Left hemianomia of musical symbols caused by callosal infarction

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DISCUSSION

Our patient developed severe and refractory generalised neuromyotonia, with evidence of autonomic nervous system dysfunction, 5 weeks after apparent recovery from an anaphylactic reaction to multiple wasp stings. Both VGKC antibodies and wasp venom specific IgE levels were raised, and both fell in parallel with clinical recovery. We cannot be certain which of the treatment strategies, if any, were responsible for the eventual resolution of the condition in our patient; recovery may simply have reflected the natural course of a monophasic autoimmune process.

A delayed syndrome, consisting of central and peripheral nervous system demyelination with a relapsing and remitting course, was described in another patient also stung by a yellow jacket wasp (*V. pennsylvanica*).[1] Cerebral infarction, acute inflammatory polyradiculoneuropathy, encephalomyeloradiculopathy, optic neuropathy, and atrial arrhythmias have all been described as relatively acute sequelae of stings from creatures of the wider order Hymenoptera. Isaacs referred to his (later eponymous) syndrome as one of "continuous muscle fibre activity", though the term neuromyotonia has now become synonymous with spontaneous muscle fibre hyperactivity as a result of peripheral nerve hyperexcitability, frequently resulting in visible "undulating" myokymia such as that seen in our patient. The CK level is frequently found to be raised. There was no evidence for rhabdomyolysis in our patient.

Neuromyotonia is most frequently an acquired condition. It has been found associated with myasthenia gravis, and as a paraneoplastic entity associated with underlying thymoma and small cell lung carcinoma (11% and 6% of cases respectively in one series[2]), but there was no evidence for this in our patient. About 40% of cases are associated with antibodies to VGKCs that are present on peripheral nerves, with the hypothesis that the mechanism is one of failure to repolarise the distal motor nerve terminal, leading to hyperactivity.

Our patient also developed autonomic dysfunction with prominent hyperhidrosis, emotional lability, insomnia, and cardiac arrhythmia. The "maladie de Morvan" (or fibrillary chorea) has been used to describe neuromyotonia occurring with central nervous system features including insomnia, hallucinations, and hyperhidrosis.[3] Cerebral imaging has been reported as normal, as in the present case. Others have detected oligoclonal bands in the cerebrospinal fluid, not found in the present case. VGKC antibodies have been frequently demonstrated in reported cases of Morvan's syndrome, and in a form of limbic encephalitis,[4] suggesting that they may be present in a spectrum of neurological conditions.

Acute focal myokymia has been reported in relation to the venom of the timber[5] and Mojave rattlesnakes. We postulate that the delayed onset syndrome in our patient was due to the development, during the 4 week period after the stings, of underlying VGKC antibodies—that is, an autoimmune, hypersensitivity-type response to an unidentified antigen of the many found in the venom of yellow jacket wasps,[6] possibly sharing epitopes with human VGKCs. The parallel decline in the IgE and VGKC antibody titres with clinical improvement provides limited evidence in support of this hypothesis.

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REFERENCES

1. **Means ED**, Barron KD, Van Dyne BJ. Nervous system lesions after sting by yellow jacket. A case report. *Neurology* 1973;**23**:881–90.
2. **Hart IK**, Maddison P, Newsom-Davis J, *et al.* Phenotypic variants of autoimmune peripheral nerve hyperexcitability. *Brain* 2002;**125**:1887–95.
3. **Loscher WN**, Wanschitz J, Reiners K, *et al.* Morvan's syndrome: clinical, laboratory, and in vitro electrophysiological studies. *Muscle Nerve* 2004;**30**:157–63.
4. **Vincent A**, Buckley C, Schott JM, *et al.* Potassium channel antibody-associated encephalopathy: a potentially immunotherapy-responsive form of limbic encephalitis. *Brain* 2004;**127**:701–12.
5. **Brick JF**, Gutmann L, Brick J, *et al.* Timber rattlesnake venom-induced myokymia: evidence for peripheral nerve origin. *Neurology* 1987;**37**:1545–6.
6. **Hoffman DR**. Allergens in hymenoptera venom. V. Identification of some of the enzymes and demonstration of multiple allergens in yellow jacket venom. *Ann Allergy* 1978;**40**:171–6.

