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Histopathological Examination of a Symptomatic Carotid Web: A Case Report

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Abstract

Carotid webs cause ischemic stroke in young people and are associated with a high rate of stroke recurrence. Histopathological examination is crucial for clarifying the pathogenesis and mechanisms underlying the occurrence of carotid webs, although the mechanisms generally remain unclear. Here, we report a case of a symptomatic carotid web in a woman in her 50s who had a medical history of two ischemic strokes. She was diagnosed with a right carotid web and underwent carotid endarterectomy 18 days after the second stroke. Histopathological examination clearly revealed several phases of intimal hyperplasia. Furthermore, a thrombus attached to the carotid web showed invasion by fibroblasts and capillaries, and organization had begun. We presume that after the appearance of the carotid web, the thrombus formed by stagnant flow and became organized, causing the carotid web to grow and change in shape.

Keywords: stroke, cerebral ischemia, carotid web, carotid endarterectomy, stroke in young adults

Introduction

A carotid web (CaW) is a cause of cryptogenic ischemic stroke in young patients.[1)] Some case-control studies have shown that CaWs are present in 9%-37% of patients aged <60 years with cryptogenic stroke and that CaWs increase the risk of ischemic stroke by approximately 10-20-fold.[2)] Identifying CaWs as the etiology of stroke is crucial for secondary prevention; however, the underlying pathophysiology and mechanisms remain unclear. Here, we report a case of symptomatic CaW with dynamic pathological findings and summarize the pathological features of CaW in this case.

Case Report

A woman in her 50s presented to our hospital with a sudden onset of severe left hemiparesis, conjugate eye deviation, left facial droop, dysarthria, visuospatial neglect, and sensory loss. She had a medical history of cerebral infarction involving the ipsilateral territory 2 months previously and was taking clopidogrel at 75 mg/day. Her National Institutes of Health Stroke Scale (NIHSS) score at admission was 21 points. Magnetic resonance imaging (MRI) and angiography showed right internal carotid artery (ICA) occlusion and acute and subacute infarctions in the ICA territory on MRI diffusion-weighted imaging sequences (Fig. 1A, B). Because of a lack of information regarding her medical history and usual medicines, a tissue plasminogen activator was not administered, and the patient directly proceeded to endovascular treatment. Digital subtraction angiography revealed that the right ICA was occluded (Fig. 1C). We performed mechanical thrombectomy using a stent retriever and an aspiration catheter. The thrombus was easily traversed. The stent retriever was deployed from the proximal portion of M1 to the ICA, and the aspiration catheter was inserted beyond the top of the ICA to integrate the removal system. We achieved thrombolysis in cerebral infarction grade 3 reperfusion in a single pass (Fig. 1D). Additionally, a shelf-like narrowing was

