

## CASE REPORT

### Autopsy findings of SUDEP in adolescence

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#### Abstract

Sudden unexpected death in epilepsy (SUDEP) is a rare in children; the risk of SUDEP in children is up to 10-fold less than adults. Herein, we report a case of SUDEP in a 14-year-old boy. The post-mortem findings in neuropathological examination in SUDEP are not pathognomonic. Tongue and lip bites marks are only an indication of a seizure before death. Basically, there are no lesions that could explain the incidence of seizures before death. However, post-mortem examination is mandatory in order to determine the diagnosis of SUDEP. Autopsy, histopathological, and toxicologic examinations and a proper medical history of epilepsy are required to come to diagnosis of SUDEP. This case report further demonstrates the importance of medicolegal autopsy in allegedly dead victims.

**Keywords:** Adolescence, autopsy finding, neuropathological, seizure, sudden unexpected death in epilepsy (SUDEP)

#### INTRODUCTION

The risk of death for a person with epilepsy is increased compared with the risk in the general population. The overall risk of SUDEP is more than 20 times higher in an individual with epilepsy than the general population. Sudden unexpected death in epilepsy (SUDEP) is more common in hospital-based studies. The frequency of sudden death in epilepsy depends on the severity of epilepsy.<sup>1-3</sup>

There are relatively less number of studies on SUDEP in children and adolescents. SUDEP rarely occurs in children; the risk of SUDEP in children is approximately ten times less frequent than adults.<sup>4,5</sup> The incidence of SUDEP in children varies from 0.2 to 0.7 per 1000 person-years.<sup>6-8</sup> The risk of SUDEP was 7% in a study in Finland<sup>9</sup> and 12% in a study in the USA<sup>10</sup> in all epilepsy-related deaths in children. In individuals with normal neurological appearance, the risk of SUDEP increases in adolescence. Children whose epilepsy are not in control are at a high-risk group for the occurrence of SUDEP.<sup>6,7,9,11</sup>

There were no reported cases of SUDEP in Indonesia, after an electronic search for the terminology “SUDEP,” “sudden unexpected death in epilepsy patients,” “paediatric SUDEP,” “sudden unexpected death in epilepsy patients

and children,” or “death-related epilepsy” in the medical literature. Herein, we described the first report of autopsy findings of SUDEP in adolescence in Indonesia.

#### CASE REPORT

A 14-year-old boy’s corpse was sent by police investigators to the Forensic Medicine and Medicolegal Studies Department for medicolegal autopsy examination. An autopsy was conducted to determine the cause of death because the victim allegedly died upon being beaten by his friend in a fight. However, the fight never happened. Several witnesses reported that the victim experienced a generalised seizure (less than 5 minutes) before dead. All these incidents occurred at the victim’s school. Post-mortem examination was performed at 10 hours after death.

##### *External examination*

A pale palpebral conjunctival membrane was found. On the right inner lip mucosa there were three contusions, which were fresh tooth marks (Fig. 1A). No injuries were found on other body parts.

##### *Internal examination*

The heart showed no remarkable change and

weighed 200 grams. The lungs were blackish red in colour and collapsed. The weight of the right and left lungs was 450 grams and 350 grams, respectively. The liver was reddish purple in color, smooth, glistening surface, showed no remarkable change, and weighed 1500 grams. The kidneys were reddish brown with the weight of the right and left kidneys being 150 grams and 100 grams, respectively. The brain weighed 1400 grams and presented moderate congestion. Venous congestion on the surface of the brain was observed. No injury was found (Fig. 1B).

#### *Histopathological findings*

Brain tissue showed stromal oedema and dilation of the blood vessels. The obtained pale regions of the cerebral area revealed an infarction (global cerebral oedema and infarction) (Fig. 2A and B). Furthermore, pulmonary, heart, venous liver, and venous renal congestion were found (Fig. 2C-F). There were no signs of infection or malignancy in the internal organs.

#### *Toxicological findings*

There was no poison found in the blood, stomach content, urine, brain or liver.

