

Familial Multiple Trichoepithelioma Associated With Subclavian-Pulmonary Collateral Vessels and Cerebral Aneurysm

—Case Report—

Yuichiro INATOMI, Toshiro YONEHARA, Shodo FUJIOKA, Joji URATA*,
Katsuro OHYAMA**, and Makoto UCHINO***

Stroke Center and *Department of Radiology, Saiseikai Kumamoto Hospital, Kumamoto;
Ohyama Dermatological Clinic, Kumamoto; *Department of Neurology,
Kumamoto University School of Medicine, Kumamoto

Abstract

A 63-year-old woman presented with cerebellar infarction caused by occlusion of the right posterior inferior cerebellar artery. She had papules on her face that were identified histologically as multiple trichoepithelioma. Angiography revealed right subclavian-pulmonary collateral vessels and a cerebral aneurysm arising from the bifurcation of the right middle cerebral artery. Her grandmother, mother, and uncle had had similar papules, and the deaths of her mother and uncle were due to subarachnoid hemorrhage.

Key words: familial multiple trichoepithelioma, vascular abnormality, cerebral aneurysm, subarachnoid hemorrhage, subclavian-pulmonary collateral vessels

Introduction

Multiple trichoepithelioma is a congenital dermatosis characterized by the presence of many small tumors located predominantly on the face, and is inherited as an autosomal dominant gene.^{3,4,7)} Systemic complications have been observed in some cases,^{1,5)} but vascular abnormalities have not been reported.

We treated members of a family suffering from multiple trichoepithelioma associated with systemic vascular abnormalities, including subclavian-pulmonary collateral vessels and cerebral aneurysm.

Case Report

A 63-year-old woman, the proband, was admitted to our hospital after 2 days of vertigo, speech disturbance, and difficulty in standing. She had a history of hypertension and smoking. The patient had not experienced either heart disease or surgical treatment of the chest. Physical examination revealed horizontal gaze nystagmus, scanning speech, right

limb ataxia, and unsteadiness. She had many skin-colored, soft and firm, asymptomatic papules of varying sizes on her face, mainly around the root and ala of her nose and on her forehead (Fig. 1). The papules were smaller than 5 mm in diameter. No telangiectatic vessels or ulcerations were found on the papules. No other types of eruptions, including cylindroma, were seen. The patient had noticed her papules before the age of 20 years. The papules had gradually increased in size and number. Blood cell and biochemical examinations were normal, except for hypercholesterolemia. Chest radiography revealed no abnormalities in the lung field. Blood gas analyses using samples from both arms were normal. Electrocardiography, transthoracic echocardiography, and abdominal ultrasonography did not reveal any abnormalities.

Angiography was performed on admission. Right subclavian arteriography disclosed abnormal dilation of the branches of the right subclavian artery (Fig. 2A). In addition, capillary vessels filled via these subclavian artery branches in the upper site of the right lung were demonstrated, whereas the pulmonary artery in the right lung was not visualized (Fig. 2B). Finally, the right upper pulmonary veins

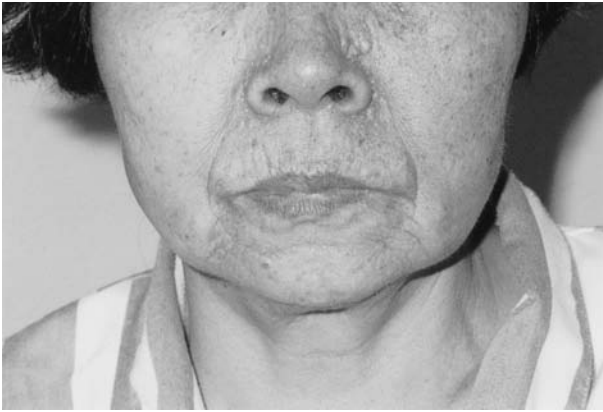


Fig. 1 Photograph of the patient's lower face showing many skin-colored, soft and firm, asymptomatic papules of varying sizes. The papules are smaller than 5 mm in diameter, primarily located around the root and ala of her nose and on her forehead. No telangiectatic vessels or ulcerations are present on the papules.

were demonstrated (Fig. 2C). Brachiocephalic arteriography disclosed an abnormally dilated anastomosis between the right vertebral artery and the thyrocervical trunk (Fig. 2D). Right vertebral arteriography demonstrated a defect in the right posterior inferior cerebellar artery (Fig. 2E, F). Left subclavian arteriography did not reveal any vascular abnormalities. Right common carotid arteriography disclosed a saccular aneurysm arising from the right middle cerebral artery (Fig. 2G).