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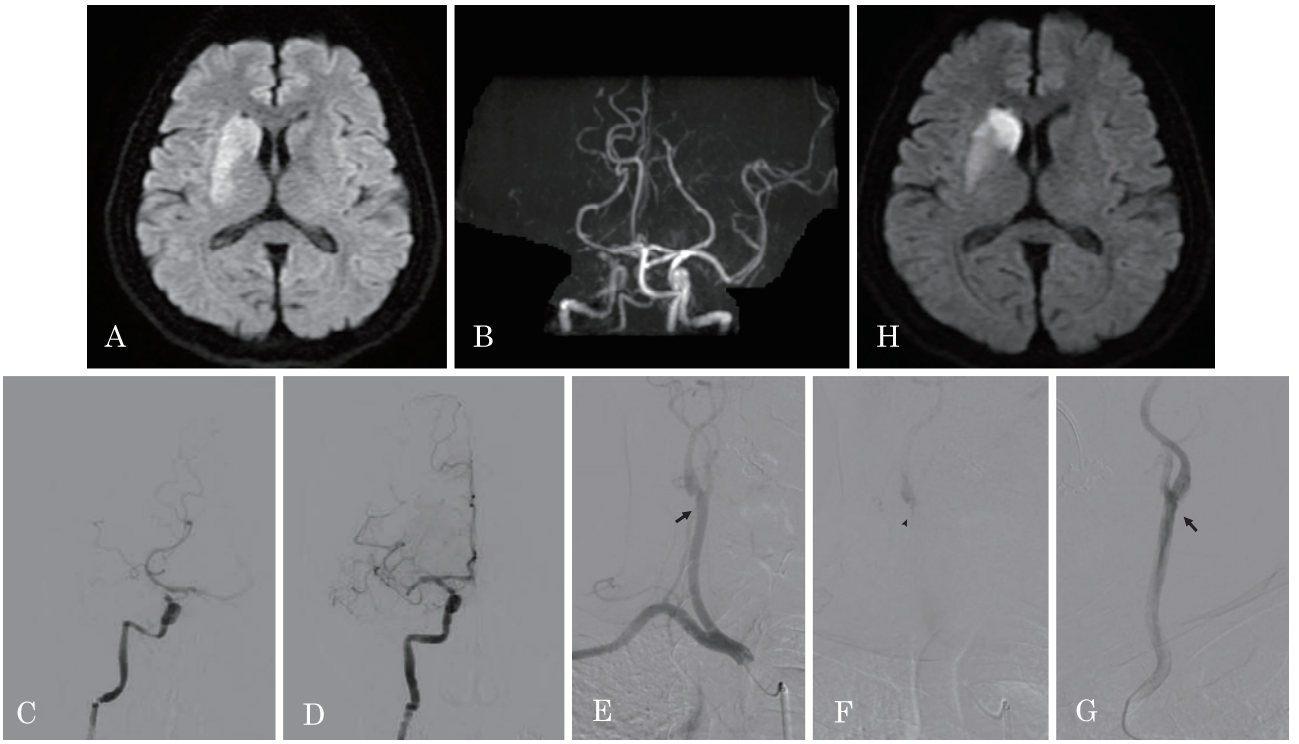

Fig. 1 (A) Diffusion-weighted magnetic resonance imaging demonstrated a high-intensity signal at the right caudate and putamen. (B) Magnetic resonance angiography showed right internal carotid artery occlusion. Digital subtraction angiography at presentation showed that the right internal carotid artery was (C) occluded and then (D) recanalized after mechanical thrombectomy. (E) A small protruding lesion (black arrow) was observed along the posterior wall of the right carotid bulb. (F) The contrast injection cleared the right internal carotid artery, whereas marked contrast stagnation (black arrowhead) was observed distal to the carotid web. (G) A tiny triangular filling defect was present along the posterior wall of the left carotid bulb (black arrow). (H) Diffusion-weighted imaging demonstrated an infarction in the right caudate and putamen after mechanical thrombectomy.

observed at the proximal right ICA (Fig. 1E) and was believed to be due to blood flow stagnation (Fig. 1F). The left common carotid artery injection also showed small protruding lesions at the proximal ICA (Fig. 1G). After endovascular treatment, the patient's NIHSS score was 0. MRI showed infarction changes only in the putamen and caudate nucleus (Fig. 1H).

The patient started treatment with prasugrel at 2.5 mg/day. Then, we initiated an etiological search. The investigation results showed that she was negative for diabetes or hyperlipidemia, and 24-h Holter monitoring and transthoracic echocardiography findings were normal. Computed tomography angiography, especially the sagittal view, revealed a membranous-like structure on the proximal right ICA consistent with a CaW (Fig. 2A, B) and a thin membranous filling defect on the posterior wall in the proximal left ICA (Fig. 2C, D). T1 plaque imaging also revealed an isointense structure and a suspicious filling defect along the posterior wall of the right ICA (Fig. 2E), distal to the carotid bifurcation in the sagittal view (Fig. 2F).

