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 autopsies; only 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 internal carotid artery and its 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.3

Agenesis and hypoplasia should be differentiated. Agenesis is the complete developmental failure of an organ and its primary manifestations are absence, whereas hypoplasia is the incomplete development of a structure. The primordial internal carotid artery is well defined by the fourth embryonic week, whereas it 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, whereas the primary manifestation of internal carotid agenesis is the hypoplastic internal carotid artery within a hypoplastic carotid canal.4 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 between the two 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 bilateral ophthalmic artery, which might be the explanation of agenesis and hypoplasia of both internal carotid arteries, with a preliminary note on the developmental history of the stapedial artery.7 Anat 1914:48:37-46.4

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 the pathogenesis of myasthenia gravis. Confalonieri et al1 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 al2 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, 5, and 5, 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. Patents' serum samples were frozen at -70°C until assayed for sIL-2R and antibody to AChR. The sIL-2R was measured by the cell free interleukin-2 receptor bead- assay kit (T cell diagnosis Co Ltd, Cambridge CA, 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 intraassay coefficient of variance was 9.3%. Antibody to human AChR was measured by immunoprecipitation. The antibody was used undiluted. It is also well established from rhombomyoarcoma cell line TE 61. The normal value (mean ± 3SD) was 0.12 nM. Intra-assay coefficient of variance was 9.0%.

Some publications1 have shown a positive correlation between sIL-2R and disease activity in myasthenia gravis, which does not coincide with our results. 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 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. Most patients with myasthenia gravis could induce impairment of chemical transmission at neuromuscular junctions in mice.4 Cohen-Kaminsky et al2 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.1 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 anuclear antithyroid disease.
muscle autoantibodies whereas the generalised type showed a high titre and incidence of autoantibodies including AChR antibody. Seronegative patients or those with low AChR antibody may form a low responder subgroup of myasthenia gravis distinct from the high responders, who show a high titre of AChR antibody.

Twelve patients (37.5%) were of the ocular type, which is higher than the incidence in the report of Confalonieri et al. All subjects in Cohen-Kaminsky's report had generalised myasthenia gravis of type IIA or IIB. Chiu et al. reported a difference in the generalised myasthenia gravis expression between Chinese and Caucasians. The characteristic population pattern in our study may be common to east Asians and may partly cause a different correlation between SL2R and disease activity. The study of this characteristic population may lead to the elucidation of the pathogenesis of low responder myasthenia gravis.

We thank Ms Ichikawa (SRL, Tokyo, Japan) for technical assistance in detecting SL2R. The work was supported partly by Grant in Aid of Scientific Research No 04670604 from the Ministry of Education, Science, and Culture of Japan.

Correspondence to: Dr Masatoshi Hayashi, Department of Pediatrics, Ehime University School of Medicine, Shigenobu-cho, Onsen-gun, Ehime 791-02, Japan.


Decreased magnetisation transfer ratio due to demyelination: a case of central pontine myelinolysis

Conventional T2 weighted MRI has a high sensitivity for detecting multiple sclerosis lesions and is widely used for diagnosis and monitoring the efficacy of new treatments. An important limitation of T2 weighted images is their low pathological specificity: they do not identify the two pathological features that are the most important in multiple sclerosis—namely, demyelination and axonal loss. This lack of pathological specificity contributes to the weak relation between MRI abnormalities and disability in multiple sclerosis. Magnetisation transfer (MT) imaging indirectly visualises immobile water protons tightly bound to macromolecular structures that have very short T2 relaxation times and are invisible on conventional images. Measurement of MT ratio (MTR) in lesions provides information about structural integrity and by inference, myelin and axons. To explore the hypothesis that demyelination itself has an important effect on MTR, we performed MT imaging of a patient with central pontine myelinolysis—a condition in which demyelination is the predominant pathological feature.

A 50 year old woman presented with memory disturbance and poor balance. There was a long history of alcohol misuse leading to hospital admission with delirium tremens three months previously. There was no other history of note. Since then she had abstained from alcohol, after noticing residual poor balance and memory loss for recent events. Both problems worsened considerably in the weeks leading to her most recent admission. She also developed peripheral paraesthesiae, ankle swelling, and weight loss. Mental state examination showed a specific deficit in recent memory and formation of new memory, although registration was intact. On neurological examination she had a broad based ataxic gait and positive Romberg's test. Examination of the peripheral nerves showed bilateral gaze-evoked non-sustained horizontal nystagmus, but no other abnor-

malities. Ataxia was present in upper and lower limbs, more pronounced in the legs. Tone was increased in the lower limbs. There was no ankle reflex and plantar responses were extensor. Vibration sense was absent in both legs and joint position sense was decreased in the toes. Light touch and pinprick sensation were reduced in the hands.

T2 weighted MRI demonstrated a single high signal symmetric lesion confined to the basis pontis which appeared hypointense on T1 weighted images (fig 1). There was no enhancement after intravenous injection of gadolinium-DTPA. Mild cerebral atrophy was also noted. Further imaging was carried out on a 1.5 Tesla GE Signa MRI scanner with standard quadrature headcoil to obtain calculated MT images (fig 2). A dual spin echo sequence was used (TR 1730, TE 31/80, 28 contiguous 5 mm slices) both with and without presaturation pulse of the pons of five normal age matched female controls). Values for MTR in the surrounding rim of intact pontine tissue were normal. The greatest decrease in MTR was at the centre of the lesion, gradually increasing towards the outer edge.

The pathological findings associated with central pontine myelinolysis are remarkably homogeneous: a single large symmetric lesion is found in the basis pontis. There is usually a rim of intact pontine tissue. Microscopically the main abnormality is destruction of myelin, with relative neuronal preservation. Myelin destruction is typically and not severe preservation of the axons, becoming less pronounced towards the edge. There are no inflammatory changes and oedema is absent. In our patient we were confident that the lesion was due to the central pontine lesion, becoming less pronounced towards the edge.

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M Hayashi, K Kida and J Yoshinaga

J Neurol Neurosurg Psychiatry 1996 61: 207-208
doi: 10.1136/jnnp.61.2.207