Left hemianomia of musical symbols caused by callosal infarction

Musical scores consist of two components, musical symbols and pitch notations. Musical symbols are elements of notation that do not denote pitch. Examples include time symbols (for example, "4/4", "rit.") and dynamic marks ("*f*", "*cresc.*") as indicated by roman letters.[1] Pitch may be defined as the quality of a sound that fixes its position on a scale, indicated by "notes" written on, between, above, or below the five lines comprising the musical stave.[1] Case studies suggest that the left hemisphere is dominant in reading pitch notations,[2 3] but opinions are divided on the left hemisphere's superiority for naming musical symbols. In order to investigate this problem, we assessed hemispheric function in a patient with a callosal lesion.

In November 1997, a 69 year old, right handed businessman who suffered from hypertension and diabetes mellitus suddenly developed impairment of the movement of his left hand. When opening a desk drawer with his right hand, his left hand involuntarily caught in the drawer as the result of a cerebrovascular event. He was an amateur violinist and had been active in concerts as a soloist, or as a member in an ensemble. For example, at the opening ceremony of the concert hall of our city, he performed Beethoven's Romance in F major accompanied by the piano. He had been a member of a semiprofessional orchestra for 30 years. He met criteria for Grison's sixth level of musical culture.[4] After this cerebrovascular event, he was unable to play the violin as well as before. Even with familiar musical pieces, his left fingers could not move with their previous accuracy. Left fingers require finer movements than the right, as they press the violin strings. He could read musical scores, and movement of the bow with his right hand was unimpaired. Brain magnetic resonance imaging (MRI) showed an infarct of his corpus callosum (fig 1) which affected the whole of the body and the anterior half of the splenium.

In April 2001, we undertook neurological and neuropsychological examinations. For the statistical analysis, we used Fisher's exact test. A score of 24 points on a revision of Annett's hand preference questionnaire[5] confirmed that he was right handed. He was fully conscious and attained a normal score on the Mini-Mental State Examination (28/30) and Raven Coloured Progressive Matrices (27/36). He clearly remembered daily and social events. A Japanese version of the Rivermead Behavioural Memory Test yielded a normal score: a standard profile score of 18 (mean (SD), 19.73 (2.93)), and a screening score of 9 (mean (SD), 9.15 (1.78)). He had no weakness in any of his limbs, and no sensory disturbances, aphasia, dyscalculia, or visual discrimination difficulties were observed.

Examination of callosal functions revealed left unilateral ideomotor apraxia. To investigate somaesthetic transfer between cerebral hemispheres, the examiner touched a point on the patient's hand with a pen while the patient's eyes were closed, and then asked him to touch the corresponding place on the ipsilateral and contralateral hand using his thumb. When the examiner touched the patient's left hand, the patient correctly identified 16/16 on the left hand and 6/16 on the right hand ($p = 0.0002$); when his right hand was touched, he correctly identified 4/16 on the left hand and 16/16 on the right hand ($p = 0.00002$). Thus our patient

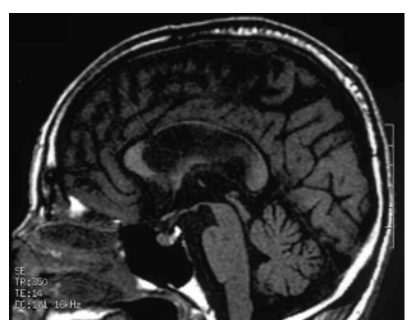

Figure 1 Brain magnetic resonance imaging showed an infarct of the corpus callosum affecting the whole of the body and the anterior half of the splenium.