We performed a right carotid endarterectomy (CEA) 18 days after stroke to prevent recurrent stroke. After arteriotomy, the CaW was confirmed to have an approximately 10-mm-diameter thrombus attached to its distal aspect (Fig. 3 A, B). The adventitia and media were in contact with one another, and we dissected into the media and removed the CaW specimen (Fig. 3C). The internal surface of the CEA specimen showed marked localized intimal thickening corresponding to CaW. Histopathological examination indicated that the most proximal portion was composed of dense elastic fibers, most of which were arranged vertically (Fig. 4A-①). The middle of the web was mainly composed of brown collagen fibers, different from the proximal portion (Fig. 4A-②). The most distal portion of the web appeared to override the two aforementioned portions, where elastic fibers were arranged horizontally (Fig. 4A-③). A fresh thrombus was attached to the end of the web. These findings indicated that CaW comprised different pathological phases (Fig. 4A, B). The most proximal portion of the CaW comprised dense elastic fiber proliferation admixed with collagen fibers and alpha-smooth muscle actin-positive myofibroblasts, and the distal portion had a similar tissue component but more prominent collagen fibers (Fig. 4C, D). The edge of the distal portion of the CaW contained a mural thrombus in the early stage of organization (Fig. 4E). The thrombus collected during thrombec-

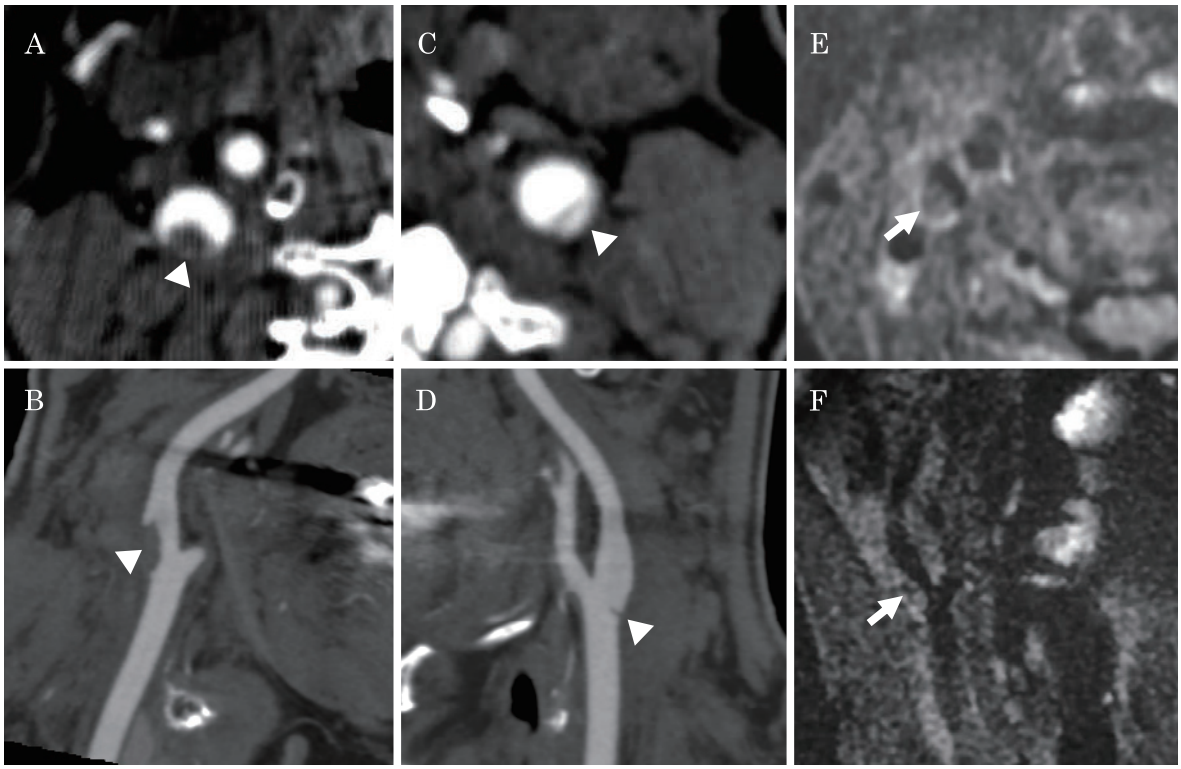

Fig. 2 (A, B) Computed tomography angiography demonstrated a carotid web (white arrowheads) in the right internal carotid artery visible as a septum on axial imaging and a defect of contrast material emerging from the posterior wall. (C, D) A protruding shelf-like lesion (white arrowheads) was observed on sagittal imaging in the left internal carotid artery. (E, F) Magnetic resonance imaging of the vessel wall revealed a curvilinear, intraluminal filling, isointense object along the posterior wall of the right internal carotid artery at its origin (white arrows).

tomy also showed signs of organization (Fig. 4F).

