jected to PMF that uses matrix-assisted laser desorption ionization/time-of-flight mass spectrometry system (Voyager-Elite Biospectrometry Workstation, Applied Biosystems) combined with sequence database searches (MS-fit) (fig. 2C) and partial amino acid sequencing with automatic peptide sequencer (Model 492HT, Applied Biosystems) after digesting the proteins on 2-DE gels with endoprotease Lys-C [5]. Protein identification by PMF showed that the 49-kDa protein was α-enolase (fig. 2C). Meanwhile, the partial amino acid sequencing retrieved the sequences PDDPS and YON, corresponding to codons 264–268 and 407–409 of α-enolase, respectively (fig. 2D).

Discussion

The patient reported here presented progressive sensorimotor neuropathy and encephalopathy with changes in personality, disturbed consciousness and cognitive decline associated with occult gastric adenocarcinoma. His sera contained antineuronal autoantibody that labeled the patient's carcinoma tissue and specifically reacted with a 49-kDa protein in the mouse brain. We biochemically identified this 49-kDa protein as α-enolase. Although it has still not been proven that the anti-α-enolase antibodies in the patient's serum have anything to do with his sensorimotor neuropathy and encephalopathy, we consider that the anti-α-enolase antibodies are likely to contribute to his multifaceted neurological disturbances for the following reasons: his neurological symptoms temporarily went into remission with IVIg therapy that may have blocked the harmful action of autoantibodies and, furthermore, his symptoms improved dramatically and were not exacerbated again after removal of his gastric adenocarcinoma which cells intensely expressed α-enolase in their cell bodies, which were immunoreacted with the patient's serum.

α-Enolase is one of the subunits of mammalian enolase, a glycolytic enzyme, and expressed ubiquitously [6]. Some may argue against our interpretation that anti-α-enolase antibody emerging in association with gastric cancer specifically caused disturbances confined to the nervous system, because α-enolase is a ubiquitously expressed enzyme. Usually organ-specific autoimmune diseases have tissue-specific enzymes as target autoantigens [7]. However, like enolase, other ubiquitously expressed enzymes have been associated with organ-specific autoimmunity, for example, dihydrolipoamide acetyltransferase is an autoantigen in primary biliary cirrhosis [8]. Furthermore, there have been a few reports that α-enolase was the target antigen that reacted with autoantibodies detected in cancer-associated retinopathy [9] and Hashimoto's encephalopathy [10].

The patient presented here had occult gastric adenocarcinoma that is uncommon in paraneoplastic neurological syndromes, but it has been reported that gastric adenocarcinoma may be associated with paraneoplastic encephalopathy that usually precedes the diagnosis of cancer [11]. Furthermore, insofar as we are aware, this is the first report that shows α-enolase may be associated with paraneoplastic encephalomyelitis in the setting of gastric cancer. We would also like to emphasize that PMF combined with 2-D PAGE is an easy and useful technique in identifying autoantigens in paraneoplastic syndromes.

References

1 Graus F, Cordon-Cardo C, Posner JB: Neuronal antinuclear antibody in sensory neuronopathy from lung cancer. Neurology 1985;35:538–543.
2 Dropcho EJ: Antiamphiphysin antibodies with small-cell lung carcinoma and paraneoplastic encephalomyelitis. Ann Neurol 1996;39:659–667.
3 Voltz R, Gultekin SH, Rosenfeld MR, Gerstner E, Eichen J, Posner JB, Dalmau J: A serologic marker of paraneoplastic limbic and brain-stem encephalitis in patients with testicular cancer. N Engl J Med 1999;340:1788–1795.
4 Honnorat J, Aguera M, Zalc B, Goujet C, Quach T, Antoine JC, Belin MF: POP66, a paraneoplastic encephalomyelitis-related antigen, is a marker of adult oligodendrocytes. J Neuropathol Exp Neurol 1998;57:311–322.
5 Kaneko K, Nakamura A, Yoshida K, Kametani F, Higuchi K, Ikeda S: Glial fibrillary acidic protein is greatly modified by oxidative stress in aceruloplasminemia brain. Free Radic Res 2002;36:303–306.
6 Marangos PJ, Schmechel D, Zis AP, Goodwin FK: The existence and neurobiological significance of neuronal and glial forms of the glycolytic enzyme enolase. Biol Psychiatry 1979;14:563–579.
7 Banga JP, McGregor AM: Enzymes as targets for autoantibodies in human autoimmune disease: Relevance to pathogenesis? Autoimmunity 1991;9:177–182.
8 Coppel RL, McNeilage LJ, Surh CD, Van de Water J, Spithill TW, Whittingham S, Gershwin ME: Primary structure of the human M2 mitochondrial autoantigen of primary biliary cirrhosis: Dihydrolipoamide acetyltransferase. Proc Natl Acad Sci USA 1988;85:7317–7321.
9 Adamus G, Aptsiauri N, Guy J, Heckenlively J, Flannery J, Hargrave PA: The occurrence of serum autoantibodies against enolase in cancer-associated retinopathy. Clin Immunol Immunopathol 1996;78:120–129.
10 Ochi H, Horiuchi I, Araki N, Toda T, Araki T, Sato K, Murai H, Osoegawa M, Yamada T, Okamura K, Ogino T, Mizumoto K, Yamashita H, Saya H, Kira J: Proteomic analysis of human brain identifies alpha-enolase as a novel autoantigen in Hashimoto's encephalopathy. FEBS Lett 2002;528:197–202.
11 Graus F, Keime-Guibert F, Rene R, Benyahia B, Ribalta T, Ascaso C, Escaramis G, Delattre JY: Anti-Hu-associated paraneoplastic encephalomyelitis: Analysis of 200 patients. Brain 2001;124:1138–1148.