showed a somaesthetic transfer defect. A dichotic listening test revealed auditory suppression (left 14/120, right 68/120; $p<0.0001$). Pure tone audiometry was within normal limits and showed no difference in threshold between right and left ears. Using a tachistoscope, visual stimuli were presented for 70 ms in each visual hemifield, beside a yellow spot 3° in visual angle. The presence of left hemialexia of Japanese kana was identified (left 16/30, right 25/30, $p = 0.025$). Some graphically simple kanji are learned by the end of the first grade of elementary school, and many of them are pictographic (for example, "□" for the mouth). Reading of such Japanese kanji revealed no significant differences between left and right (left 20/30, right 23/30, $p = 0.57$). The following callosal disconnection syndromes were absent: left visual anomia (left 10/10, right 10/10, $p = 1.0$); left agraphia of kanji (left 44/46, right 46/46, $p = 0.49$) and kana (left 43/46, right 46/46, $p = 0.24$); left tactile anomia (left 20/20, right 20/20, $p = 1.0$); and right constructional apraxia, which was examined using the block design test of WAIS-R (Wechsler Adult Intelligence Scale–Revised) (left 8/10, right 9/10, $p = 1.0$).

Using the tachistoscope, we also assessed hemispheric superiority for the naming of musical symbols. Thirty musical symbols (G, F, and C clefs, up and down bow, accent marks, repeat marks, 16th-, 8th-, quarter-, half-, and whole-notes and rest, a couple of eight notes, sharp, double sharp, flat, double flat, natural, ¢, segno, tenuto, flageolet) were randomly ordered and briefly presented in each visual hemifield. Time and dynamic symbols were not included because they were composed of actual letters, the reading of which involves the left hemisphere. The patient showed left hemianomia for musical symbols (three times examined: left 22, 20, 20/30; right 28, 27, 28/30, total left 62/90, right 83/90, $p = 0.0001$). He mistook up bow, accent, 16th-note and rest, 8th-note and half rest, double sharp, natural, segno, and flageolet in the left visual hemifield, and, in the right, double sharp and flageolet. It was possible that the patient could not represent verbal answers even if his right hemisphere was able to understand the meaning of those musical symbols, because of the disconnection between two cerebral hemispheres. In order to clarify this, a way of answering that did not require verbal processing was recommended. We undertook the same hemispheric superiority task for naming of musical symbols described above. Only 13 symbols were chosen this time (up and down bow, 16th-, 8th-, quarter-, half, and whole-notes and rest, sharp, flat), because the other symbols are hard to express in a non-verbal way. Each symbol was presented twice (26 trials in all). The patient was asked to answer by pointing to a symbolic representation of the musical symbol with the hand that was ipsilateral to the represented visual hemifield. These representations consisted of figures which did not contain any words. For example, for the up and down bow, an upward and a downward arrow was used. For the quarter tone or rest, four columns with four divided rooms were shown, each column having one to four painted rooms. On this test, the patient showed no significant differences between the two visual hemifields (left 21/26 and 22/26; right 24/26 and 24/26; total left 43/52, right 48/52; $p = 0.23$).

The results of our examination showed left hemisphere dominance in naming musical symbols. This result is in agreement with reports showing dominance of the left hemisphere in musicians when dealing with musical stimuli.[6] Owing to the callosal lesion, the right hemisphere had lost access to the contralateral speech control centres, so reading musical symbols aloud was impaired. It is widely accepted that visual information is delivered through the splenium of corpus callosum. The callosal lesion in our patient affected the anterior half of the splenium of the corpus callosum, suggesting that information contained in musical symbols is mediated there. Our patient also showed left hemialexia of kana, but not of kanji. The kanji used in our experiment convey pictographic meaning, whereas kana are purely symbolic. Musical scores, except for time and dynamic symbols, are also symbolic. It seems reasonable to conclude that similar neuropathological mechanisms are at work in the patient's alexia of both kana and musical symbols.

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References

1 **Sadie S**, editor. *Grove's concise dictionary of music*. London: Macmillan, 1994.
2 **Brust JCM**. Music and language; musical alexia and agraphia. *Brain* 1980;**103**:367–92.
3 **Kawamura M**, Midorikawa A, Kezuka M. Cerebral localization of the center for reading and writing music. *Neuroreport* 2000;**11**:3299–303.
4 **Grison B**. Une etude sur les alterations musicales au cours des lesions hemispheriques [These]. Paris, 1972. [Cited by Benton AL. The amusias. In: Critchley M, Henson RA, editors, *Music and the brain*, London:Heinemann, 1977:378–97.].
5 **Annett M**. The bimodal distribution of right, mixed and left handedness. *Q J Exp Psychol* 1967;**19**:327–33.
6 **Evers S**, Dannert J, Roedding D, *et al*. The cerebral haemodynamics of music perception: a transcranial Doppler sonography study. *Brain* 1999;**122**:75–85.