After the operation, the patient discontinued prasugrel and exhibited no cerebrovascular ischemic events during a follow-up of 12 months.

Discussion

CaW has been highlighted recently as a cause of cryptogenic stroke in young people.[3] However, its etiology, natural history, and treatment remain unclear. The etiopathogenesis of CaW is controversial, and its origin, either congenital or developmental or acquired, has been the subject of debate. Vercelli et al.[4] reported the *de novo* formation of a CaW from an intimal dissection, and dissections similarly splitting the intimal fibrous content are reported.[2,4] A focal intimal dissection has been indicated to be an underlying cause of CaW. The posterolateral wall of the proximal ICA is believed to have low shear stress, which may explain why CaWs are predisposed to occur in this location. Our patient exhibited localized loss of smooth muscle cells and irregularity of the elastic laminae in the media, indicating signs of dissection. These observations support the hypothesis that CaW develops secondarily and may be associated with local vascular dissection.

Because of the lack of high-quality clinical trials, a unified standard for the medical treatment of symptomatic CaWs has not been established. One case-control study showed that nearly 30% of patients receiving active antiplatelet monotherapy developed recurrent ischemic events.[5] A cohort study also demonstrated that among seven (29%) patients with symptomatic CaWs exhibiting a recurrent ischemic stroke, three were already taking antiplatelet monotherapy and two were using dual antiplatelet therapy.[6] Only a few reports have angiography findings, indicating an overlying thrombus trapped in the CaW, and the thrombus disappeared under anticoagulation therapy Several reports have advocated that a thrombus might respond best to anticoagulation therapy[1,2,7] because blood stagnation may lead to thrombus formation distal to the CaW, followed by artery-to-artery embolism; this mechanism of thrombus formation could be similar to the mechanisms of thrombus formation in the left atrial appendage. We confirmed that antiplatelet therapy did not play a role in preventing either thrombus formation or stroke recurrence. The effectiveness of anticoagulation therapy for symptomatic CaWs requires further verification.

The surgical treatment of symptomatic CaW was first

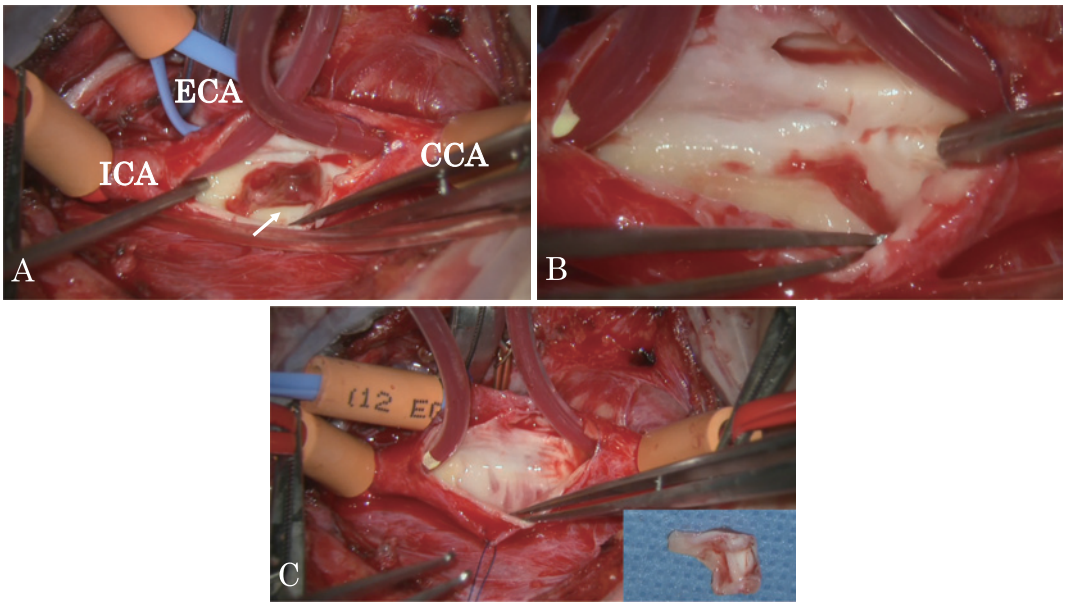

Fig. 3 (A, B) The carotid web had a smooth contour, was in the posterior wall of the ICA, and had a superimposed thrombus (white arrow) over the web pocket. (C) The carotid web was dissected from the intima of the proximal ICA. After removal, the luminal contour became normal.
ECA, external carotid artery; ICA, internal carotid artery; CCA, common carotid artery