Takahiko Tokuda, Third Department of Internal Medicine
Shinshu University School of Medicine
3-1-1 Asahi, Matsumoto 390-8621 (Japan)
Tel. +81 263 372673, Fax +81 263 340929
E-Mail ttokuda@gipac.shinshu-u.ac.jp

Eur Neurol 2004;51:233–235
DOI: 10.1159/000078548

Bilateral Anterior Inferior Cerebellar Artery Territory Brachium pontis Infarcts of Probable Hemodynamic Cause

Roger Kalla[a], *Thomas Mayer*[b], *Gerhard F. Hamann*[a]
Departments of [a] Neurology and [b] Neuroradiology,
Ludwig Maximilian University, Klinikum Grosshadern,
Munich, Germany

Introduction

Infarcts in the territory of the anterior inferior cerebellar artery (AICA) are rare [1–3]. The clinical signs first described by Adams [4] in 1943 in a patient who experienced rotational vertigo, vomiting, tinnitus and dysarthria are dominated by brain stem signs. This is due to the fact that the AICA supplies the middle and lower third of the lateral pontine region and the anterolateral parts of the cerebellum with the middle cerebellar peduncle, the flocculus and the anterior part of the cerebellar lobules [2]. We present the case of a 51-year-old man with a symmetrical infarct in the bilateral middle cerebellar peduncles and the left flocculus. The occlusion of both vertebral

