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Case Report

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Aneurysmal Rupture of the Internal Carotid Artery in a Presumed Neurofibromatosis Type Ⅰ Patient

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Aneurysm of the internal carotid artery is a rare disease and is known to be associated with congenital arterial anomalies such as neurofibromatosis type Ⅰ (NF-Ⅰ). NF-Ⅰ is an autosomal dominant neurocutaneous disorder characterized by a variety of manifestations that involve the central and peripheral nervous systems, skin, vascular system, and skeleton. In particular, the involvement of vascular abnormalities in NF-Ⅰ is well known. Any vessel may be affected by this condition, although the renal artery is most frequently involved. The vascular abnormality can be occlusive or an aneurysmal degenerative change. Therefore, symptomatic presentations might assume an indolent pathophysiologic course such as hypertension, or manifest as a catastrophic event such as arterial rupture that could result in sudden death. We report a rare autopsy case of an aneurysmal rupture of the internal carotid artery in a woman with suspected NF-Ⅰ, who collapsed in her home.

Key words : Aneurysmal rupture, Autopsy, Internal carotid artery, Nerurofibromatosis type Ⅰ

Introduction

Carotid artery aneurysms are uncommon but have the potential of catastrophic clinical events. The aneurysms, as we know, lead to severe neurologic symptoms like embolization and even sudden death from rupture. Aneurysms of the carotid artery result from injury or may be a long term sequel of spontaneous dissection. It could be also caused by congenital arterial anomalies such as Neurofibromatosis type Ⅰ (NF-Ⅰ).

NF-Ⅰ, so-called von Recklinghausen disease, is an autosomal dominant disorder affecting one per 3,500-4000 live births.[1] NF-Ⅰ is developed by mutations in, or deletions of, the NF-Ⅰ gene that is located on 17q11.2. This gene controls neurofibromin, a GTPase-activating protein that is thought to have a possible tumor-suppressor function by maintaining the ras proto-oncogene in an inactive form. Over 250 mutations in the NF-Ⅰ gene have been identified. The inheritance is autosomal dominant type with 50% of the cases representing new mutations.[2] Clinical features of NF-Ⅰ include multiple hyperpigmented macules (so-called café au lait spots), various benign and malignant tumors including neurofibroma, iris hamartomas (so-called Lisch nodules), and freckling in the axillary or inguinal regions (so-called Crowe's sign), and abnormalities of blood vessels.[1] Vascular abnormalities, mostly in the form of aneurysms or stenoses, affect medium- and large-sized vessels and are presented in NF-Ⅰ. The renal artery is the most frequently involved one, but abdominal aortic coarctation, internal carotid artery aneurysms, and

cervical vertebral arteriovenous malformations have also been described. Internal carotid artery aneurysms are rare but often present with spontaneous rupture or neurological complications.[3]

Case Report

A 41-year-old female suddenly collapsed in her place while walking into her home after shopping. When she arrived at home the right side of her neck was perceived suddenly swollen and she got lost her mentality. She was immediately transferred to hospital and cardiopulmonary resuscitations were performed but in vain. The given medical documents showed that an emergency room doctor felt considerable difficulty in doing tracheal intubation because the patient's upper airway lumen got narrowed at that time.

At postmortem examination, there was no evidence of external injury without swelling and subcutaneous hemorrhage in the right neck and shoulder area (Fig. 1). Numerous café au lait spots and pigmented macules were noted on the body (Fig. 2). The conjunctiva of eyelid and oral mucosa showed multiple petechiae. A hyperpigmented, 5.5 × 3.0 cm sized mass was noted on the lateral malleolar region of the ankle (Fig. 3). On internal examination, 200 ml of hematoma was found in the soft tissue layer of the right neck. Aneurysmal rupture of the right internal carotid artery was revealed (Fig. 4).