reported in 1968 and has since been widely performed.[2,8] A systematic review showed that among 35 patients who underwent CEA, none of them developed procedural complications or stroke recurrence for a median follow-up of 14 months.[9] CEA has been described as safe and potentially efficient. However, in recent years, with the increasing safety of carotid artery stenting,[10,11] there has been a growing number of reports on carotid artery stenting for symptomatic CaWs. Several reports have indicated technical feasibility without complications and no recurrent ischemic events or other complications during follow-up of 3-60 months.[1,12] Additionally, there was no evidence of restenosis during a median follow-up of 10 months (interquartile range, 3-18 months).[13] The clinician must regard anatomical considerations and the patient's overall condition to determine the appropriate surgical approach. For example, CEA can eliminate the need for antiplatelet therapy. Because patients with CaW are young and not at substantial risk of ischemic disease, resolving CaW-related issues would render antiplatelet therapy unnecessary and eliminate the risk of bleeding. Moreover, the best advantage of CEA is the possibility of pathological diagnosis. In several studies, pathological examinations revealed that a CaW is a subtype of fibromuscular dysplasia.[1,2,14,15] A typical characteristic of CaW is intimal fibrous hyperplasia with minimal medial degeneration,[2,16] sometimes containing fibroelastic tissue with muscular tissue[17] and fibroelastic tissue with areas of myxoid degeneration.[18] In our case, the CaW showed different developmental phases with new intimal hyperplasia overlying the CaW distally. At the distal aspect of the CaW, a white thrombus had formed secondary to turbulent blood flow and had begun to organize. Thrombus attachment to a CaW was reported in 29% of cases in previous studies.[2,6] The frequent observation of a thrombus adhering to a CaW supports the theoretical possibility that webs lead to blood flow stagnation, increasing the likelihood of thromboembolism. Among the cases reported to date, there have been no confirmations of a thrombus adhering to a CaW undergoing organization. Here, we have reported the first of such cases. We considered that the organizing process of the thrombus might have contributed to the distal growth of CaW, as indicated by histopathological examination. Whether CaWs undergo dynamic morphological changes has not been definitively concluded. Although continued CaW enlargement, secondary to hemodynamic changes in blood flow has been indicated, there is no clear evidence supporting this phenomenon.[19] One case report described an increase in the CaW thickness in a patient who underwent a second digital subtraction angiography after a second ipsilateral stroke; however, it was unclear whether the thickening was associated with a superimposed thrombus or indicated proliferative thickening of the web.[20] Few reports have described morphological changes among the pathological findings. The histological findings in our case may support the theory that CaW progresses throughout the patient's lifespan. Histopathological examinations are crucial not only to diagnostic purposes but also to understand better this disease's pathophysiology.[21,22] Accumulating precise histological analyses of CEA specimens containing CaWs is essen-