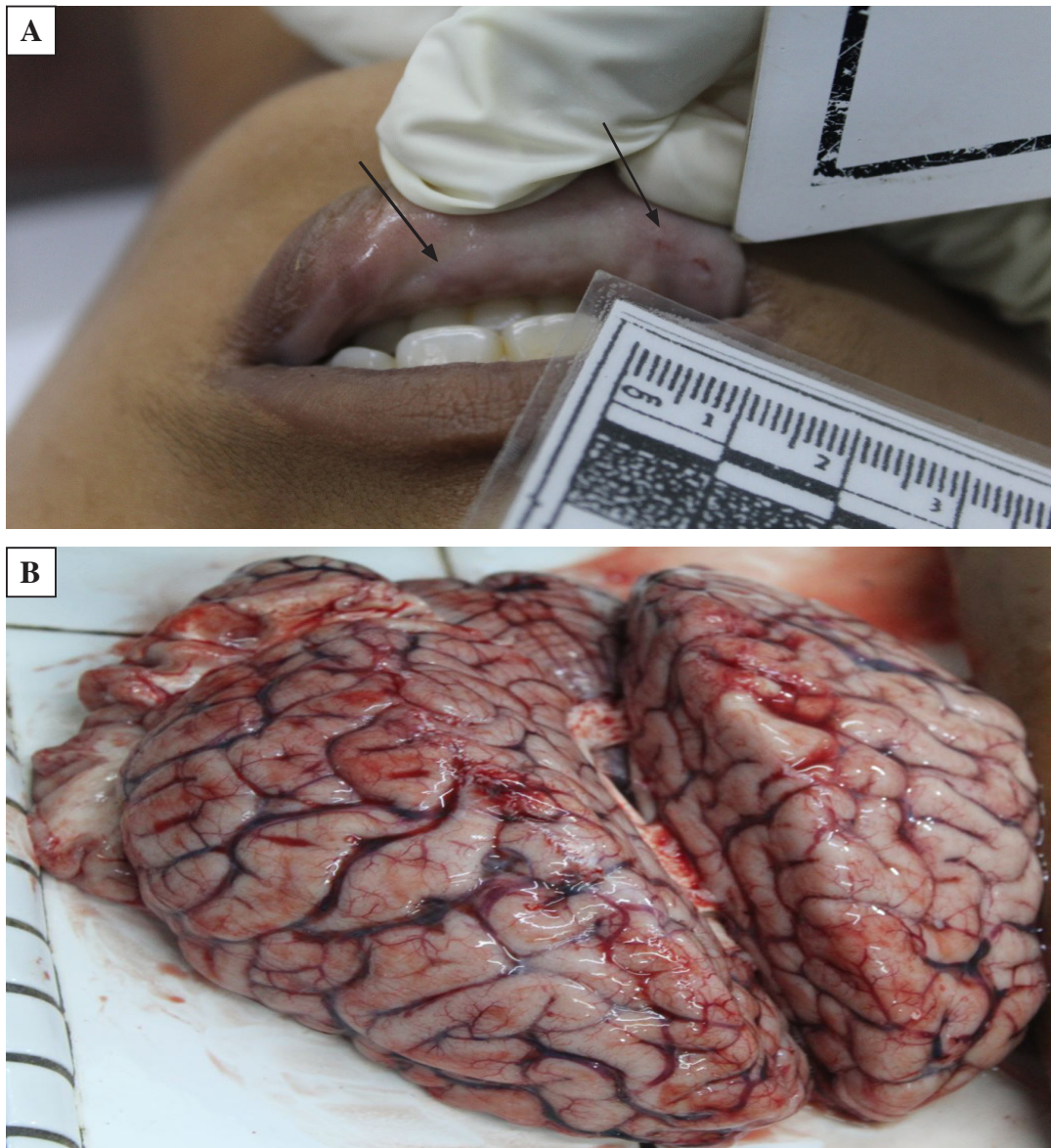


FIG. 1: Macroscopic post-mortem findings. A: Contusions on inner lip mucosa. B: Venous congestion on the surface of the brain, soft, friable and fragile.

*Additional information*

We received information that victim often experienced seizures in school. The last convulsion before the victim died was three months ago. The victim was an orphan, so information was obtained from a relative. His relative confirmed that the victim suffered from

epilepsy since childhood: previously treated, but not completely. The victim had not been taking antiepileptic medication for the last 5 years.