Magnetic resonance imaging demonstrated an infarction at the lower region of the right cerebellar hemisphere that was supplied by the posterior inferior cerebellar artery (Fig. 3). Magnetic resonance angiography showed that pulmonary arteries appeared normal.

Histological examination of the papules revealed numerous horn cells, islands of basaloid cells with palisading periphery, absence of cytological atypia, positive foreign body giant cell reaction, and fibrocellular stroma (Fig. 4). The diagnosis was multiple trichoepithelioma.

Figure 5 charts the pedigree of the family. The proband's grandmother, mother, and uncle had similar eruptions on their faces, although we were unable to obtain their photographs. The proband's mother died of subarachnoid hemorrhage at the age of 84 years, and her uncle died of subarachnoid hemorrhage in his middle age. The diagnoses were based on computed tomography, without angiography. The cause of her grandmother's death is

unknown. Genetic analyses were not performed in any members of this family.

The patient's symptoms were relieved immediately after medication with ozagrel sodium and thromboxane A₂-inhibitory agents. We provided information regarding surgical treatment for the cerebral aneurysm, but she refused surgical intervention. At one year after her initial examination, the aneurysm has not ruptured.

Discussion

The proband was admitted to our hospital after suffering right cerebellar infarction due to occlusion of the right posterior inferior cerebellar artery. Further examinations revealed multiple trichoepithelioma and vascular abnormalities, including right subclavian-pulmonary collateral vessels and a cerebral aneurysm.

In our case, the right subclavian-pulmonary collateral vessels anastomosed at the capillary vessel level of the right lung. Patients with tetralogy of Fallot, with or without pulmonary atresia, show major aortopulmonary collateral arteries, which originate primarily from the descending aorta and supply peripheral pulmonary arteries.⁶⁾ Occasionally, the abnormal collateral arteries originate from other arteries, including the subclavian artery. In our proband, no congenital heart disease was found and the right subclavian-pulmonary collateral vessels directly supplied capillary vessels in the lung, but not the pulmonary arteries. Therefore, the collateral vessels in our proband were different from such major aortopulmonary collateral arteries. Moreover, patients with inflammatory pulmonary diseases or surgical treatment of the chest may suffer secondary dilation of the bronchial artery. In our proband, the right subclavian-pulmonary collateral vessels did not originate from the aorta, and none of these complications were found.

In addition to the arterial abnormalities, our proband also harbored an unruptured cerebral aneurysm. Some members of her family had suffered subarachnoid hemorrhage, and may also have had cerebral aneurysms. Occasionally, cerebral aneurysm occurs in members of the same family.⁸⁾ However, all members in this family who suffered subarachnoid hemorrhage or cerebral aneurysm had multiple trichoepithelioma. Therefore, we suggest that multiple trichoepithelioma is strongly associated with cerebral aneurysm in this family.

Cerebral aneurysms or other vascular abnormalities are a complication in some patients with tuberous sclerosis.^{2,9)} Patients with trichoepithelioma may show systemic abnormalities including