Histological evaluation found the carotid artery being marked degeneration of the elastic fiber of the

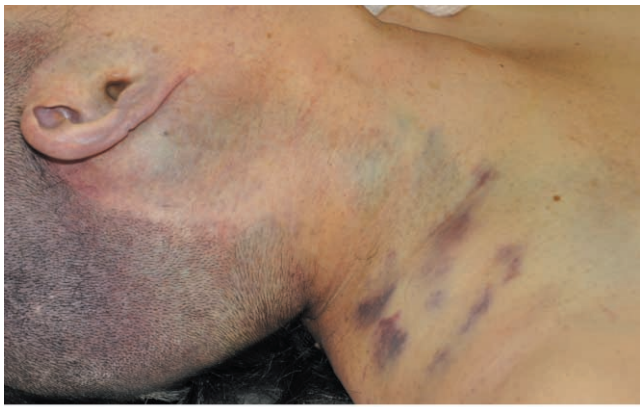

Fig. 1. Postmortem examination shows no evidence of external injury, but swelling and subcutaneous hemorrhage in the right neck and shoulder region are noted.

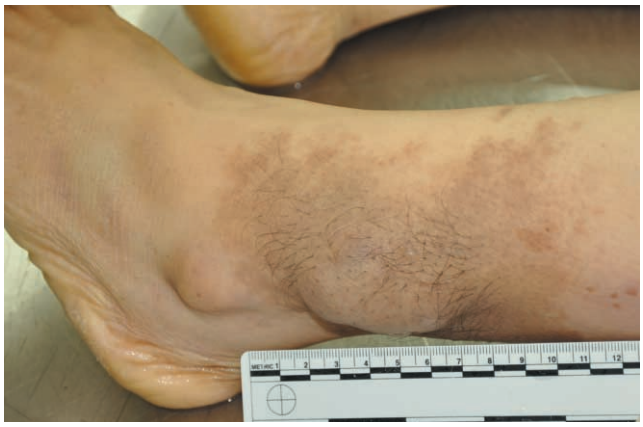

Fig. 3. A hyperpigmented mass is noted above the lateral malleolus of the left ankle.

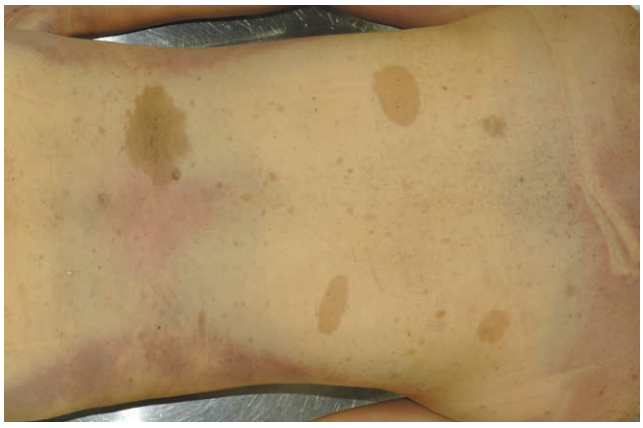

Fig. 2. Numerous café au lait spots are multifocally formed on the body.

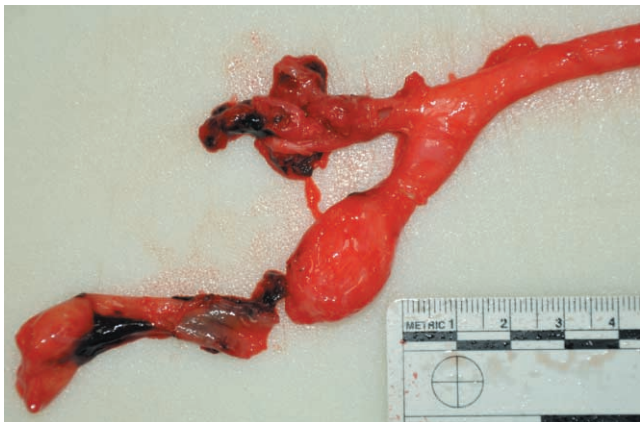

Fig. 4. Internal examination reveals aneurysmal rupture of the right internal carotid artery.

media and dissection with intimal thickening. There was intimal proliferation of spindle cells which were positive on the smooth muscle actin (SMA) and negative on the S100 protein (Fig. 5). Although these proliferative lesions often obliterated the lumen of the vessel, marked degenerative change of the arterial wall was thought to lead to formation of an aneurysm. Toxicologic study of the blood and gastric contents was unremarkable. Considering the autopsy findings and medical records, the cause of death was ruled as suffocative asphyxia sustained by massive hematoma which was from aneurysmal rupture of the right internal carotid artery in the neck region.

