

dysarthria is usually associated with other symptoms, such as vomiting, limb ataxia, or axial lateropulsion.

In posterior inferior cerebellar artery and anterior inferior cerebellar artery territory infarcts dysarthria is an unusual symptom.⁴ There were no detailed phonetic descriptions in the cases reported, and brain stem signs were present as well. So, it might be suspected that his speech impairment resulted from an involvement of brain stem structures.

Lechtenberg and Gilman² first noted that dysarthria developed most often after damage extending into the superior paravermal segments of the left cerebellar hemisphere. Amarenco *et al*³ confirmed this finding in a patient with an isolated cerebellar dysarthria after a small infarction in the left paravermal zone; but they considered a minute mirror image lesion to be of no importance, the patient's hand dominance was not reported, and MRI was not performed. Nevertheless, both studies strongly implicated the left cerebellar hemisphere in the development of dysarthria. Ackermann *et al*¹ did not corroborate the notion of an exclusive left sided paravermal cerebellar speech cortex; three of the four dysarthric patients in their study had unilateral right sided ischaemia due to occlusion of the superior cerebellar artery; all of them were right handed. The fourth had a bilateral cerebellar infarction.

More recently, increasing evidence suggests a role for the cerebellum in cognitive functions such as language. Silveri *et al*⁵ reported a patient with agrammatical speech after a posterior inferior cerebellar artery infarction, suggesting a right cerebellar hemispheric dominance for language function. It is not clear if that hemispheric dominance exists for speech function.

The well delineated lesion in our patient agrees with the hypothesis that the right cerebellar hemisphere is the most likely site for cerebellar speech function as cerebro-cerebellar connections are predominantly contralateral and the left cerebral hemisphere is dominant for speech function in right handed people. However, it may also be possible that the site of the infarct (the paravermal zone) is more important than the side.

In conclusion, as well as describing an exceedingly uncommon clinical presentation of a superior cerebellar artery infarction, our report suggests the superior right paravermal zone as the possible site of the cerebellar speech centre, and supports the hypothesis of functional interrelation between supratentorial structures and cerebellum in functional domains outside the motor system.

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- 1 Ackermann H, Vogel M, Petersen D, Poremba M. Speech deficits in ischaemic cerebellar lesions. *J Neurol* 1992;239:223-7.
- 2 Lechtenberg R, Gilman S. Speech disorders in cerebellar disease. *Ann Neurol* 1978;3: 285-90.
- 3 Amarenco P, Chevrie-Muller C, Roulet E, Boussier MG. Paravermal infarct and isolated cerebellar dysarthria. *Ann Neurol* 1991;30: 211-3.
- 4 Barth A, Bogousslavsky J, Regli F. The clinical and topographic spectrum of cerebellar

infarcts: a clinical-magnetic resonance imaging correlation study. *Ann Neurol* 1993;33: 451-6.

- 5 Silveri MC, Leggio MG, Molinari M. The cerebellum contributes to linguistic production: a case of agrammatical speech following a right cerebellar lesion. *Neurology* 1994;44: 2047-50.

Bilateral internal carotid artery agenesis

Bilateral internal carotid artery agenesis is extremely rare. Agenesis of the internal carotid artery may cause cerebrovascular diseases such as subarachnoid haemorrhage or cerebral ischaemia. We describe a patient with bilateral internal carotid artery agenesis manifesting as intracerebellar haemorrhage.

A 57 year old woman suddenly developed vertigo and vomiting with severe headache, and was brought to our hospital by ambulance on 19 November 1993. She was alert with slight ataxia on the right side. Brain CT showed a haematoma 2 cm in diameter in

the subcortical region of the right cerebellar hemisphere. Brain MRI showed no vascular malformation near the haematoma, but an MR angiogram (base view) showed abnormal dilatation of the basilar artery and absence of the internal carotid arteries. Both anterior cerebral arteries and middle cerebral arteries were filled from the enlarged posterior communicating arteries. Transfemoral cerebral angiography showed no bifurcation of either common carotid artery and absence of bilateral internal carotid arteries. The ophthalmic arteries were supplied through the middle meningeal artery. Left vertebral angiography showed an enlarged and tortuous basilar artery. A high resolution CT of the skull base showed complete absence of the carotid canals on both sides, indicating bilateral internal carotid artery agenesis.

The patient gradually improved with conservative medical treatment and was discharged on 13 December with no neurological deficit. She died suddenly at home of heart failure on 30 January, 1994.

Congenital internal carotid artery agenesis is a very rare anomaly, with only about 100



Figure 1 Left: CT showing a haematoma in the subcortical region of the right cerebellar hemisphere. Right: High resolution skull base CT showing complete absence of the carotid canals on both sides.

