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Pathomorphological differentiation between traumatic rupture and nontraumatic arterial dissection of the intracranial vertebral artery

Ayako Ro [a,b,*], Norimasa Kageyama [b]

[a] Department of Legal Medicine, Tokyo Women's Medical University, Tokyo 160-8666, Japan
[b] Tokyo Medical Examiner's Office, Tokyo Metropolitan Government, Tokyo 112-0012, Japan

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ABSTRACT

We aimed to establish an objective indicator for differential diagnosis between traumatic rupture of the intracranial vertebral artery (TRIVA) and nontraumatic rupture from intracranial vertebral artery dissection (NIVAD). We investigated 19 intracranial vertebral artery (IVA) samples, including three from TRIVA, seven from NIVAD and nine non-IVA rupture cases using 0.2-mm serial histological sections through the IVA. The internal elastic lamina (IEL)–adventitia ratio for each slide was calculated as the ratio of the traced length of the adventitia to the length of the IEL as measured by digital photomicrography. NIVAD cases showed a significant peak in the IEL–adventitia ratio around the area of rupture, whereas TRIVA and non-rupture cases showed no specific increase or decrease in IEL–adventitia ratios throughout the IVAs. All NIVAD cases had a significantly higher average IEL–adventitia ratio across 10 slides at the site of the rupture lesion than at the site furthest from the rupture. In contrast, two out of three TRIVA cases showed no significant difference between the two points. The other TRIVA case showed a significantly lower IEL–adventitia ratio at the point nearest the rupture compared with that at the point farthest from the rupture. Other histological characteristics considered specific to either TRIVA or NIVAD were observed. Our results indicate that measuring and comparing IEL–adventitia ratios at ruptured and non-ruptured sites of the IVA could be a useful practical indicator for differential diagnosis between TRIVAs and NIVADs.

1. Introduction

Isolated traumatic subarachnoid hemorrhage (SAH) is a rare but serious outcome of head or neck injury [1–4]. Vessels of the posterior circulation are usually involved. In addition to complete transectional rupture of the basilar artery, the intracranial vertebral artery (IVA), is known as a common sites of rupture [2–4]. Because of the vulnerability of the IVA to longitudinal extension [5], the stretching force induced by hyperextensional or rotational neck movement is thought to be an etiology of IVA rupture [2–4], Short-lasting oscillation of the brain or momentary severe increases in intra-arterial pressure have also been proposed as possible mechanisms of IVA rupture [2]. In contrast, the IVA is also susceptible to idiopathic intracranial artery dissection [6,7]. Therefore, differentiations between traumatic rupture of the IVA (TRIVA) and nontraumatic rupture from IVA dissection (NIVAD) is required in medicolegal autopsies when a person suddenly dies from SAH owing to a ruptured IVA with head or neck injury just before death.

The previous criteria for isolated traumatic SAH may be summarized as follows: (a) basal SAH due to (b) a transmural tear of vessel(s) at the relevant site, usually without preexisting pathology, (c) with biomechanically and temporally consistent evidence of blunt impact that can cause abrupt hyperextension and/or rotation of the head and neck [8–10]. However, histological differentiation is not included in these criteria.

In contrast, NIVADs form fusiform aneurysms with a small rupture at the top of the vascular wall protrusion [11]. Microscopically, medial dissecting hematomas are observed at the rupture site [6,11]. The pathogenesis of NIVAD remains unclear; however, our previous study detected medial defects as a predisposing vessel pathology [11].

Based on our autopsy experience, we concluded that the adventitial extension at the ruptured point is the most specific histopathological characteristic of NIVAD [12–14]. According to our conclusion is, we propose a new index, the internal elastic lamina (IEL)–adventitia ratio, for pathomorphological differential diagnosis between TRIVA and NIVAD. In the present study, we applied

* Corresponding author at: Department of Legal Medicine, Tokyo Women's Medical University, 8-1 Kawada-cho, Shinjuku-ku, Tokyo 162-8666, Japan. Tel./fax: +81 3 5269 7300.
E-mail address: chaeja@nifty.com (A. Ro).

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the index to cases of TRIVA and NIVAD, and cases without rupture. Three-dimensional reconstruction and pathomorphometry of the lengths of ruptures were also performed.

2. Materials and methods

2.1. Study subjects

Nineteen IVAs from 19 medicolegal autopsy cases were investigated. The subjects' causes of death were determined based on the results of medicolegal autopsies performed at the Tokyo Medical Examiner's Office between April 2006 and September 2012. Ten subjects died of diffuse basal SAH from a ruptured IVA. Among them, three subjects were diagnosed with TRIVA. TRIVA in this study was defined as patients when subjects were affected by a sudden witnessed accident including head or neck impact and subsequent consciousness disorder. This resulted in death with autopsy confirmation of massive basal SAH from rupture of the IVA. Additionally, histological sections revealed an acute transmural rupture without any preexisting vascular disorder. Clinical and general autopsy information regarding TRIVA summarized below.