Discussion

Aneurysms of the carotid artery are rare and they are usually caused by atherosclerosis, trauma, or infection. Overall, the incidences of theses aneurysms are from 0.4% to 4% of all peripheral arterial aneurysms.[4] Aneurysmal degeneration has also been associated with congenial arterial anomalies, such as NF-Ⅰ. The vascular manifestations of NF-Ⅰ were first described by Reubi in 1945,[5] and since then, there have been several reports regarding stenosis, occlusions, aneurysms, arteriovenous malformations and fistulae. In the presenting case, the deceased had

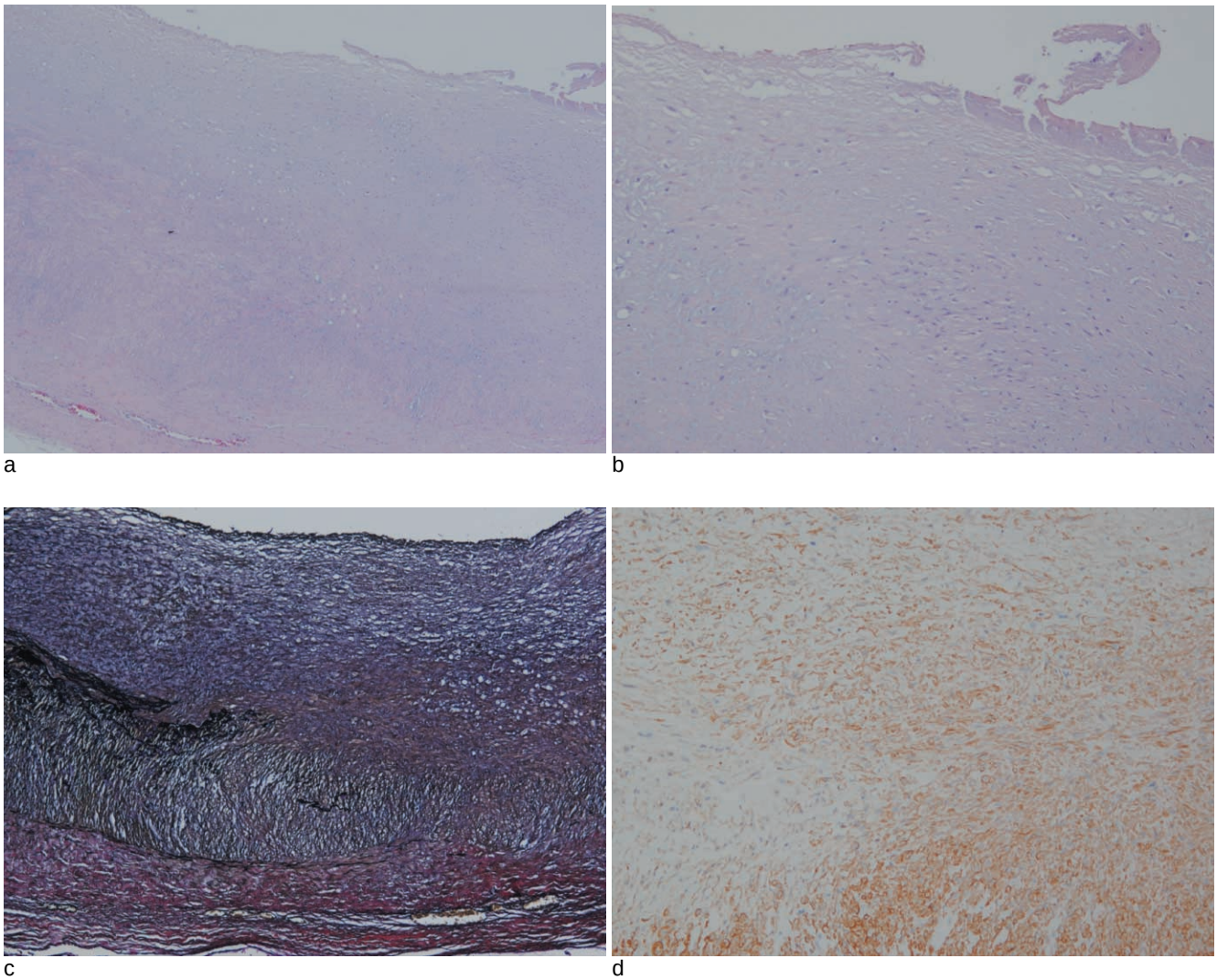

Fig. 5. Disrupted elastic lamina and thickened tunica intima are noted accompanying spindle cell proliferation (Fig. 5a, H&E, x40; 5b, H&E, x100; 5c, elastic stain, x40). Proliferating spindle cells which are positive on the smooth muscle actin (SMA) are presented in the tunica intima of the right internal carotid artery (Fig. 5d, SMA, x100).

numerous café au lait spots on the body and about 5 cm sized hyperpigmented mass above the lateral malleolar region of the left ankle. We presumed that she suffered from a NF-Ⅰ patient. NF-Ⅰ vasculopathy has been used by medical geneticists to describe the vascular lesions in NF-Ⅰ.[6] The frequency of this vasculopathy is hard to be defined, but the prevalence of vascular lesions in large clinical series is about 0.4% to 6.4%.[7] The renal artery involvements are most common (41%), and more often stenotic than aneurysmal. The carotid, vertebral, or cerebral artery lesions seen in 19% of patients are commonly aneurysms, occur in the third decade of life, and occur more often in women (72%).[8] The usual NF-Ⅰ vascular lesions result from an intrinsic process involving the walls of arteries that are not directly associated with neurofibromas. The blood vessel continuously responds to changes in its environment, and vascular remodeling and repair occur constantly. Intimal proliferation is an essential component of vascular remodeling and repair. And intimal thickening with cellular proliferation is characteristic feature in the NF-Ⅰ vasculopathy. This proliferation often causes luminal obliteration, but elastic degenerations causing aneurysmal change and dissection are another characteristic feature in the NF-Ⅰ.