of diabetes or other metabolic disorder.
- Hair for anti-epileptic drug analysis to assess compliance if indicated, e.g. allegations of medical negligence or of possible homicide by inappropriate drug administration.
- Store fresh frozen brain tissue for biochemistry, to be performed later if brain histology suggests inherited metabolic disorder.

The clinicopathological summary

1. Documentation of all morbid anatomical, histological and toxicological findings.
2. Description of how epilepsy has caused or contributed to death, and the aetiology of the epilepsy, if ascertained.

Specimen cause of death opinions/statements

- 1a. Sudden and unexpected death in epilepsy (SUDEP)

(SUDEP is defined as "sudden, unexpected, unwitnessed or witnessed, non-traumatic and non-drowning deaths in patients with epilepsy, with or without evidence for a seizure, and excluding documented status epilepticus, where necropsy examination does not reveal a toxicological or anatomical cause of death.")

- 1a. Drowning
- 1b. Idiopathic primary generalised epilepsy
2. Hypertensive cardiomegaly

- 1a. Diffuse hypoxic brain damage
- 1b. Status epilepticus
- 1c. Left frontal astrocytoma.

References

1. Black M, Graham DI. Sudden death in epilepsy. *Current Diagnostic Pathology* 2002;8: 365–372.
2. Nashef L, Brown S. Epilepsy and sudden death. *Lancet* 1996;348:1324–1325.
3. Love S (editor). *Current Topics in Pathology. Volume 95: Neuropathology. A guide for practising pathologists*. Berlin: Springer-Verlag, 2001. Appendix, pp. 267–271.
4. Love S. Review. Post-mortem sampling of the brain and other tissues in neurodegenerative disease. *Histopathology* 2004;44:309-317. (Standard sampling scheme is presented with illustrations.)

The RCPATH Working Party on the Autopsy

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