CD25+ and CD4+ CD25^{high}), although this test was not performed in the CSF. Such expansion may be playing a role in the progression of cancer.⁶ Indeed, regulatory T cells have been reported to selectively inhibit autologous immune response in the local tumour environment in patients with LC.⁷

The main initial MRI features were located at the cerebellum, which showed swelling and an abnormal signal of the cerebellar cortex concomitant with CSF pleocytosis, probably translating the inflammatory autoimmune process. These findings are unusual, as other authors have described cerebellar atrophy in PCD particularly later in the process, compatible with our second MRI. We hypothesise that in most cases, the diagnosis of PCD is carried out at later stages of the disease, when the cerebellar atrophy has been established after an initial inflammatory response. Supporting this idea, we found close similarities between our case and the case of Shoji *et al*⁸ with acute infectious cerebellar ataxia. In that case, the cerebellar oedema disappeared 1 month later, whereas in our case evolved to atrophy.

Altogether, our data suggest that the paraneoplastic syndrome is a dynamic process initially inducing inflammation and oedema and subsequently evolving to loss of brain tissue, and that the inflammatory autoimmune process contributes to the secondary brain degeneration.

Acknowledgements

We wish to thank C Aristimuño for expertise in flow cytometry.

C de Andrés, A Esquivel

Department of Neurology, Hospital General Universitario Gregorio Marañón, Madrid, Spain

J G de Villoria

Department of Radiology, Hospital General Universitario Gregorio Marañón, Madrid, Spain

F Graus

Department of Neurology, Hospital Clinic, Barcelona, Spain

S Sánchez-Ramón

Department of Immunology, Hospital General Universitario Gregorio Marañón, Madrid, Spain

Correspondence to: Dr C de Andrés, Department of Neurology, Hospital General Universitario "Gregorio Marañón", C/Doctor Esquerdo 46, 28007, Madrid, Spain; claradeandres@hotmail.com

doi: 10.1136/jnnp.2005.073379

Competing interests: none

References

- 1 Voltz R. Paraneoplastic neurological syndromes: an update on diagnosis, pathogenesis, and therapy. *Lancet Neurol* 2002;1:294–305.
- 2 Vernino S, Tuite P, Adler CH, *et al*. Paraneoplastic chorea associated with CRMP-5 neuronal antibodies and lung carcinoma. *Ann Neurol* 2001;49:146–54.
- 3 Kinirons P, Fulton A, Keoghan M, *et al*. Paraneoplastic limbic encephalitis (PLE) and associated with CRMP-5 neuronal antibody. *Neurology* 2003;61:1623–24.
- 4 Pashenkov M, Huang YM, Haglund M, *et al*. Two subsets of dendritic cells are present in human cerebrospinal fluid. *Brain* 2001;124:480–92.
- 5 McDermott RS, *et al*. Tumor antigens and antigen-presenting capacity in breast cancer. *Pathobiology* 2002;70:324–32.
- 6 Shimizu J, Yamazaki S, Sakaguchi S. Induction of tumour immunity by removing CD25+CD4+ T cells: a common basis between tumour immunity and autoimmunity. *J Immunol* 1999;163:5211–18.
- 7 Yo E, Yeh H, Chu CS, *et al*. Regulatory T cells from lung cancer patients directly inhibit autologous T cell proliferation. *J Immunol* 2002;168:4272–6.
- 8 Shoji H, Hirai S, Ishikawa K, *et al*. CT and MRI imaging of acute cerebellar ataxia. *Neuroradiology* 1991;33:360–1.

Abscess of the medulla oblongata following endotracheal intubation

A 71 year old man was admitted for a myocardial infarction following which he was successfully resuscitated for a cardiac arrest secondary to ventricular fibrillation. He was intubated and ventilated in the peri-arrest period. After extubation, he complained of neck pain and dysphagia. A flexible laryngoscopy examination revealed an oedematous left larynx. He was subsequently lost to follow up. His symptoms worsened over the next 2 months. He lost 15 kg in weight and suffered fevers and night sweats.

On readmission, he was cachectic. He had discomfort on moving his neck. He had a chest wall abscess and a hard lymph node attached to the left trapezius muscle. Magnetic resonance imaging (MRI) of the neck revealed a large retropharyngeal abscess with osteomyelitis of the C1 and C2 vertebrae. Aspiration of the chest wall abscess revealed methicillin resistant *Staphylococcus aureus*. Intravenous vancomycin and metronidazole were commenced and the neck was stabilised with a hard collar.

One week later, he complained of acute onset severe neck pain. He developed bulbar palsy and right sided weakness. MRI revealed an abscess in the posterior part of the medulla in continuity with the retropharyngeal collection (fig 1A) and multiple lung abscesses. He required a tracheostomy and positive pressure ventilation. It was felt that

surgical aspiration of the medulla abscess would be too risky, thus a halo traction brace was applied and conservative management with antibiotics was adopted.

