博士学位論文

錐体部出血：その特異性と病態機序について

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Doctoral　Dissertation

Petrous bone hemorrhage: Specificity and pathogenesis

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Abstract

Whether or not temporal petrous bone hemorrhage is drowning/asphyxia specific or not has been controversial. This issue was investigated by analyzing 151 judicial autopsy cases using semi-3-dimensional microscopic observations of the bones. This systematic evaluation revealed the hemorrhages in all 151 cases, not only of the drowning/asphyxia group, but also of the others. Therefore, it was concluded that the hemorrhage was non-specific. Venous congestion was also one of the most consistent features of the bones. During agonal periods, hypoxia seemed unavoidable. The "hypoxic pulmonary vasoconstriction" increases the central venous pressure. Even in the agonal periods, arterial blood flow to the brain is relatively maintained by cerebral autoregulation. In addition, the small petrous veins do not have sufficient supporting structures. These mechanisms might contribute to the pathogenesis of perimortal petrous bone hemorrhage. There is no single sign which proves drowning/asphyxia as the cause of death. The judgment about the cause should be based on the overall assessment.

Key words : Petrous bone, hemorrhage, drowning, asphyxia, congestion, pathology

Introduction

In 1963, the first report was published concerning the hemorrhagic changes in the petrous part of the temporal bone (petrous bone hemorrhage) in cases of drowning by Niles NR1. Thereafter, several authors reviewed the hemorrhage. Some concluded that petrous bone hemorrhage was specific to drowning and/or asphyxia[1-4]. However, others considered that the hemorrhage was non-specific[5, 6]. The pathognomonics of it are still unclear. The barotrauma hypothesis had been favored to the pathogenesis of petrous bone hemorrhage in drowning[7]. However, if the hemorrhage is non-specific, other mechanism (s) should be discussed. The author investigated these points by analyzing 151 judicial autopsy cases, using not only macroscopic inspections, but also semi-3-dimensional microscopic observations of petrous bones in all cases.

Materials and Methods

Materials

From September 15th, 2010 to July 31st, 2011, 209 serial judicial autopsies were performed in the Department of Legal Medicine, Kinki University Faculty of Medicine. The cases in which erythrocytes could not be evaluated histologically because of postmortem decomposition were excluded, and the remaining 151 cases were chosen as the subjects. They consisted of 91 males and 60 female, with ages ranging from a 35-week fetus to 95 years old, (average, 55.3 years old). The time from presumption-of-death to dissection was about 9 hours to about a month (average 70.1 hours). The immersed victims, in which the other causes than drowning were excluded, were judged as drowning. The deaths caused by the compression or obstruction of the air ways, by the compression of neck or chest, or by the awkward positioning of the body were diagnosed as asphyxia. In this study, chemical asphyxia, like as CO poisoning, was classified in burn or poisoning. The cases, in which the causes of death other than drowning or asphyxia were specified, were classified as non-drowning and non-asphyxia. The causes of death are shown in Table 1. Twenty-three cases of drowning and 14 cases of asphyxia were made into the drowning/asphyxia group, and the other 114 cases made up the control group.

Methods

Macroscopic inspection of petrous bone

After the removal of brains, the basal skull dura maters were exfoliated, and the external laminae of petrous bone were exposed. The hemorrhagic changes were inspected macroscopically from the surfaces of the laminae. The macroscopic judgment criteria which are original in this study, are shown in Table 2. It was difficult to distinguish mild hemorrhage from the congestion or postmortem hemoglobin leakage. Therefore, definite macroscopic petrous bone hemorrhage was defined expediently as more than "intermediate-grade" hemorrhage in the criteria.

Table 1　The causes of death

Extrinsic		Intrinsic	
Injury	44	Pneumonia	9
Drowning	23	Heart disease	6
Burn	22	Pulmonary thromboembolism	5
Asphyxia	14	Sepsis	4
Intoxication	8	Systemic inflammatory response syndrome	4
Hypothermia	2	Cerebrovascular disease	3
Starvation	1	Gastrointestinal bleeding	2
Total　(cases)	114	Meningitis	1
		Others	3
		Total　(cases)	37

Table 2　The judgment criteria for the macroscopic grading of hemorrhage

Grading	Judgment criteria
High-grade	Definite hemorrhage in a large area
Intermediate-grade	Definite hemorrhage but not in a large area
Low-grade	No hemorrhage or possible hemorrhage

