Anterior superior alveolar neuropathy: an occupational neuropathy of the embouchure

A 31 year old French hornist was referred for evaluation of a 9 month history of pain in her right upper lip.

A member of a major symphonic orchestra, she regularly played 4-6 hours a day. Her symptoms began after a heavy period of playing, with a sensation of excess pressure in the right upper lip followed shortly thereafter by frank pain in this area. She spontaneously distinguished between two types of pain. The first was a constant dull ache, extending from the midline 1 cm laterally onto the vermilion lip. She noticed that brushing her teeth or eating could trigger pain in this region. Her second pain sensation was different from the first—electric, lancinating pain originating in the medial portion of the right lip and extending to her right nostril. There were no paraesthesias of the lips, cheeks, or jaw, and she had no symptoms of facial weakness.

She compensated for her difficulties and maintained her usual high level of professional performance. Briefs periods of rest produced temporary improvement; however, her symptoms recurred when she resumed performing. There were no other complaints and her family history and medical history were unremarkable.

Except for her right lip, neurological examination was normal including careful sensory evaluation of the anterior teeth, gums, and palate. Her right first incisor was noted to protrude slightly in front of her left. As shown in the figure, light touch sensibility was reduced in the right lip (wide cross hatching). A smaller region (narrow cross hatching) was painful to touch, lying directly over her prominent first incisor and below the contact point for the circular mouthpiece of the horn (fine stippling). Application of viscous lidocaine to the lip temporarily relieved her symptoms. An MRI of the head was obtained, showing no abnormalities along the path of the trigeminal nerve. A brief course of gabapentin at 900 mg/day was ineffective, and she declined further drug treatment. Filing down her prominent right first incisor in combination with 6 weeks of complete rest produced marked improvement in her symptoms. Her sensory loss improved as well, and she was able to return to work.

Musicians who play brass instruments (trumpet, French horn, trombone, and tuba) spend their professional lives perfecting control of the embouchure, the muscles of the lower face, lips, and tongue that control the direction and intensity of airflow into the mouthpiece. The lips and face of a brass

player experience tremendous pressure from the mouthpiece, sometimes sufficient to cause muscle strains or even traumatic tears in the orbicularis oris.¹

This patient's sensory disturbance localised to the anterior superior alveolar nerve. The superior alveolar nerve divides into a posterior, middle, and anterior group. Branches from these divisions form a plexus that innervates the dental pulp, periodontal membrane, adjacent labial and buccal gingiva, and the upper teeth. The posterior, middle, and anterior branches innervate the molar, premolar, and incisor or canine teeth, respectively. Only the anterior superior alveolar nerve travels with the infraorbital nerve to exit through the infraorbital foramen.² In our patient, her prominent right first incisor predisposed a terminal branch of this nerve to focal entrapment by the overlying mouthpiece rim.

Injuries related to occupation are increasingly recognised among performing artists. Focal entrapment neuropathies of the arm have been well described in musicians. This patient shows that similar occupational neuropathies may affect the lips and face. We are aware of two other reports of patients similar to ours.^{3,4} Given that the force exerted on the lips by the mouthpiece of a French horn has been measured to be as high as 50 N, with displacements of the central incisors of up to 180 µm during playing, it is not surprising that these neuropathies occur.⁵

French horn and trumpet mouthpieces are significantly smaller than those of the trombone and tuba, and so mouthpiece forces are concentrated onto a very small lip surface area. We suspect that there are other French horn and trumpet players who have experienced similar symptoms to our patient.

Entrapment neuropathy is a potentially reversible cause of disability in brass players, and should be considered in the differential diagnosis of embouchure dysfunction.

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- 1 Papsin BC, Maaske LA, McGrail S. Orbicularis oris muscle injury in brass players. *Laryngoscope* 1996;106:757-60.
- 2 Campbell WW. The numb cheek syndrome: a sign of infraorbital neuropathy. *Neurology* 1986;36:421-3.
- 3 Lederman RJ. Trumpet player's neuropathy. *JAMA* 1987;257:1526.
- 4 Lederman RJ. AAEM minimonograph 43: neuromuscular problems in the performing arts. *Muscle Nerve* 1994;17:569-77.
- 5 Borchers L, Gebert M, Jung T. Measurement of tooth displacements and mouthpiece forces during brass instrument playing. *Med Eng Phys* 1995;17:567-70.