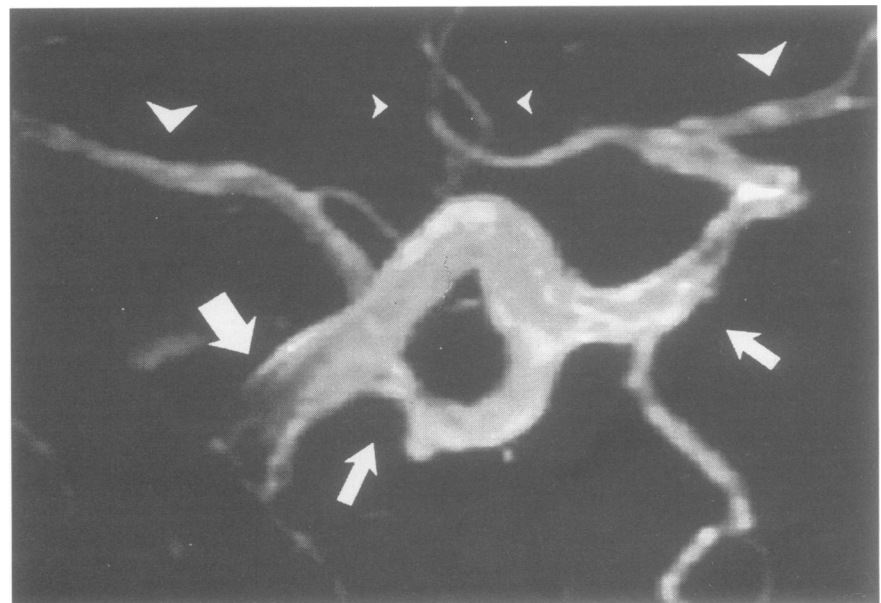


Figure 2 MR angiogram (base view) showing abnormal dilatation of the basilar artery (large arrow) and absence of the bilateral ICAs. Both anterior cerebral arteries (small arrow heads) and middle cerebral arteries (large arrow heads) were filled from the enlarged posterior communicating arteries (small arrows).

patients described since the first description in 1787.¹ In most cases, agenesis is unilateral, with only 26 reported cases of bilateral agenesis. Most of the early cases were discovered by cadaver dissection. In 1972 Boudin reported the first living patient with bilateral internal carotid artery agenesis, based on an angiographical diagnosis.² There is no agreement on the development of the common carotid artery and its two branches, the internal carotid artery and the external carotid artery. The two theories for the embryogenesis of these arteries are that the common carotid artery and the proximal parts of the internal carotid artery and external carotid artery arise together from the third aortic arch; or that only the proximal part of the internal carotid artery arises from the third aortic arch, and the common carotid and external carotid arteries arise from the aortic sac.⁴

Agenesis and hypoplasia should be differentiated. Agenesis is the complete developmental failure of an organ and its primordium, whereas hypoplasia is the incomplete development of a structure. The primordial internal carotid artery is well defined by the fourth embryonic week, whereas the skull base does not form until the fifth to sixth weeks of fetal life. Therefore, if the embryonic primordium of the internal carotid artery fails to develop (agenesis), no internal carotid artery is present when the skull base is formed, and no carotid canal develops. By contrast, a relatively mild or relatively late insult occurring in the course of development of the skull base portion of the internal carotid artery will result in a hypoplastic internal carotid artery within a hypoplastic carotid canal.³ Therefore, agenesis and hypoplasia of the internal carotid artery can be differentiated by the demonstration of the carotid canal in the skull base. Some authors have confused agenesis with hypoplasia, and carotid canals or internal carotid arteries were found in their patients.

The anterior cerebral circulation is most commonly supplied through enlarged basilar and posterior communicating arteries in patients with agenesis of the internal carotid artery. Occasionally an abnormal trans-sellar anastomosis or an anastomosis between the external carotid and intracranial systems provide collateral flow. Brain CT or MRI can demonstrate the enlarged abnormal vessels. In our patient, MRI showed abnormal dilatation of the basilar artery and absence of the internal carotid arteries. Therefore, MRI is a useful diagnostic tool for this disease. Especially, MR angiography can show the further relation between anterior and posterior cerebral circulation clearly. This is the first report to describe the value of MR angiography.

Agenesis of the internal carotid artery may mainly cause cerebrovascular disease. Previous manifestations included subarachnoid haemorrhage in seven patients, cerebral ischaemia in five, seizure in three, brain tumour in two, intracerebral haemorrhage in one, chronic subdural haematoma in one, syncope in one, cancer in one, and cardiac anomaly in one. Ours is the first patient to present with intracerebellar haemorrhage. The haematoma was located in the subcortical portion of the cerebellar hemisphere, and there was no lesion near the haematoma. Spontaneous haemorrhage of the cerebellum usually occurs in the dentate nucleus region. In this case the location of the haematoma was unusual, suggesting that the haemor-

rhage might be caused by haemodynamic stress.

The prognosis for internal carotid artery agenesis is unknown, because of the lack of detail in previous reports. Our patient died of heart failure, but no necropsy was permitted. Her death may have been related to the recurrence of cerebrovascular disease.