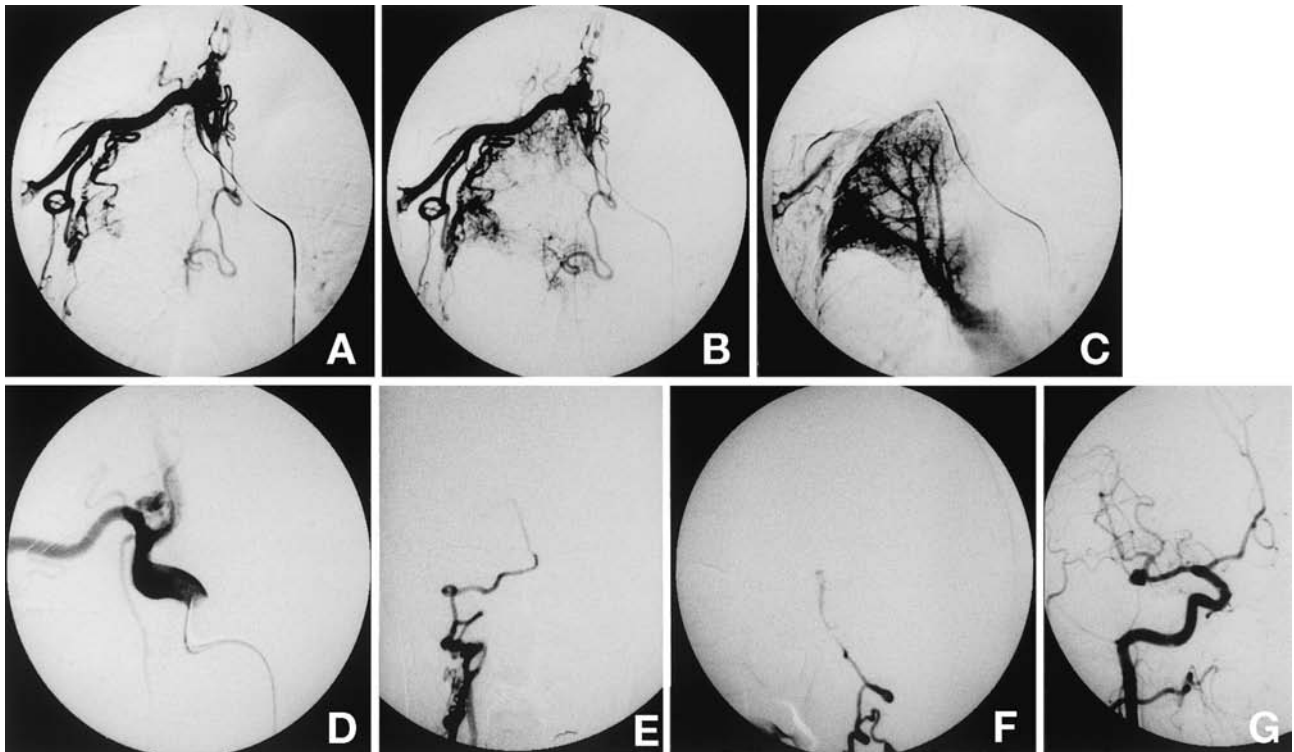


Fig. 2 Angiograms performed on admission. A-C: Right subclavian arteriograms revealing abnormal dilation of branches from the right subclavian artery (A, arterial phase). The capillary vessels in the upper region of the right lung are filled via these branches, but the pulmonary artery in the right lung is not visualized (B, capillary phase). The right upper pulmonary veins are demonstrated (C, venous phase). D: Brachiocephalic arteriogram demonstrating an anastomosis between the vertebral artery and the abnormally dilated thyrocervical trunk. E, F: Right vertebral arteriograms, anteroposterior (E) and lateral views (F), demonstrating a defect in the right posterior inferior cerebellar artery. G: Right common carotid arteriogram demonstrating a cerebral aneurysm arising from the right middle cerebral artery.

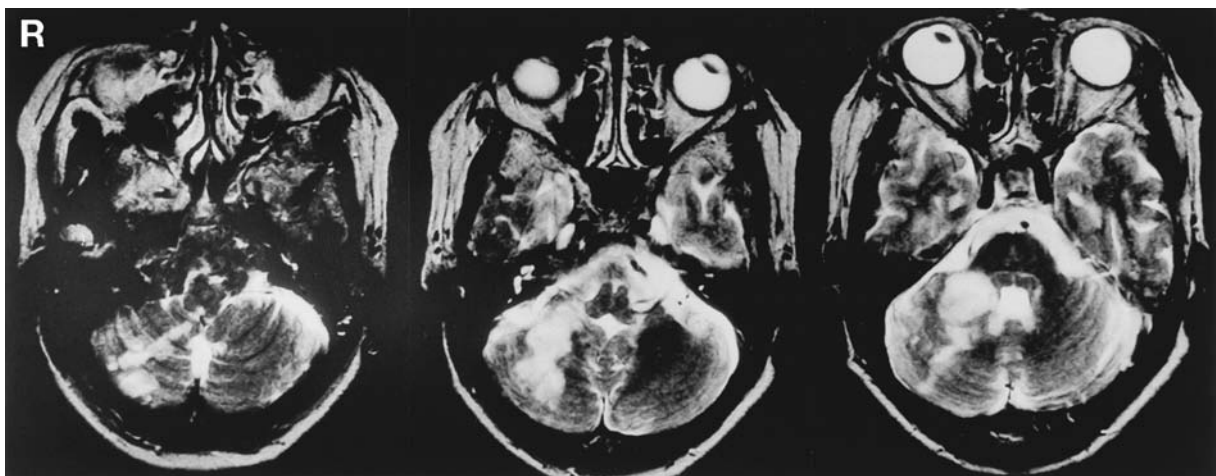


Fig. 3 Magnetic resonance images demonstrating infarction in the lower region of the right cerebellar hemisphere supplied by the posterior inferior cerebellar artery.