Clinical and MRI discordance in a case of delayed radiation myelopathy

Delayed radiation myelopathy (DRM) is a rare complication of radiotherapy, especially when the total dose delivered to the spinal cord is less than 50 Gy.¹ From the limited data reported on the radiological features of DRM, typical MRI changes of cord swelling and gadolinium enhancement on T1 weighted images and increased intramedullary signal on T2 weighted images often correlate well with progression of neurological

symptoms. We report a case of DRM in which the clinical features remained static at a level corresponding only to the lower end of the abnormal intramedullary lesion seen on MRI, without radiological evidence of blood-brain barrier breakdown, suggesting that pathological changes to the spinal cord after radiation are not always displayed as visible changes on MRI.

A previously well 71 year old woman presented in December 1997 to the ear, nose and throat department with hoarseness and difficulty swallowing, having discovered a lump in the right side of her neck. Laryngoscopy showed a right pyriform fossa tumour, histologically confirmed as a lymphoepithelioma after biopsy. Staging neck CT showed extensive tumour in the right pyriform sinus and lateral pharyngeal wall with associated lymphadenopathy extending to the thoracic inlet.

Between April and May 1998, she received chemotherapy comprising 5-fluorouracil and cis-platinum. Radiotherapy was started in June 1998 with fields covering the pyriform sinus and neck, anterior supraclavicular fossa, and posterior neck. The calculated dose delivered to the cervical spinal cord was 42.5 Gy in 2 Gy equivalent fractions.

Over the next 4 months, she improved clinically and on review in October 1998 there were no signs of tumour recurrence, confirmed on laryngoscopy. She remained well until November 1998 when she began to notice progressive numbness and weakness spreading proximally up both legs over a period of 6 weeks, such that she was unsteady when walking. Soon thereafter, she developed urinary incontinence and constipation. At this time, cervical and thoracic spine MRI (figure) disclosed cervical cord swelling with a spindle shaped cavity of low signal intensity on T1 weighted images and high signal intensity on T2 weighted images extending from C4 to the upper end of T1. There was no cord enhancement after the administration of gadolinium.

On neurological review in January 1999, she was incontinent of urine and faeces and was able to mobilise only with the aid of a walking frame. There was generalised wasting in both legs with mild reduction in strength of hip flexion, knee flexion, and extension, but no detectable weakness in the arms. There was a loss of spinothalamic sensation below the level of T5 bilaterally, with a subjective feeling of altered sensation in both hands.

Over the ensuing 4 months, her level of disability progressed such that she was unable to walk or transfer independently. Further examination disclosed flaccid paralysis of both legs and minor weakness of the intrinsic muscles of both hands. There was reduced perception of pain and temperature sensation below the level of C8. She commenced hyperbaric oxygen therapy given on a daily basis for 3 weeks but there was no symptomatic recovery.

After a recurrence of her original swallowing difficulties, she was found to have a tumour recurrence in her pyriform fossa at biopsy, with associated lymphadenopathy. No further radiotherapy was given. At last review in February 2000, she had no movement in her lower limbs and marked weakness of the intrinsic muscles of both hands, with preserved power in proximal upper limb muscles. Sensation above the level of C8 was intact.

Diagnostic criteria of DRM as outlined by Pallis *et al*² stated that the spinal cord should

Sensory loss (wide cross hatching), focal pain (narrow cross hatching), and lancinating pain (arrow) are shown overlying a diagram of the lips. Dashed lines indicate the position of the first incisors, and the contact of the french horn mouthpiece with the lips is shown as a stippled circle.