He was weaned off the ventilator and the halo traction was replaced by a hard collar. It was not possible to wean him from his tracheostomy, because of a residual left sided bulbar palsy. He also required permanent gastrostomy feeding. His right hemiparesis improved, although he was left wheelchair bound. Repeat MRI 6 months after admission showed near resolution of the medulla abscess (Fig 1B). Antibiotics were continued for 10 months. The patient was discharged to a nursing home 8 months after admission and has shown continuing physical improvement in outpatient follow up.

Retropharyngeal abscesses are a rare but recognised complication of intubation.¹ They usually occur following foreign body ingestion (usually fish or chicken bones), pharyngotonsillitis, peritonsillar abscesses and dental infections.² They can cause great morbidity. Reported complications include airway obstruction, mediastinitis, empyema, septicaemia, osteomyelitis, and epidural abscesses.^{2–4} To our knowledge, this is the first case reported of an intraparenchymal brainstem abscess occurring as a complication of a retropharyngeal abscess.

Brainstem abscesses may arise spontaneously, or from haematogenous or contiguous spread, usually from the ears.⁵ Case mortality is thought to be high, but reports in the literature have, like this one, mainly been of single cases that have had a successful outcome. There is no consensus over management. Options include open surgical drainage, stereotactic aspiration, and medical management with antibiotics alone.⁵ Conservative management may be useful where the causative organism is known and/or the lesion would present too great a surgical risk, as in this case. Operative intervention is useful for identifying the

Figure 1 Post-gadolinium T1 weighted magnetic resonance imaging of the brainstem and cervical spinal cord. (A) One week post admission, showing the development of a medullary abscess in continuity with the retropharyngeal collection and C1/2 osteomyelitis; (B) 6 months later after prolonged antibiotic therapy demonstrating near resolution.

causative organism, for decompressing large lesions, and when the patient is deteriorating despite antibiotic therapy.⁵ The duration of antibiotic treatment is to an extent empirical. In previous reports of brainstem abscesses treated with antibiotics, the treatment was usually continued for 6–8 weeks. In our case, antibiotics were continued for 10 months because of the coexistent cervical osteomyelitis.

This case illustrates a devastating complication arising from endotracheal intubation and the possibility of conservative management in the management of medulla abscesses owing to the obvious risks of surgical intervention.

S J L Payne

Department of Medical Oncology, St. Bartholomew's Hospital, West Smithfield, London, UK

S J Hickman, R S Howard

Department of Neurology, St Thomas's Hospital, Lambeth Palace Road, London, UK

Correspondence to: Dr S Payne, Department of Medical Oncology, St. Bartholomew's Hospital, West Smithfield, London EC1A UK; sarah_146@hotmail.com

doi: 10.1136/jnnp.2005.075994

Competing interests: none

REFERENCES

- 1 **Heath LK**, Peirce TH. Retropharyngeal abscess following endotracheal intubation. *Chest* 1977;**72**:776–77.
- 2 **Sharma HS**, Kurl DN, Hamzah M. Retropharyngeal abscess: Recent trends. *Auris Nasus Larynx* 1998;**25**:403–6.
- 3 **Furst I**, Ellis D, Winton T. Unusual complication of endotracheal intubation: Retropharyngeal space abscess, mediastinitis, and empyema. *J Otolaryngol* 2000;**29**:309–11.
- 4 **Jang YJ**, Rhee CK. Retropharyngeal abscess associated with vertebral osteomyelitis and spinal epidural abscess. *Otolaryngol Head Neck Surg* 1998;**119**:705–8.
- 5 **Fuentes S**, Bouillot P, Regis J, et al. Management of brain stem abscess. *Br J Neurosurg* 2001;**15**:57–62.

Anti-MuSK antibodies in a case of ocular myasthenia gravis

In 10–20% of patients with generalised myasthenia gravis and in up to 50% of patients with ocular myasthenia gravis there are no detectable antibodies to the acetylcholine receptor (AChR). In such cases the disease is commonly referred to as seronegative myasthenia gravis. Seronegative myasthenia gravis has been recognised as an antibody mediated disease, and recently antibodies to muscle specific kinase (MuSK) were demonstrated in the sera of patients with generalised seronegative myasthenia gravis.¹ Anti-MuSK antibodies were not found in seropositive myasthenia gravis. Myasthenia gravis patients with these antibodies have been described as having more prominent bulbar and neck weakness and more respiratory crises.^{2–4} These studies differ in the degree of ocular involvement reported, however, only one previous case of anti-MuSK antibodies being found in purely ocular myasthenia gravis has been described.⁵ We would like to describe a further case of seronegative ocular myasthenia gravis associated with anti-MuSK antibodies.

Case report

A 21 year old male student presented with a four month history of variable diplopia and bilateral ptosis. He did not complain of any limb weakness or speech, swallowing, or respiratory problems. He had no past medical history of note and was not taking any regular medication. He is the youngest of eight siblings and there is no family history of neuromuscular disease.

On examination he had bilateral ptosis with fatigue and Cogan's lid twitch sign was positive. Extraocular movements were limited in all directions, and particularly pronounced on eye abduction bilaterally. The ptosis and ophthalmoplegia varied between clinical assessments. He had no facial or neck weakness, and bulbar function and limb power was normal with no evidence of fatigability.