Procedures for microscopic specimens of petrous bone

The bilateral petrous bones were excised en bloc. They were fixed in 10% folmaldehyde for a week, and were decalcified by Osteomol (JEM-1200EX II, JEOL, Tokyo, Japan) for 11 days. Then, they were trimmed using the semi-3-dimensional method, as follows. Firstly, they were cut perpendicularly to body axes through the planes containing the internal and external acoustic meatus. From the perpendicular planes, namely, the horizontal planes, the parts containing the inner ear, middle ear and external meatus were trimmed for the specimens. Secondly, the remaining petrous bones were cut in parallel to body axes, namely, vertically. The vertical slices were also trimmed for the microscope (Figure1). They were embedded in paraffin, sectioned and stained by hematoxylin-eosin (HE) for the general observasions, elastica van Gieson (EVG), and silver impregnation methods to evaluate the vascular system. In some cases, the materials were decalcified by Osteosoft (HC946396, Merck, Tokyo, Japan) for about 3 months. After postfixation by 1% osmium tetraoxide, they were embedded in EPON. The ultrathin sections were stained by uranium acetate for the electron microscopic studies. The other organs were also trimmed and processed for light microscopic observation with special attensions to evaluate the vasculature and the degrees of congestion.
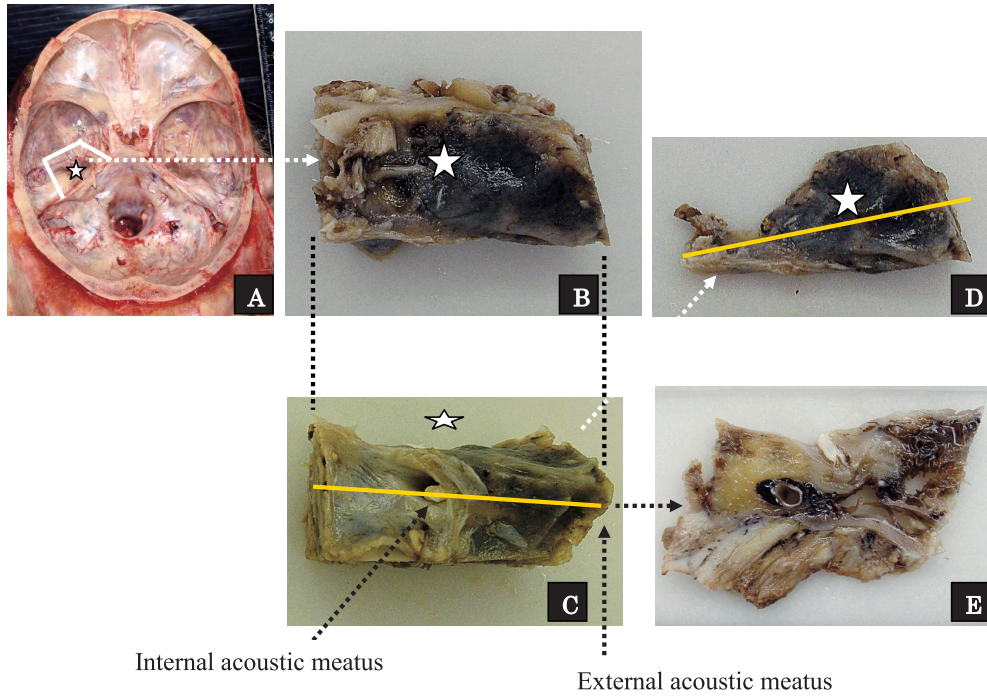
Internal acoustic meatus

External acoustic meatus

Fig. 1　Procedures of semi-3-dimmensional trimming of petrous bone
A, B；The petrous bone（star）was excised en bloc. C；it was cut perpendicularly to body axis through the plane containing the internal and external acoustic meatus. D；the upper half of the petrous bone was cut in parallel to body axis, namely, vertically. The vertical slice was trimmed for the microscope. E；From the perpendicular plane, namely, the horizontal plane, the part containing the inner ear, middle ear, and external meatus was also trimmed for the specimens.

Methods of histological evaluation

Evaluation of hemorrhage

　To exclude the artificial erythrocytic extravascular displacement due to pathological procedures, the hemorrhages were diagnosed only when more than 100 erythrocytes were observed at the extravasucular spaces, and, in addition, the erythrocytes were observed in the same microscopic visual dimensions with the background tissues.