Sagittal T2 weighted MRI showing a spindle shaped area of increased signal extending from C4 to T1.

be included in the irradiated area; the main neurological lesion should be within segments of the cord exposed to radiation; and that other causes for the neurological disorder have been excluded.

Despite the almost syrinx-like appearance of radiation myelopathy on MRI, the clinical presentation of DRM is usually one of progressive rostral spread of sensorimotor symptoms, where the final clinical level usually corresponds to a level well within the boundaries of the length of abnormal signal seen on MRI, typically within 1 year of symptomatic onset.^{3,4} All but one of the reported cases of MRI features of DRM in the literature have shown ring-like enhancement after gadolinium administration, suggesting breakdown of the blood-brain barrier.^{3,4} As yet, there are insufficient data on precise clinical sensorimotor cord levels in relation to MRI appearances (and possible gadolinium enhancement) in the studies of DRM currently published to enable prediction of clinical outcome based on radiological findings at presentation. Our patient's symptoms and signs plateaued at a level which would indicate an upper level of spinal cord damage at C8/T1, whereas MRI showed extensive cord changes from C4 to the upper end of T1. There was no gadolinium enhancement, but T2 weighted images disclosed evidence of marrow change in the vertebral bodies of C1 to T3, suggesting that the lesion was within the irradiated area. Pathological studies in DRM have shown white matter changes of demyelination and malacia, often affecting the lateral and posterior aspects of the cord, with associated vascular changes of fibrinoid necrosis, thrombosis, perivascular oedema, and haemorrhage.¹

The high signal T2 weighted MRI findings with cord swelling resemble those of syringo-

myelia. However, almost all patients with cervical syrinx formation develop marked sensorimotor symptoms or signs in the upper limbs, and a clinical picture of isolated spastic paraparesis is unusual.⁵ The main areas of cord damage after radiotherapy would seem to be the lateral corticospinal tracts and posterior columns from radiological-pathological studies.⁶ Peripheral ring enhancement of the cord after gadolinium administration suggests that the major focus of cord damage or at least blood-brain barrier breakdown does not lie within the central cord regions. Consequently, the central cord swelling seen on T2 weighted images may well represent oedema, produced in response to altered vascular permeability after radiation damage to the vascular endothelium. In direct intrinsic cord compression, this spindle shaped region of cord oedema has limited correlation with clinical signs, as would be suggested by our case. The presence of gadolinium ring enhancement of the cord, missing in our case, serves as a more reliable marker of structural cord damage, but even in its absence, the diagnosis of DRM can be made in a patient with ascending sensorimotor symptoms within months of radiation therapy, where the only clue to radiation damage to the cord is central cord swelling and vertebral body marrow change with increased signal on T2 weighted images. Follow up MRI shows cord atrophy only in the region of previous gadolinium enhancement, correlating with clinical findings.⁷ Our case has shown that the ultimate level of disability cannot be judged from the extent of the T2 weighted central cord changes seen on initial MRI.

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- Schultheiss TE, Kun LE, Ang KK, *et al*. Radiation response of the central nervous system. *Int J Radiat Oncol Biol Phys* 1995;31:1093-112.
- Pallis CA, Lewis S, Morgan RL. Radiation myelopathy. *Brain* 1961;84:460-79.
- Wang PY, Shen WC, Jan JS. MR imaging in radiation myelopathy. *AJNR Am J Neuroradiol* 1992;13:1049-55.
- Michikawa M, Wada Y, Sano M, *et al*. Radiation myelopathy: significance of gadolinium-DTPA enhancement in the diagnosis. *Neuroradiology* 1991;33:286-9.
- Barnett HJM, Foster JB, Hudson P. *Syringomyelia*. London: WB Saunders, 1973:11-29.
- Komachi H, Tsuchiya K, Ikeda M, *et al*. Radiation myelopathy: a clinicopathological study with special reference to correlation between MRI findings and neuropathology. *J Neurol Sci* 1995;132:228-32.
- Wang PY, Shen WC, Jan JS. Serial MRI changes in radiation myelopathy. *Neuroradiology* 1995;37:374-7.