**DISCUSSION**

SUDEP has been defined as a “sudden,

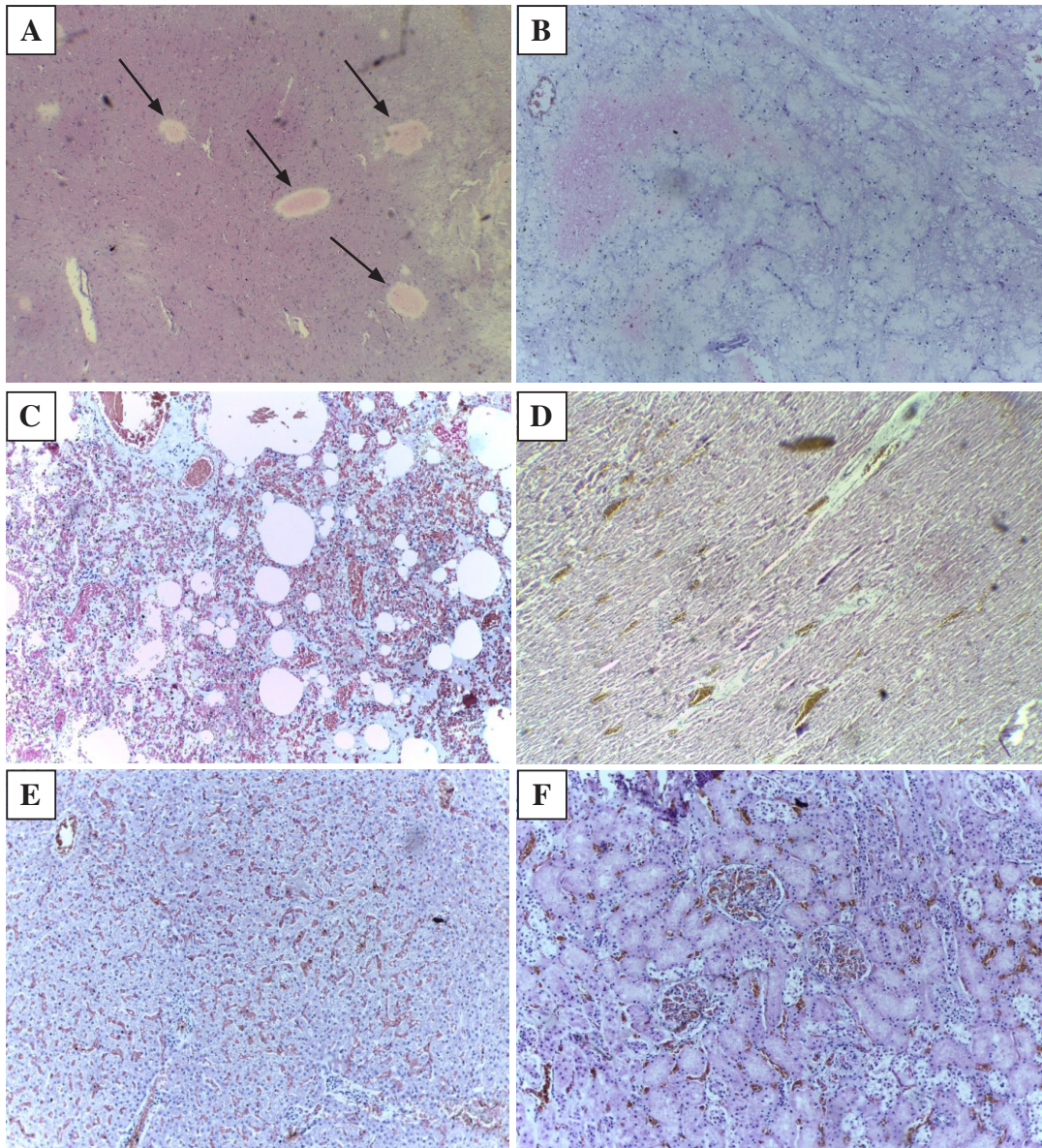


FIG. 2: Histopathologic findings (H&E stains). A: Multiple cerebral infarct (x40 magnification); B: Cerebral tissue with stromal oedema and dilation of blood vessels. Obtained parts of impression area infarct (x100 magnification); C: The blood vessels in the lung were generally widened with extravasated erythrocytes. The stroma is oedematous with presence of macrophages containing pigment and a few inflammatory cells. (x100 magnification); D: Myocardial tissue is arranged elongated, including blood vessels widened contained erythrocytes (x100 magnification); E: Vascular liver congestion (x100 magnification); F: Renal tissue with dilated blood vessels containing erythrocytes (x100 magnification).