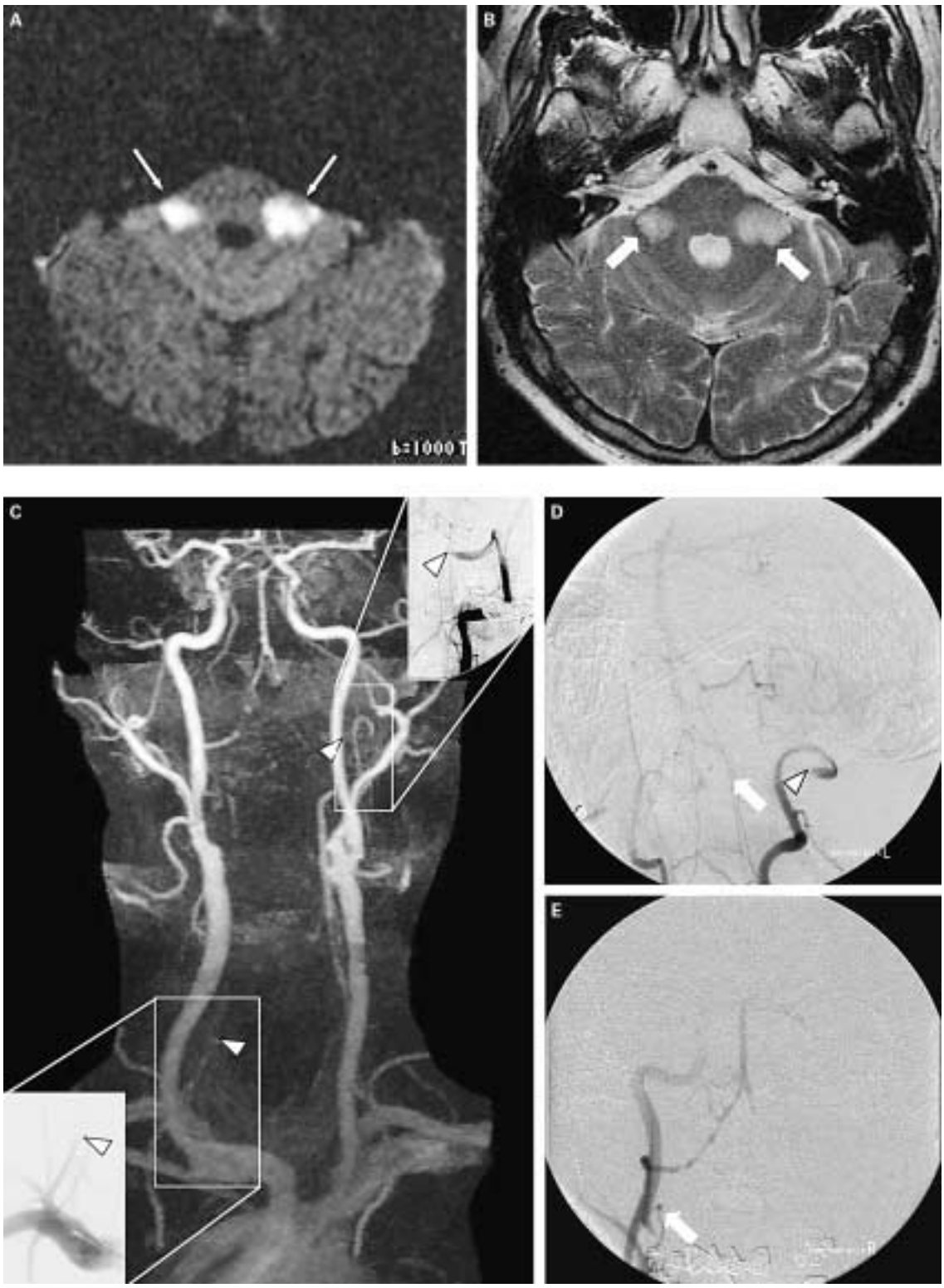

Fig. 1. A, **B** Cranial magnetic resonance imaging revealed bilateral middle cerebellar peduncular infarctions (**A**, arrows, diffusion-weighted MRI, b = 1,000; **B**, arrows, T2 MRI) and an infarction in the flocculus on the left side. All infarcts were confined to the territory of the anterior inferior cerebellar arteries. **C–E** Vertebral angiography showed occlusion of the right and left vertebral arteries (**C**, arrowheads) and collateralization of both vertebral arteries (**D**, **E**, arrows).

arteries suggested a hemodynamic mechanism involving hypoperfusion and subsequent infarction in the middle cerebellar peduncles.

Case Report

The patient was admitted to our hospital after 3 days of progressive gait and postural imbalance, dizziness, numbness of the left side of the face and dysarthria. Three months before admission, he had had recurrent episodes of rotatory vertigo and visual disturbances lasting several seconds. He also had vascular risk factors, hypertension, peripheral arteriosclerosis and had smoked for 20 years. The patient history documented an infarct of the right middle cerebral artery territory 7 years before which caused no neurological deficits. The MRI revealed microangiopathy, but no territorial infarct. Neurological examination at admission showed a conscious and oriented patient with bilateral horizontal gaze nystagmus, ocular tilt reaction to the left, numbness of the left side of the face, slight right-sided facial weakness, dysarthria, ataxia in all four limbs and axial lateropulsion to both sides, which made it impossible for him to stand. Muscle strength, deep tendon reflexes and sensations were all normal. Babinski's sign was not present. An electrocardiogram was normal, and a transthoracic and transesophageal echocardiogram revealed a moderately dilated left atrium without thrombi. The MRI with fast echoplanar diffusion-weighted images (1.5 T, Siemens, Vision) showed marked hyperintensity signals (fig. 1A, arrows) bilaterally in the middle cerebellar peduncles on the left more than on the right side and in the left flocculus as a cause of the symptoms. Other areas in the brain stem or cerebellum were not involved. Blood chemistry including homocysteine and screening for thrombophilic risk factors was normal. The Doppler sonography and transcranial Doppler sonography revealed a 50% stenosis of the arteria carotis interna and bilateral low flow in the vertebral arteries. Digital subtraction arteriography via a transfemoral approach disclosed extracranial occlusion of the left vertebral artery at the level of C1 (fig. 1C, arrowheads) and a 50–60% stenosis at the origin of the vertebral artery. The intradural segment of the left vertebral artery was collateralized by the arteria spinalis anterior (fig. 1D, arrowhead). The right vertebral artery was occluded at the exit from the subclavian artery (fig. 1C) and had a collateralization through muscle branches at the level of C2 (fig. 1E). The top of the basilar artery up to the issue of the superior cerebellar artery was supplied by the right internal carotid artery via the posterior communicating artery on the same side. The left posterior cerebral artery was filled by a leptomeningeal anastomosis, and the left carotid artery showed an arteriosclerotic narrowing in the pars petrosa. The AICAs and superior cerebellar arteries could be clearly visualized. Under the misconception that the occlusion of the left vertebral artery was relatively fresh, we treated the patient with 24-hour infusion therapy with Aggrastat, which might have led to a recanalization of the left vertebral artery. However, the unchanged findings on angiographic reexamination the next day prompted us to administer heparin intravenously. The patient improved under stroke unit treatment over the next days. He became able to sit independently, the limb ataxia lessened and there were no more attacks of vertigo during mobilization. However, the pronounced dysarthria remained. Long-term secondary stroke prevention was achieved by oral anticoagulation.