　The microscopic judgment criteria, which are also original, are shown in Table 3.

Table 3　The judgment criteria for the microscopic grading of hemorrhage

Grading	Judgment criteria
High-grade	Hemorrhage, easily identified under the visual field of x1 object lens
Intermediate-grade	Hemorrhage, identified under the visual field of x2 object lens
Low-grade	Hemorrhage, identified under the visual field of x4 or more object lens

Histological observation of vasculature

The vasculatures of the petrous bones, maxillary sinuses, and subcutaneous tissues of the forearms were compared histologically with a special attention to the vascular wall structures and the surrounding supporting tissues. Ultrathin sections were observed using a transmission electron microscope（Nihon Densi, S1000, Tokyo, Japan）, concerning the supporting structures just beneath the endothelial basement membrane.

Evaluation of degree of congestion

The degree of congestion was also investigated in the various organs and tissues, using HE sections.

Results

Macroscopic inspection of petrous bone hemorrhage

The results are shown in Table 4. Macroscopically definite hemorrhage was observed in 67.6% of the drowning/asphyxia group, and in 64.9% of the control group. There were no significant differences between them.

Table 4　The macroscopic grading of petrous bone hemorrhage in the drowning/asphyxia and control groups

	Drowning/asphyxia group	Control group
High-grade	12 cases (32.4%)	38 cases (33.3%)
Intermediate-grade	13 cases (35.1%)	36 cases (31.6%)
Low-grade	12 cases (32.4%)	40 cases (35.1%)
Total	37 cases	114 cases

Microscopic observation of petrous bone hemorrhage

The results are shown in Table 5. Microscopically, the hemorrhage was confirmed in all cases bilaterally. There were no significant differences in the frequency, location and grading between the 2 groups. In total, the frequency of hemorrhage was highest at the bone marrow, followed by mastoid air cells and middle ear. The frequency was relatively low at the external ear and inner ear. The total frequency according to the location is shown in Table 6.

Table 5　The microscopic grading of petrous bone hemorrhage in the drowning/asphyxia and control groups

	Drowning/asphyxia group	Control group
High-grade	13 cases (35.1%)	43 cases (37.7%)
Intermediate-grade	11 cases (29.7%)	37 cases (32.5%)
Low-grade	13 cases (35.1%)	34 cases (29.8%)
Total	37 cases	114 cases

Table 6　The frequency according to the location of microscopic petrous bone hemorrhage

Bone marrow	Mastoid air cell	Middle ear	External ear	Inner ear
100%	92.6%	68.2%	8.1%	8.0%

Correlativity of macro- and microscopic petrous bone hemorrhage

　Although, a certain amount of correlativity could be accepted, there were many disagreements. One of the causes of the disagreement seemed the thickness of the external lamina. Namely, it seemed more difficult to detect the hemorrhage macroscopically in case with the thicker external lamina. In macroscopically low-grade/microscopically high-grade group, the thickness of the external lamina was 0.48 ± 0.32 mm, and in macroscopically high-grade/microscopically low-grade group, it was 0.12 ± 0.13 mm. In addition, it seemed also more difficult to recognize the hemorrhage macroscopically in cases with the deeper situated bleedings. The correlativity is shown in Table 7. Typical cases are shown in Figure 2.
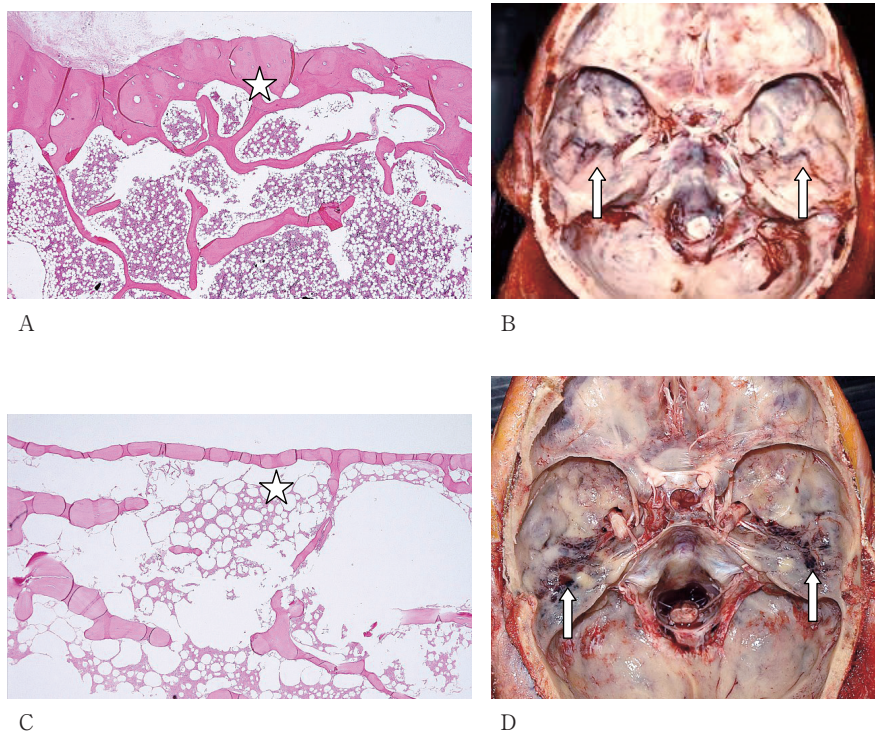
Other histological findings