Leucocytoclastic vasculitic neuropathy diagnosed by biopsy of normal appearing skin

Leucocytoclastic vasculitis (LCV) is a clinicopathological entity that preferentially involves capillaries or small vessels rather than the medium sized or large arteries typical of polyarteritis nodosa. Its histopathological features are characterised by the presence of perivascular polymorphonuclear leucocytes with fragmented nuclear debris (leucocytoclasis).[1] It may be limited to skin lesions such as erythematous macules, purpuric papules, and haemorrhagic vesiculobullous lesions. Although LCV often involves organ systems other than the skin, it is rarely associated with neurological complications, unlike polyarteritis nodosa or Churg-Strauss syndrome. We report a patient who presented with leucocytoclastic vasculitic neuropathy without skin lesions, and discuss the value of doing a combined biopsy of the skin, nerves, and muscle in this patient for the detection of vasculitis.

A 44 year old man was admitted to our hospital because of progressive asymmetrical paraesthesiae in all four limbs. Eight months before admission, a tingling sensation had begun in the second finger of his left hand, but it disappeared spontaneously within one month. Over the next seven months, he experienced dysaesthesia which spread gradually on the lateral sides of his feet, and later to his left hand, and he developed drop foot on the right. Two weeks before admission, he had dysaesthesia in his right hand and left thigh. There was no weight loss, fever, general malaise, alcoholism, toxin exposure, or nutritional deficiency. He had no history of asthma, only seasonal allergic sinusitis in recent years.

On admission, he was afebrile. A general physical examination was normal. No skin erythema or purpura was present. On neurological examination, he had a pattern of multiple mononeuropathy. No cranial nerve dysfunction was found. There were peroneal nerve palsy on the right and ulnar nerve palsy on both sides. On the MRC scale, muscle strength was graded as 1/5 for the right tibialis anterior, and 4/5 for the bilateral abductor digiti minimi and dorsal interosseous muscles. The strength of the other muscles was normal. Tendon reflexes were normal, and plantar responses were flexor. Sensory examination showed mild impairment of pain and touch sensations in the bilateral ulnar nerve and right peroneal nerve territories.

Laboratory tests showed a white cell count of 6900/μl with 3% eosinophils, and 0.0 mg/dl serum C reactive protein. Haemoglobin, urea, and serum creatinine values were all normal. Serological markers for hepatitis B virus, hepatitis C virus, Epstein-Barr virus, cytomegalovirus, and syphilis were negative. Rheumatoid factors, antinuclear antibody, and antineutrophil cytoplasmic antibody were all negative. Cerebrospinal fluid analysis showed a normal cell count (2 lymphocytes/mm^3) and normal protein (42 mg/dl). Nerve conduction studies showed asymmetrically reduced amplitudes of compound muscle action potentials and sensory nerve action potentials, particularly in the clinically affected nerves, indicative of multiple mononeuropathy and axonal degeneration.

Combined biopsies were performed on the left sural nerve, peroneus brevis muscle, and skin at the ankle. The skin was taken as a full thickness biopsy from the incision site. Three or more sections were examined for each specimen. Sural nerve biopsy findings showed reduced myelinated fibre density ($3587/mm^2$), but no significant vessel changes, inflammatory cells, and findings suggestive of demyelination. The skin biopsy showed vasculitis, mainly involving capillaries in the dermis, with leucocyte infiltration and fragmented nuclear debris (fig 1), indicative of LCV. Findings in the peroneus brevis muscle biopsy were normal.

Intravenous methylprednisolone (1 g/day for three consecutive days) was given in two series, followed by oral methylprednisolone (80 mg on alternate days). After the start of corticosteroid treatment, the symptoms gradually lessened. There was good recovery of movement of the right foot two months later