Lack of association between *IL-1A* and *IL-1B* promoter polymorphisms and multiple sclerosis

Multiple sclerosis is an autoimmune and inflammatory disease of the CNS characterised by recurrent destruction of myelin which results in heterogeneous and unpredictable clinical manifestations. Although the factors able to foster the initial changes leading to CNS demyelination in patients with multiple sclerosis are still unknown, a discrete number of genes are likely to predispose to the occurrence of multiple sclerosis and to influence its clinical variables.

Due to the inflammatory nature of the pathogenic mechanisms mediating CNS damage during multiple sclerosis, association studies have been focused on candidate genes coding for immunorelevant molecules. The interleukin (IL)-1 gene cluster (including *IL-1A*, *IL-1B*, *IL-1RN*), located on the long arm of chromosome 2 (2q12-22; OMIM Database of National Center for Biotechnology Information; www3.ncbi.nlm.nih.gov:80/Omim) and polymorphic in different sites, represents a good target for association studies in multiple sclerosis. *IL-1*, in fact, has been detected within multiple sclerosis lesions.¹ Moreover, lipopolysaccharide stimulated peripheral blood monocytes of patients with multiple sclerosis produce more *IL-1α* and *IL-1β* than controls.² Due to the potential involvement of *IL-1α* and *IL-1β* in multiple sclerosis, a genetically determined polymorphic variation in their production may contribute to the occurrence of multiple sclerosis, or modulate its clinical features. Furthermore, we have recently reported the association between the variable number of tandem repeat polymorphism (VNTR) of *IL-1RN* with multiple sclerosis susceptibility and prognosis.³ *IL-1A*-889 and *IL-1B*-511 polymorphic loci are located 375 and 320 kb respectively from *IL-1RN* VNTR. To determine whether a particular allele or genotype of *IL-1A* or *IL-1B* affects occurrence or clinical variables of multiple sclerosis, we performed a case-control association study in a large cohort of patients with multiple sclerosis and age and ethnicity matched healthy controls.

Patients were clinically diagnosed at the multiple sclerosis centre of the San Raffaele Hospital in Milano as affected by clinically definite multiple sclerosis according to Poser's criteria. All patients had a relapsing-remitting course. Genotype frequencies of the *IL-1A*-889 polymorphism were calculated in a cohort of 399 patients with sporadic relapsing-remitting multiple sclerosis (247 women, 152 men; age 37.3 (SD 12); mean age at disease onset 27.3 (SD 9.3)) and 439 healthy controls (151 women, 288 men; mean age 37.6 (SD 10.6)). Gene frequencies of the *IL-1B*-511 polymorphism were calculated in a cohort of 321 patients with sporadic relapsing-remitting multiple sclerosis (203 women, 118 men; mean age 38 (SD 12); mean age at disease onset 27.4 (SD 9.2)) and 403 HC (146 women, 257 men; mean age 38 (SD 10.9)).

IL-1A-889 and *IL-1B*-511 C/T polymorphisms were characterised by polymerase chain reaction (95°C 30 seconds, 55°C 30 seconds, and 72°C 40 seconds; 40 cycles) using genomic DNA and following primers: *IL-1α* FW 5'-AAGCTTGTCTACACCTGAAGTAGGC-3', *IL-1α* RV 5'-TTAATATGAGCCTTCCATG-3'; *IL-1β* FW 5'-TGGCATTGATCTGGTTCATC-3', *IL-1β* RV 5'-GTTTAGGAATCTTCCACTT-3'. Amplified products were digested with restriction endonuclease (NcoI and Aval).

Statistical analyses were performed with the SAS statistical package (SAS Institute Inc, Cary, NC, USA). The p values were considered not significant (NS) when greater than 0.05. Gene frequencies were compared by χ^2 test with two degrees of freedom. The homogeneity of Kaplan-Meier disease free curves over strata was tested using the rank statistics (log-rank and Wilcoxon tests).

The *IL-1A* and *IL-1B* alleles were in Hardy-Weinberg equilibrium in all populations and their distributions were not affected