Fig. 2　Correlativity of macro- and microscopic petrous bone hemorrhage
　　A：Petrous bone hemorrhage was classified as high-grade. The thickness of the external lamina (star) was 0.52 mm (x1.4, HE).
　　B：Macroscopically, the hemorrhage (arrows) was judged as low-grade in the case of photomicrograph A.
　　C：The hemorrhage was classified as low-grade. The thickness of the external lamina (star) was 0.11 mm (x1.4, HE).
　　D：Macroscopically, the hemorrhage (arrows) was judged as high-grade in the case of photomicrograph C.

Table 7 Correlativity of the macro- and microscopic grading

Macroscopic grade		Microscopic grade			
		high	intermediate	low	Total
	high	31	7	12	50
	intermediate	12	26	11	49
	low	13	15	24	52
	Total (cases)	56	48	47	151

Microstructure of vasculature

The venules of the maxillary and subcutaneous tissues showed well developed supporting structures composed of smooth muscle cells, elastic fibers and reticulin fibers around them. On the contrary, the petrous bone venules almost lacked such structures（Figure 3）. On electron microscopy, the petrous venules showed only faint supporting structures just beneath the endothelial basal lamina（Figure 4）.

Degree of congestion

In every case, the congestion was consistently in the head, neck, and lung. In other organs, the degree was variable. The microscopic findings of congestion in petrous bone, maxillary sinus, and subcutaneous tissue of the forearm were shown in Figure 5.
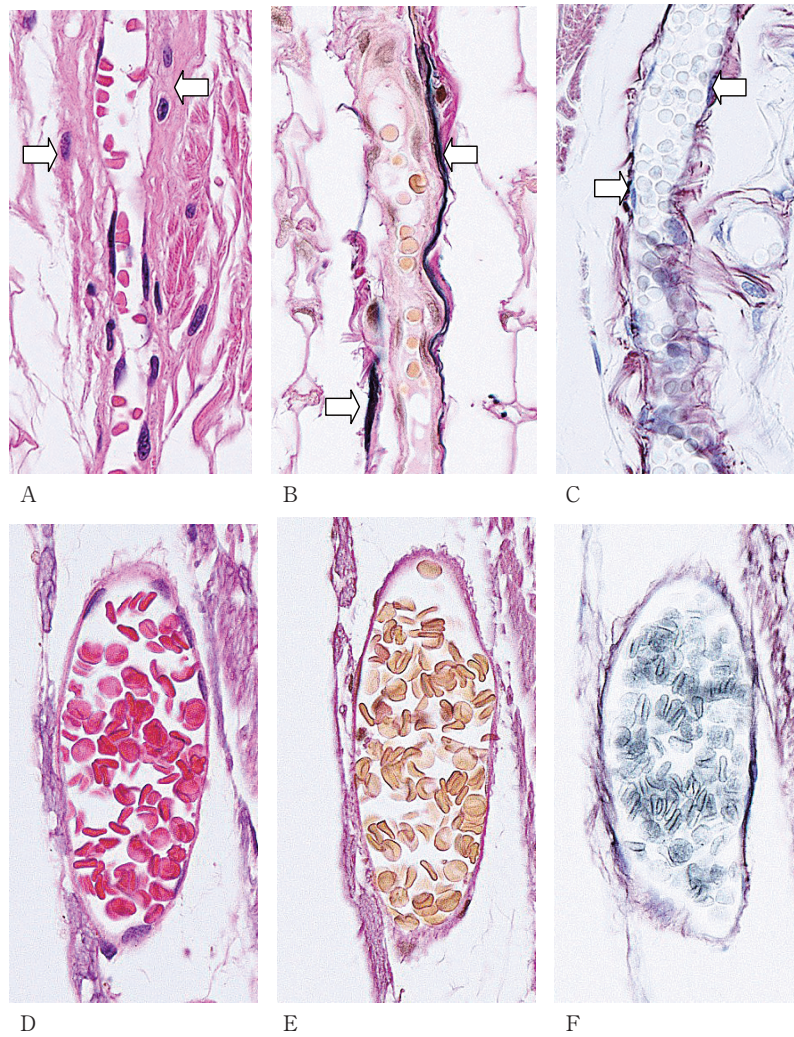
Fig. 3　Light microscopic structure of vasculature
A：The venule of the forearm subcutaneous tissue showed well developed supporting structures composed of smooth muscle cells（arrows）（x280, HE）.
B：The venule also had elastic fibers（arrows）（x280, EVG）.
C：The small vein also had reticulin fiber（arrows）（x280, silver impregnation）.
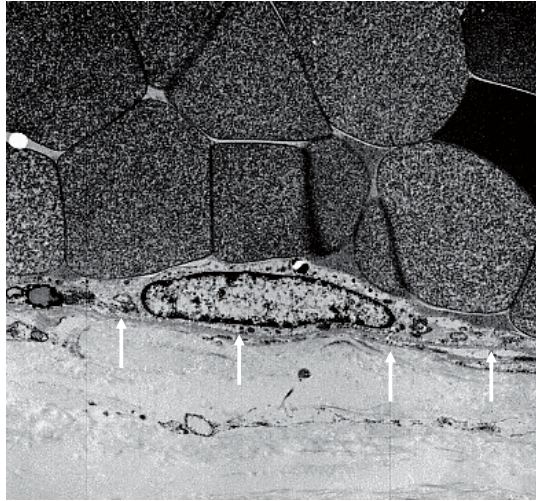D－F：The venule of petrous bone lacks such supporting structures（x280, D：HE, E：EVG, F：silver impregnation）.

Fig. 4　Ultrastructure of petrous bone venule
　　　On electron microscope, the petrous venule showed only faint supporting structures just beneath the endothelial basal lamina （arrows） （x5, 500）.
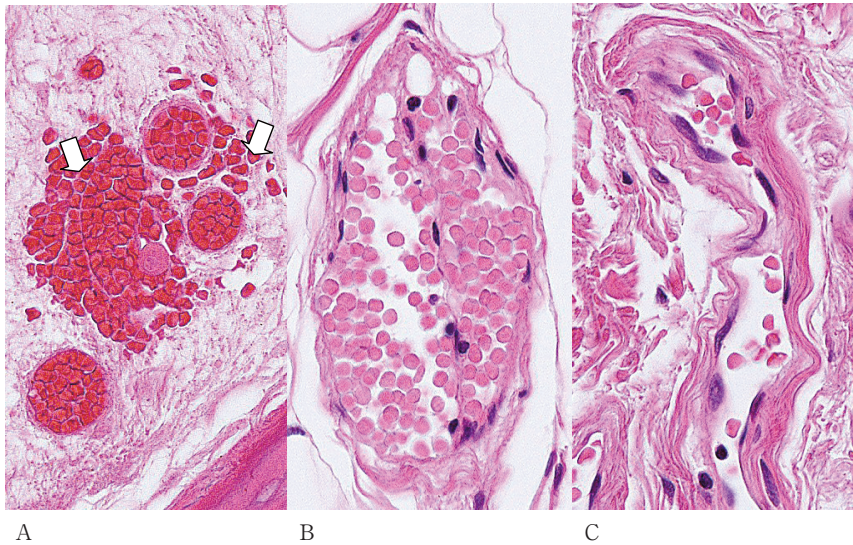

A　　　　　　　　　　B　　　　　　　　　　C

Fig. 5　Degree of congestion
　　　In the cephalic regions, the congestion was severe （A：petrous bone, B：maxillary sinus, C：subcutaneous tissue of forearm）. Photomicrograph A also showed congestive hemorrhage （arrows） （A-C：x280, HE）.