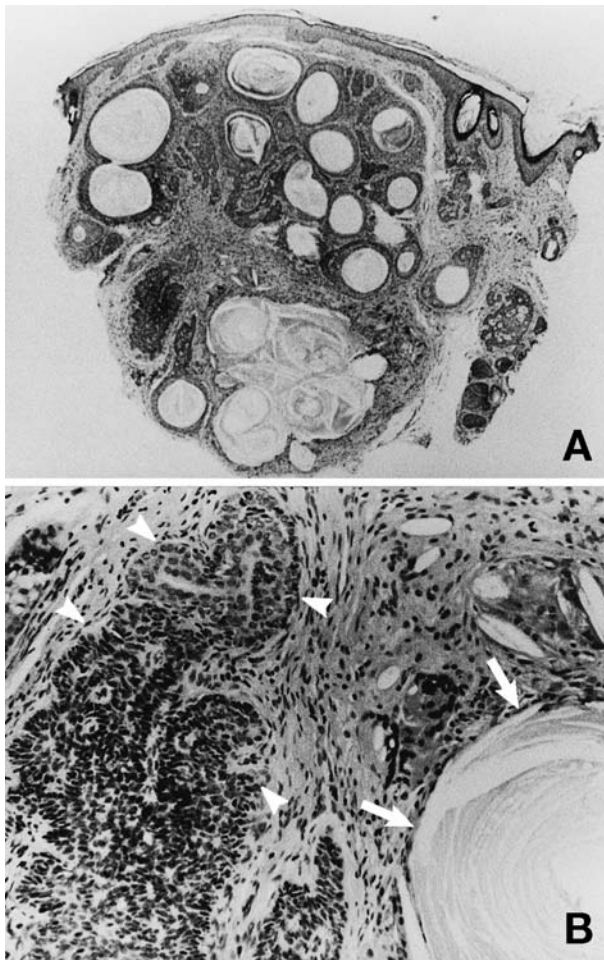


Fig. 4 Photomicrographs of the papules showing the presence of numerous horn cells (arrows), islands of basaloid cells (arrowheads) with peripheral palisading, absence of cytological atypia, positive foreign body giant cell reaction, and fibrocellular stroma. Hematoxylin-eosin stain, $\times 20$ (A), $\times 100$ (B).

cheilognathopalatoschisis, jaw cyst, epilepsy, oligophrenia, bradykinesia, labyrinthine deafness, adipositas, Dupuytren contracture, and disturbance of micturition.^{1,5,7}) However, familial multiple trichoepithelioma associated with systemic vascular abnormalities, including subclavian-pulmonary collateral vessels and cerebral aneurysm or subarachnoid hemorrhage, has not been reported. These are new and important complications of familial multiple trichoepithelioma. Moreover, no causative gene mutation has been reported, although there are many factors other than genetic factors involved in the etiology and pathogenesis of intracranial aneurysms. The present case and other

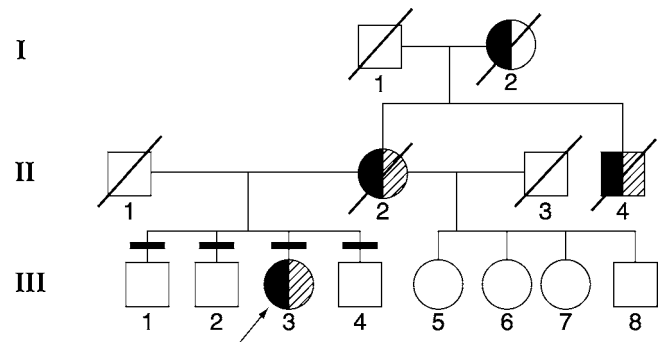


Fig. 5 Pedigree of the patient's family. Proband's grandmother (I-2), mother (II-2), and uncle (II-4) had similar eruptions on their faces. The patient's mother and uncle died of subarachnoid hemorrhage at the age of 84 years and in middle age, respectively. The diagnoses were based on computed tomography, but not angiography. The cause of her grandmother's death is unknown. arrow: present case, ■: facial eruption, ▨: subarachnoid hemorrhage or cerebral aneurysm, —: examined only physically by authors, /: died.

studies of cerebral aneurysms suggest that the dermatological assessment of pedigrees is important in the investigation and understanding of familial intracranial aneurysms.

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Address reprint requests to: Y. Inatomi, M.D., Stroke Center, Saiseikai Kumamoto Hospital, 5-3-1 Chikami, Kumamoto 861-4193, Japan.