Case 1: A man in his 70s with a history of small cerebral infarction. He fell from stairs to the floor. After initially recovering from cardiopulmonary arrest on hospital arrival, he died 15 h after the accident. Head computed tomography revealed diffuse basal SAH. At autopsy, basal SAH and an occipital bone fracture were detected. Blood alcohol was not detected.
Case 2: A man in his 80s without any previous medical history fell from stairs to the floor. Head computed tomography showed diffuse basal SAH. He died 14 h after the accident. Autopsy revealed basal SAH, occipital bone fracture and a slight brain contusion. Blood alcohol was not detected.
Case 3: A man in his 30s suffering from obsessional neurosis fell from a platform. He was in cardiopulmonary arrest on hospital arrival and died 1 h after the accident. Head computed tomography was not performed. Autopsy revealed basal SAH with neither skull fracture nor brain contusion. His blood alcohol level was 1.13 mg/ml.

Another six subjects were diagnosed with fatal SAH from NIVAD. NIVAD in this study was defined as when subjects had no preexisting episode of head or neck injury within at least 24 h before death. Additionally, there was autopsy confirmation of massive basal SAH from rupture of the IVA with histological evidence of an acute rupture of arterial dissection. The last case of SAH was a man in his 50s who died of NIVAD owing to a traffic accident just prior to death; this case was previously reported in this journal [15]. The remaining nine autopsy cases died of non-cerebrovascular disorders with no IVA rupture nor recent head or neck injury within at least 24 h before their death. These cases comprised eight men and one woman, and the mean age was 55.8 ± 19.5 years [standard deviation]. A summary of their clinical data is shown in the supplemental data (Supplemental Table 1).

2.2. IVA examinations with serial histological sections

The IVAs on the ruptured side were investigated in the 10 SHA cases. In the nine non-SAH cases, the IVA on one side was randomly selected and examined. IVAs were removed from brains at autopsy and fixed with formalin. The IVA was embedded in a paraffin block as one long packed block. Serial cross-sectioning at 5 μm was then performed through the block, longitudinally. Among whole sections, every 40th 5-μm cross-section was selected and stained with the Elastica van Gieson methods, such that observations of the ruptured IVA were made every 0.2 mm. The mean number of observed slides per case was 101 ± 23. Photomicrographs of all slides were digitalized using an DP71 Microscope Digital Camera (Olympus corp. Tokyo, Japan).

2.3. Three-dimensional reconstruction

The digital photomicrographs were aligned and three dimensionally reconstructed using Avizo 6.1 software (Visualization Sciences Group, Massachusetts, USA). Three main vascular elements, namely, the IEL, media, and adventitia, were segmented from each of the aligned photomicrographs and reconstructed for three-dimensional models (Video 1).

2.4. Pathomorphometry of the lengths of rupture

Pathomorphometry for the longitudinal lengths of ruptured adventitia and the ruptured IEL was performed by calculating the number of slides containing ruptures. The longitudinal lengths of the ruptures were calculated by multiplying 0.2 mm by the numbers of slides showing lesions.

2.5. Measurement of the IEL–adventitia ratio

The IEL and adventitia were traced and measured from digital photomicrographs using Image J 1.43 software (National Institutes of Health, Maryland, USA). Every IEL and adventitia throughout the histological sections were traced manually. The length of the traced lines was then measured as the number of traced pixels. The IEL–adventitia ratio was calculated as the ratio of the number of pixels for the measured adventitia to the number for the IEL in each histological slide.

The mean IEL–adventitia ratios throughout the IVA were measured in all cases. Additionally, the mean IEL–adventitia ratios across 10 slides taken at each of the nearest and farthest points relative to the adventitial rupture were compared for the 10 SAH cases.

Analyses were performed using JMP 9.0 software. Non-ordinal statistical analysis of the mean IEL–adventitia ratios for the 10 slides from each of the nearest and farthest points relative to the adventitial rupture was performed using the chi-square test (Mann–Whitney *U* test). A probability value of <0.01 was considered to represent significance.

3. Results

3.1. Morphological characteristics

All cases suffered diffuse SAH, especially around the cerebral base (Figs. 1a and 2a). The morphological characteristics of TRIVA and NIVAD are summarized in Table 1. Macroscopically, adventitial ruptures in the TRIVA cases showed longitudinal tears (Fig. 1b), v-shaped tears or partial tears at the bifurcation of the posterior inferior cerebellar artery. Adventitial ruptures in the NIVAD cases showed pin-point adventitial tears at the top of the vascular wall protrusion, which are usually termed fusiform aneurysms (Fig. 2b). Variations of IVAs were not detected in either of the TRIVA and NIVAD groups.

The most specific histopathological characteristic observed was that all TRIVA cases showed transmural rupture without extension of the adventitia (Fig. 1c). Conversely, extension of the adventitia was observed in all NIVAD cases (Fig. 2c). The three-dimensional reconstructed model also showed that the adventitia and IEL of TRIVA cases were ruptured at the same position, without adventitial extension (Fig. 1d and e).