Discussion

The present data showed that petrous bone hemorrhage was non-specific, and is able to occur due to many different causes of death. This was the first report in which the petrous bones were observed microscopically using semi-3-dimensional trimmings. This method seemed to make the histological evaluation more reliable to detect the hemorrhage. The macroscopic observations were considered to show a tendency to cause underestimation in such cases with thick external laminae and/or deep hemorrhages. It was also difficult to distinguish the hemorrhage from congestion or hemoglobin leakages on macroscopic inspection, as previously mentioned. Therefore, it was deduced that the systematic microscopic observation is necessary to diagnose petrous bone hemorrhage.

There had been several reports which said that the petrous hemorrhage was drowning/asphyxia-specific, such as by Niles[1], Mueller[2], Ueno[3] and Ito[4]. Niles analyzed 24 cases of drowning and only 2 victims of non-drowning as the control. In addition, he did not observe all cases microscopically. Mueller et al. and Ueno also did not investigate their all cases histologically. Ito et al. studied all cases microscopically. However, there were no descriptions of whether the petrous bones were observed 3-dimensionally in their report. The differences in the results between the present study and their seemed to be caused by the differences in methodology.

In the present study, special attention was paid for the petrous bone, which had been famous as the hemorrhagic point in drowning, traditionally. However, the vulnerability of small veins was not specific for the bone. The other parts of the basal skull also showed mild hemorrhagic changes. Therefore, it was considered that the basal bone small veins are vulnerable for congestive hemorrhage in general, and at the petrous part, they seemed more sensitive.

The barotrauma theory had been the most favored regarding the pathogenesis of petrous bone hemorrhage in drowning[1, 2]. However, the present report clarified that the hemorrhage could occur under normal atmospheric pressure. In addition, the hemorrhage occurred more frequently in the petrous bone marrow than in the mastoid air cells, which seemed most vulnerable to barotraumata[8]. Consequently, it was concluded that the barotrauma theory was not applicable in all cases. Aspiration of water via the eustachian tube was also reported as a cause of petrous hemorrhage in drowning[2]. The single case, on which the theory was based, was a baby that had aspirated amniotic fluid into the middle ear[9]. However, the baby also suffered from asphyxia. Therefore, it was impossible to prove that the fluid aspiration via the eustachian tube itself was the cause of the petrous bone hemorrhage. The petrous bone is frequently involved in temporal bone fracture[10]. However, there were many non-traumatic cases in the present study, so, traumatic theories also could not be applied in all cases.

Pathologically, congestion was a very consistent feature of the petrous bones, surrounding tissues, and lungs in this study. In all cases, hypoxia seemed unavoidable during the agonal periods. Generally, hypoxia induces vasodilatation in many organs. In the lung, however, it induces vasoconstriction[11-13]. The "hypoxic pulmonary

vasoconstriction" results in right cardiac failure, and induces venous congestion. Cerebral autoregulation adjusts cerebrovascular resistance in the face of changing perfusion pressures[14]. Therefore, the arterial blood flow into the brain is relatively maintained even in the agonal periods. This might make the cephalic vein more congestive. Unlike the usual vessels, the small petrous veins do not have sufficient supporting structures around them. Therefore, they may be more vulnerable to congestion, and fall into congestive hemorrhage. These mechanisms might contribute to the pathogenesis of perimortal petrous bone hemorrhage.

Conjunctival and facial petechiae had been regarded as classic signs of asphyxial death[15-17]. However, Ely SF concluded that the petechiae were non-specific, and they could occur due to various causes of death[18]. In addition, she considered that the increased cephalic venous pressure was the pathogenesis of petechiae. In that sense, the petrous bone hemorrhage and conjunctival/facial petechiae might be phenomena of the same kind.

There is no single sign which proves drowning/asphyxia as the cause of death. A judgment of the cause should be made carefully from the viewpoint of overall assessment, based on the background investigations, circumstances of death, macro- and microscopic autopsy findings and many ancillary tests.

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