Discussion

Cranial MRI demonstrated bilateral cerebellar infarction of the middle cerebellar peduncles in our patient. The middle cerebellar peduncle, the flocculus and the anterior part of the cerebellar lobules [2] are mainly supplied by the AICA. Acute infarcts in the territory of the AICA are rare, having a frequency of 0.5% of all acute strokes. They account for 5.2% of infarcts affecting the vertebrobasilar territory [5].

The complete AICA syndrome first described by Adams [4] in a single patient with vertigo, vomiting, trigeminal sensory loss, Horner's syndrome, peripheral facial palsy, ipsilateral hearing loss with tinnitus, dysmetria of the limbs, dysarthria and contralateral temperature and sensory loss sparing the face is rare [2]. The usual clinical manifestation is a crossed brain stem syndrome. Only three cases of infarcts in the territory of the AICAs and restricted to the bilateral territory of the middle cerebellar peduncles have been reported [1, 6, 7]. In our case, the vertebral angiography revealed extracranial occlusion of the left vertebral artery at the level of C1 and occlusion of the right vertebral artery at its exit from the subclavian artery; however, the AICAs were clearly visualized. This suggests that a hemodynamic mechanism with bilateral, focally lowered blood flow in the areas mainly supplied by the AICA subsequently led to an infarction in the middle cerebellar peduncles. These areas might be the most vulnerable parts of the territory affected by ischemia of the AICA [2], and thus other areas supplied by the AICA were not involved. The vertebrobasilar occlusion in our patient might have been caused by an atherothrombotic mechanism at the site of an underlying stenosis in these vessels. An atherosclerotic etiology is considered the most frequent cause of AICA infarcts. [3, 5]

Acknowledgement

We thank Ms. J. Benson for copyediting the manuscript.

References

1 Akiyama Y, Takizawa S, Takuoka K, Ohnuki Y, Kobayashi N, Shinohara Y: Bilateral middle cerebellar peduncle infarction caused by traumatic vertebral artery dissection. Neurology 2001;56:693–694.
2 Amarenco P, Hauw JJ: Cerebellar infarction in the territory of the anterior and inferior cerebellar artery: A clinicopathological study of 20 cases. Brain 1990;113:139–155.
3 Amarenco P, Rosengart A, DeWitt LD, Pessin MS, Caplan LR: Anterior inferior cerebellar artery territory infarcts. Mechanisms and clinical features. Arch Neurol 1993;50:154–161.
4 Adams RD: Occlusion of anterior inferior cerebellar artery. Arch Neurol Psychiatry 1943;49:765–770.
5 Roquer J, Lorenzo JL, Pou A: The anterior inferior cerebral artery infarcts: A clinical-magnetic resonance imaging study. Acta Neurol Scand 1998;97:225–230.
6 Sato K: Bilateral middle cerebellar peduncle infarction (in Japanese). No To Shinkei 1998;50:1036–1037.
7 Tsukamoto T, Seki H, Saitoh J, Watanabe K: A case of bilateral cerebellar peduncle infarction. Jpn J Med 1991;30:376–378.

Gerhard F. Hamann, MD, Department of Neurology
Klinikum Grosshadern, Marchioninistrasse 15
DE–81377 Munich (Germany)
Tel. +49 89 7095 3670, Fax +49 89 7095 3677
E-Mail hamann@brain.nefo.med.uni-muenchen.de