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- 1 Tode. *Medizinisch chirurgische bibliothek (Kopenhagen)* 1787;10:408. Cited by: Fisher AGT. A case of complete absence of both internal carotid arteries, with a preliminary note on the developmental history of the stapodial artery. *J Anat* 1914;48:37-46.
- 2 Boudin G. Bilateral aplasia of the internal carotid artery. *Rev Neurol (Paris)* 1972;127:329-40.
- 3 Quint DJ, Silbergleit R, Young WC. Absence of the carotid canals at skull base CT. *Radiology* 1992;182:477-81.
- 4 Lie TA. *Congenital anomalies of the carotid arteries*. Amsterdam: Excerpta Medica, 1968: 44-9.

Possible distinct pathogenesis in low responder myasthenia gravis: association of soluble interleukin-2 receptor with acetylcholine receptor antibody titre or abnormal thymus

In myasthenia gravis there is an increase in soluble interleukin-2 receptor (sIL-2R), which is associated with cellular immunity. Confalonieri *et al*¹ showed that the concentration of sIL-2R correlated with the severity or the activity of the disease, and that there was no association of sIL-2R concentration with antibody to fetal calf acetylcholine receptor (AChR). On the other hand, Cohen-Kaminsky *et al*² reported a progressive decline of sIL-2R in myasthenia gravis after thymectomy which correlated with the clinical outcome. To elucidate the pathogenesis and cellular immunity in myasthenia gravis, we studied sIL-2R concentrations in 32 patients before immunosuppressive treatment.

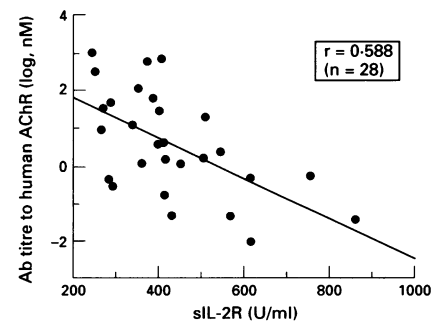
All 32 patients (eight male and 24 female) participating in this study were older than 6 years (mean 31.7 (range 7 to 72) years at onset), because sIL-2R concentration has been reported to be higher in healthy infants under 6 years old than in adults.³ The number of patients with type I, IIa, IIb, or III myasthenia gravis, according to Osserman's classification, was 12, 10, five, and five respectively. The thymus was examined for abnormality by CT, and thymectomy was performed on 21 patients, including one whose thymus was atrophic. All thymuses were categorised histologically after removal, as thymoma, hyperplasia, atrophy, or normal. Patients' serum samples were frozen at -70°C until assayed for sIL-2R and antibody to AChR. The sIL-2R was measured by the cellfree interleukin-2 receptor bead-assay kit (T cell diagnosis C Ltd, Cambridge MA, USA) using two monoclonal antibodies directed against two different epitopes on IL-2R. The normal value of sIL-2R measured in serum samples obtained from 110 unrelated healthy controls was 390.7 (SD

101.7) U/ml. Samples were assayed in duplicate and the intra-assay coefficient of variance was 9.3%. Antibody to human AChR was measured by immunoprecipitation. The antigen used was human AChR purified from rhabdomyosarcoma cell line TE 671. The normal value (mean + 3SD) was 0.12 nM. Intra-assay coefficient of variance was 9.0%.

The sIL-2R correlated negatively with antibody titre to human AChR (figure; $r = 0.588$, $P < 0.01$). Thymic histology showed an association with sIL-2R concentration (one way ANOVA, $p < 0.025$), but the Osserman clinical type did not. The sIL-2R in patients with thymoma (317.2 (64.1) U/ml) was significantly lower than in the normal subjects, or patients with atrophic or normal thymus (535.7 (174.1) U/ml; Scheffe test, $P < 0.025$), but not significantly lower than in patients with hyperplasia (426.2 (126.6) U/ml). All four patients with a high concentration of sIL-2R (more than mean + 2SD) had a low AChR antibody titre (< 1 nM).

Some publications^{1,2} have shown a positive correlation between sIL-2R and disease activity in myasthenia gravis, which does not coincide with our result. It is also well established that patients with myasthenia gravis with thymic hyperplasia or thymoma have a higher titre of AChR antibody than patients with a normal thymus. According to our results of the negative correlation pattern of sIL-2R with AChR antibody titre and the association of sIL-2R with thymic abnormality in myasthenia gravis, it is not likely that sIL-2R is merely a T cell activation marker, because AChR antibody production is T cell dependent.

The problem is to decide what the pathogenic mechanism is in seronegative patients. Mossman *et al* showed that the immunoglobulin from seronegative patients with myasthenia gravis could induce impairment of chemical transmission at neuromuscular junctions in mice.⁴ Cohen-Kaminsky *et al* pointed out that the group of patients with myasthenia gravis with low AChR antibody titre seemed to represent a particular subgroup of the disease, which might be associated with a pathogenic mechanism involving AChR antibody produced in undetectable amounts but especially pathogenic antibody.² We previously reported that ocular myasthenia gravis had a different genetic background from generalised myasthenia gravis: the ocular type showed a low AChR antibody titre and no antinuclear antithy-



Correlation between sIL-2R and antibody titre to human AChR. Correlation was assessed in 28 patients in whom AChR antibody was detected. The concentrations of sIL-2R in four patients without AChR antibody were 475, 419, 785 and 516 U/ml.