unexpected, witnessed or unwitnessed, non-traumatic and non-drowning death in patients with epilepsy with or without evidence of a seizure and excluding documented status epilepticus, in which post-mortem examination does not reveal a toxicologic or anatomic cause of death.”<sup>12</sup> Definite SUDEP can only be established with post-mortem examination. The definite diagnosis of SUDEP can be said to be a diagnosis established as *per exclusion*. In addition to the victim having a medical history of epilepsy, post-mortem findings should also rule out that the death was due to trauma, asphyxia due to aspiration or status epilepticus, drowning, or other obvious medical cause of death. Deaths due to SUDEP must also meet the criteria that the deaths occur suddenly and unexpectedly while in a reasonable state of health and during normal activities (e.g., at school, at home, in or around bed) in benign circumstances.<sup>5,13,14</sup>

After we performed the autopsy and the histopathological and toxicological examinations, we still could not determine the cause of death. No signs of injury were present except contusions on the lip, and the findings of autopsy and histopathological and toxicological examinations were not sufficient to diagnose the cause of death; thus, we considered performing verbal autopsy. The victim's history of epilepsy is the most important key to establish SUDEP as a diagnosis in this case.

Post-mortem examinations are mandatory in determining the diagnosis of SUDEP. The pathologic autopsy findings that are significant and more frequent in SUDEP can be observed in the brain, lungs, heart, and liver of patients with SUDEP.<sup>15-19</sup>

In SUDEP case, majority of victims had significant pathologic findings in brain (84%).<sup>19</sup> These neuropathological findings are in the form of cerebral oedema and infarction as well as signs of hypoxia in the hippocampal area in few of cases.<sup>15,16,19</sup> Similar pathological findings were also found in our case.

The findings in lungs, heart, and liver in SUDEP reported in the literature were congestion with slight increased in the weight of each organs.<sup>5,13,17-19</sup>

External examination of the victim revealed three contusions on the lip; these findings are in line with a study by Shield *et al*<sup>16</sup>, who reported 44%, and Clark *et al*<sup>8</sup>, who reported 60% of SUDEP cases can be determined by the presence of tongue/lip contusions. This finding is usually found in SUDEP cases preceded by seizures.

Possible SUDEP mechanisms have been proposed, generalised tonic-clonic seizure (GTCS), prone position, seizure-induced respiratory dysfunction and seizure related cardiac arrhythmia. Before terminal apnea causing cardiac arrest, changes in early post-ictal, alteration of respiratory and cardiac function induced by central due to GTCS, which will result in the death of the patient. Seizures that occur in prone position until death may promote hypoxia. However, the findings of pulmonary oedema on post-mortem examination were not significant enough to cause death. Some studies reported cardiac pacemakers are needed in many patients, indicating that there is a relationship between seizures and cardiac arrhythmias.<sup>18,20-22</sup>

The risk factors for SUDEP are early onset of seizures, generalised tonic-clonic (GTC) seizures, tonic-clonic seizures 3 months prior to death and lack of treatment with medication. The onset of seizures (<12 years) is significant to the increased risk of SUDEP. SUDEPs are also associated with GTC seizures around the time of death; In three-quarters of cases, GTC seizure had occurred near the time of the SUDEP. People with 3 or more GTC seizures per year have a 15-fold increased risk of SUDEP. Study in China<sup>22</sup> reported patients who died from SUDEP had more frequent tonic-clonic seizures 3 months before their deaths. The frequency of occurrence of seizure is one risk of SUDEP, therefore patients with epilepsy need to be treated with anticonvulsant medications.<sup>8,23,24</sup>

In conclusion, autopsy, histopathological and toxicological examinations, and a good medical history of epilepsy are required to come to a diagnosis of SUDEP. This case report demonstrates the importance of medicolegal autopsy in victims with history of seizure.

*Conflicts of interest:* The authors affirm no conflict of interest in this study.

*Consent:* Consent from relative was obtained for using the photograph of victim.