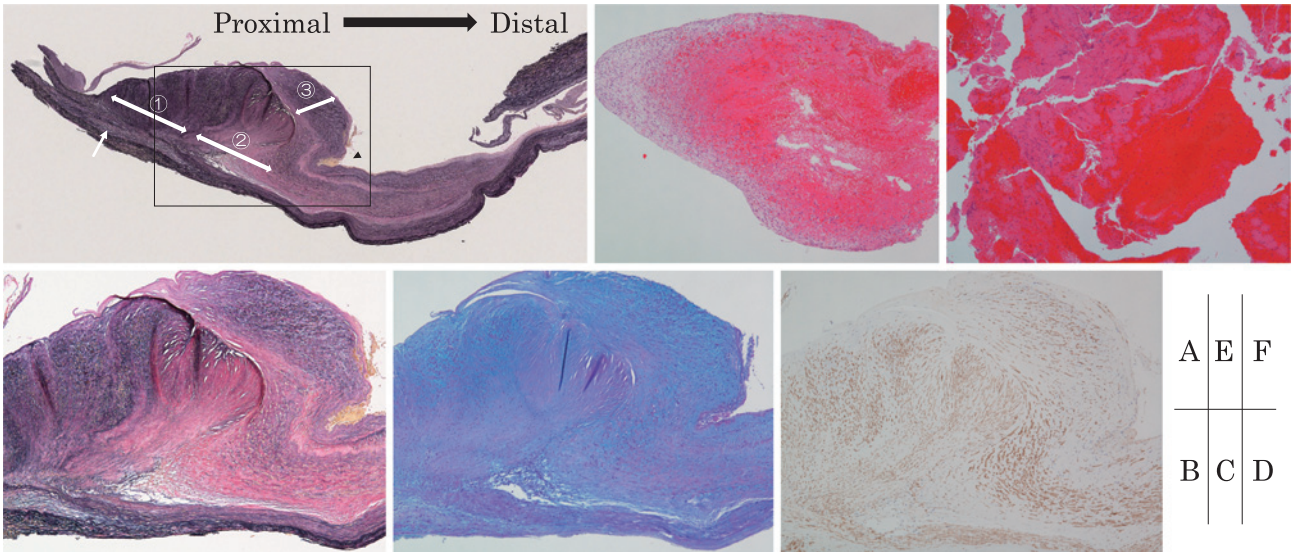

Fig. 4 (A) Histopathological examination revealed that the carotid web consisted of intimal thickening composed of elastofibrotic tissue of various stages. ① The most proximal portion was composed of dense elastic fibers that were mainly arranged vertically. ② The middle of the web was mainly composed of brown collagen fibers, different from those in the proximal portion. ③ The most distal portion of the web appeared to override the two aforementioned portions, where the elastic fibers were arranged horizontally. Localized loss of smooth muscle cells and irregularity in the elastic laminae of the media were observed (white arrow). A fresh thrombus was attached to the end of the web (black arrowhead) (Elastica van Gieson stain, original magnification ×1). (B) Magnification of the black framed area in (A). (C) The most proximal portion of the carotid web was composed of dense elastic fiber proliferation admixed with collagen fibers, and the distal portion had a similar tissue component but more prominent collagen fibers (periodic acid–Schiff–Alcian blue stain, original magnification ×400). (D) Alpha-smooth muscle actin-positive myofibroblasts were observed (original magnification ×400). (E) The thrombus had begun to organize (hematoxylin and eosin stain, original magnification ×400). (F) The thrombus obtained during mechanical thrombectomy revealed signs of organic consolidation mixed with red blood cells and fibrin (hematoxylin and eosin stain, original magnification ×400).

tial to clarify the pathogenesis and prognosis of CaWs.

Data on the clinical course of asymptomatic CaWs are limited. In one study, 58% of patients with symptomatic CaWs had an asymptomatic CaW on the contralateral side,[10] like in our case. Symptomatic CaWs have been demonstrated to be significantly larger than contralateral asymptomatic CaWs.[1] Therefore, enlargement of a CaW is considered to increase the risk of stroke. Treatment of an asymptomatic CaW is often reported to involve only medical treatment or observation, but the optimal treatment strategy remains unclear.[1,9] Antiplatelet therapy was discontinued in our patient, and at the time of this writing, she had been observed for 12 months with no new stroke events. Determining the most appropriate treatment approach and observation period for asymptomatic CaWs requires the accumulation of more cases and systematic evaluations.

In conclusion, we analyzed the characteristic histopathological examination findings of symptomatic CaWs. In our case, the intimal hyperplasia clearly showed several phases, and a thrombus had formed secondary to stagnant flow; the organization of this thrombus may have caused the CaW to grow and change in shape. Further research is required to explore the etiology, prognosis, diagnosis, and best treatment of CaWs.

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Conflicts of Interest Disclosure

None of the authors have any conflicts of interest to declare.

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