[7] Recent studies using inmmunohistochemistry and electromicroscopy suggest that the proliferating cells in the intima tunica of NF-Ⅰ patients are consistent with smooth muscle cell origin.[3] In our case, the proliferating cells of the tunica intima presented of immunoreactivity for SMA.

Despite the fact that NF-Ⅰ is one of the most commonly inherited diseases, death case is not frequently encountered in practical forensic medicine, so relevant death mechanisms may be not enough familiar to forensic pathologists.[2] The most common cause of death in NF-Ⅰ is malignancy, often from connective or soft tissue mass lesion including intracranial neoplasm, hemorrhage or brainstem compression. Vascular disease is the second leading cause of death, especially among those individuals aged less than 40 years old.[8] The vasculopathy may result in critical reduction in blood flow within the coronary or cerebral circulations, and aneurysmal dilatation may be associated with rupture leading to life-threatening hemorrhage. When forensic pathologists investigate death case like this presenting one, the following that should be recommended are review of the past medical and familial history, medical records, a full external examination with careful documentation of skin lesions and nodules, measuring of the head circumference in case of children, fine photography, radiologic study, standard forensic dissection, appropriate pathologic study of specific tumors and vasculature (renal, cerebral, and cardiac), neuropathologic examination of brain and spinal cord, examination of the eyeballs and gastrointestinal tract, toxicological study, and cytogenetic/molecular evaluation for blood and tissue should be remembered.[2]

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