Anti-AChR antibodies were negative as measured by a standard radioimmuno precipitation assay using human adult-type AChR as antigen. Repetitive nerve stimulation revealed no decrementing response in abductor digiti minimi but stimulated single fibre electromyography of orbicularis oculi demonstrated enhanced jitter (mean of 10 single fibres 31 ms; normal range >23 ms) consistent with a defect in neuromuscular transmission. A computed tomography (CT) scan of the head and orbits was normal, and a magnetic resonance scan of the brain was also normal. CT thorax showed normal residual thymic tissue in the anterior mediastinum.

A provisional diagnosis of seronegative ocular myasthenia gravis was made and he was treated with pyridostigmine up to 60 mg four times daily, which had no benefit. Treatment with 3,4-diaminopyridine (20 mg three times daily) was also ineffective. An edrophonium test was then performed which was negative. A quadriceps muscle biopsy showed mild variation in fibre size with some atrophic fibres (predominantly type II). He was subsequently found to have anti-MuSK antibodies as detected by immunoprecipitation of ¹²⁵I-recombinant MuSK extracellular domains.⁶ He was started on treatment with prednisolone 10 mg once daily which resulted in a marked symptomatic improvement.

Discussion

It could be argued that this patient will go on to develop generalised myasthenia gravis since this progression occurs in up to 85% of patients with ocular myasthenia gravis. His symptoms and signs, however, have now remained purely ocular for over a year whereas in the majority of patients the progression of ocular to generalised myasthenia gravis occurs in the first year. The frequency of anti-MuSK antibodies in generalised but seronegative myasthenia gravis has been reported as between 40% and 70% in Caucasian populations.^{1–4} The frequency of these antibodies in purely ocular myasthenia gravis is likely to be much lower. One recent report has described positive anti-MuSK antibodies in purely ocular myasthenia gravis.⁵ In other reports anti-MuSK antibodies were tested in 38 patients with purely ocular seronegative MG with all being negative.^{2–4}

Interestingly, our patient did not respond to treatment with acetylcholinesterase inhibitors and an edrophonium test was negative. Both of these findings have previously been

described in the context of MuSK positive generalised myasthenia gravis.^{2–3} In one study the edrophonium test was unhelpful in 30% of patients with anti-MuSK antibody positive generalised myasthenia gravis.³ Although our patient did not find treatment with acetylcholinesterase inhibitors beneficial he responded well to a low dose of prednisolone.

MuSK is a tyrosine kinase receptor predominantly located on the postsynaptic membrane of the neuromuscular junction. It is activated upon binding of nerve released agrin and then mediates AChR clustering and formation of the neuromuscular junction. Anti-MuSK antibodies interfere with agrin induced clustering of AChRs in cultured muscle cell lines.¹ It is unclear what effect anti-MuSK antibodies will have on the more stable adult neuromuscular junction, and indeed there is some controversy over the pathogenicity of anti-MuSK antibodies.⁷ In patients with these antibodies there was no substantial loss of AChRs or MuSK on muscle biopsy. Recent studies suggest that sera from seronegative myasthenia gravis patients may have an inhibitory effect on AChRs that is independent of the IgG fraction or the MuSK antibody itself. Despite these uncertainties the presence of anti-MuSK antibodies is a useful diagnostic marker of myasthenia gravis. Their frequency appears to be low in purely ocular myasthenia gravis. Finding anti-MuSK antibodies in a patient with purely ocular seronegative myasthenia gravis, however, may be extremely helpful. This report demonstrates their use in particularly challenging diagnostic cases where the edrophonium test is negative and there is no response to acetylcholinesterase inhibitors.

D L H Bennett

Department of Neurology, King's Neurosciences Centre, King's College Hospital, Denmark Hill, London, UK

K R Mills

Academic Unit of Neurophysiology, King's College Hospital, Denmark Hill, London, UK

P Riordan-Eva

Department of Ophthalmology, King's College Hospital, Denmark Hill, London, UK

P R J Barnes, M R Rose

Department of Neurology, King's Neurosciences Centre, King's College Hospital, Denmark Hill, London, UK

Correspondence to: D L H Bennett, Department of Neurology, King's Neurosciences Centre, King's College Hospital, Denmark Hill, London, UK; dlhbennett@talk21.com

doi: 10.1136/jnnp.2005.075812

Competing interests: none declared

References

- 1 **Hoch W**, McConville J, Helms S, et al. Auto-antibodies to the receptor tyrosine kinase MuSK in patients with myasthenia gravis without acetylcholine receptor antibodies. *Nat Med* 2001;**7**:365–8.
- 2 **Sanders DB**, El-Salem K, Massey JM, et al. Clinical aspects of MuSK antibody positive seronegative MG. *Neurology* 2003;**60**:1978–80.
- 3 **Evoli A**, Tonali PA, Padua L, et al. Clinical correlates with anti-MuSK antibodies in generalized seronegative myasthenia gravis. *Brain* 2003;**126**:2304–11.
- 4 **Zhou L**, McConville J, Chaudhry V, et al. Clinical comparison of muscle-specific tyrosine kinase (MuSK) antibody-positive and -negative