## REFERENCES

1. Lhatoo SD, Sander JWAS. Cause-specific mortality in epilepsy. *Epilepsia*. 2005; 46(Suppl.11): 36–9.
2. Callenbach PMC, Westendorp RGJ, Geerts AT, *et al*. Mortality risk in children with epilepsy: The Dutch study of epilepsy in childhood. *Pediatrics*. 2001; 107: 1259–63.
3. Zhuo L, Zhang Y, Zielke HR, *et al*. Sudden unexpected death in epilepsy: Evaluation of forensic autopsy cases. *Forensic Sci Int*. 2012; 223: 171–5.

4. Nickels KC, Grossardt BR, Wirrell EC. Epilepsy-related mortality is low in children: A 30-year population-based study in Olmsted County, MN. *Epilepsia*. 2012; 53(12): 2164–71.
5. Morse AM, Kothare SV. Pediatric sudden unexpected death in epilepsy. *Pediatr Neurol*. 2016; 57: 7–16.
6. Sillanpää M, Shinnar S. Long-Term Mortality in Childhood-Onset Epilepsy. *N Engl J Med*. 2010; 363: 2522–9.
7. Berg AT, Nickels K, Wirrell EC, *et al*. Mortality risks in new-onset childhood epilepsy. *Pediatrics*. 2013; 132(1): 124–31.
8. Clark D, Riney K. A population-based post mortem study of sudden unexpected death in epilepsy. *J Clin Neurosci*. 2016; 23: 58–62.
9. Sillanpää M, Shinnar S. SUDEP and other causes of mortality in childhood-onset epilepsy. *Epilepsy Behav*. 2013; 28(2): 249–55.
10. Moseley BD, Wirrell EC, Wong-Kisiel LC, Nickels K. Early onset epilepsy is associated with increased mortality: A population-based study. *Epilepsy Res*. 2013; 105(3): 410–4.
11. Shorvon S, Tomson T. Sudden unexpected death in epilepsy. *Lancet*. 2011; 378(9808): 2028–38.
12. Nazhef L. Sudden unexpected death in epilepsy: terminology and definitions. *Epilepsia*. 1997; 38(Suppl.11): S6–8.
13. Leestma JE, Annegers JF, Brodie MJ, *et al*. Sudden unexplained death in epilepsy: Observations from a large clinical development program. *Epilepsia*. 1997; 38(1): 47–55.
14. Johnston A, Smith P. Sudden unexpected death in epilepsy. *Expert Rev Neurother*. 2007; 7(12): 1751–61.
15. Thorn M. Neuropathologic findings in postmortem studies of sudden death in epilepsy. *Epilepsia*. 1997; 38(Suppl.11): S32–4.
16. Shields LBE, Hunsaker DM, Hunsaker JC, Parker JC. Sudden unexpected death in epilepsy: neuropathologic findings. *Am J Forensic Med Pathol*. 2002; 23(4): 307–14.
17. Thom M, Michalak Z, Wright G, *et al*. Audit of practice in sudden unexpected death in epilepsy (SUDEP) post mortems and neuropathological findings. *Neuropathol Appl Neurobiol*. 2016; 42(5): 463–76.
18. Nascimento FA, Tseng ZH, Palmiere C, *et al*. Pulmonary and cardiac pathology in sudden unexpected death in epilepsy (SUDEP). *Epilepsy Behav*. 2017; 73: 119–25.
19. Nouri S, Balish M. Sudden unexpected death in epilepsy. *Medscape* [internet] 2015 Dec 3 [cited 2017 Oct]. Available from: <https://emedicine.medscape.com/article/1187111-overview#a2>
20. Ryvlin P, Nashef L, Lhatoo SD, *et al*. Incidence and mechanisms of cardiorespiratory arrests in epilepsy monitoring units (MORTEMUS): A retrospective study. *Lancet Neurol*. 2013; 12(10): 966–77.
21. Jones LA, Thomas RH. Sudden death in epilepsy: Insights from the last 25 years. *Seizure*. 2017; 44: 232–6.
22. Chen D, Si Y, He J, Deng Y, Chen T, He Y jin, *et al*. Terminal seizure frequency and its relation to SUDEP. *Epilepsy Behav*. 2017; 70: 173–6.
23. Hughes JR. A review of sudden unexpected death in epilepsy: Prediction of patients at risk. *Epilepsy Behav*. 2009; 14(2): 280–7.
24. Beghi E, Giussani G, Sander JW, Neurologiche M, Neuroscienze D, Istituto I. The natural history and prognosis of epilepsy. *Epileptic Disord* 2015; 17 (3): 243–53.