

ligated to the pMalc vector. Plasmids were transformed into *Escherichia coli* DH5. Production of the recombinant fusion protein was induced with isopropyl- $\beta$ -D-thiogalactopyranoside. The DH5 cells were sonicated and centrifuged, after which the supernatant was applied to an amylose resin column and eluted with maltose to separate the Yo protein fused to the maltose binding protein (figure). For ELISA, the r-Yo was bound to immunoplates (0.5  $\mu$ g/well). Non-specific binding was blocked with Tris-buffered saline (TBS) containing 0.5% skimmed milk. The patient's serum then was diluted 1:5000 with the blocking solution and immunostained with avidin-biotin-peroxidase. Absorbance at 495 nm was measured with a spectrophotometer. The normal and disease control samples consisted of serum samples taken from 10 healthy young adults, from 10 patients with spinocerebellar degeneration (mean age 56 (SD 11)), and from seven patients with gynaecological cancer without neurological symptoms. The mean ELISA absorbance of serum samples from the young adult controls was 0.080 (SD 0.023) and that from the disease controls, 0.082 (SD 0.046). The absorbance for serum from the patient with PCD before treatment was 1.200. After three cycles of plasmapheresis, it rose to 1.764. On the basis of her clinical picture and the presence of the characteristic anti-Yo antibody, we did a test laparotomy with her informed consent because the conventional survey had found no tumour. A fallopian tube adenocarcinoma 1.5 cm in diameter was identified and successfully resected. Cancer chemotherapy was started 18 days after operation (cisplatin, adriamycin, cyclophosphamide, and 5-fluorouracil). Two more chemotherapy cycles were given at monthly intervals. The antibody titre of serum taken serially at various times during treatment and during the three year follow up period showed a gradual reduction to 0.401. Patients with PCD who have anti-Yo antibody have been found to have mostly breast or gynaecological cancers.<sup>1</sup> More than half of these patients with PCD showed neurological symptoms only for several months, no underlying cancer being detected despite extensive surveys for malignancy. The detection of antineuronal antibodies, therefore, is important for the early detection of the underlying cancer. These autoantibodies can be detected from the staining distribution obtained by immunohistochemical means as well as by their molecular sizes on immunoblots. But, as there are many molecules of similar size, we constructed r-Yo to use as the ELISA antigen to group patients with PCD with an autoantibody that recognises the same molecule.

In ELISA, our patient's serum and CSF both had a high titre for the anti-Yo antibody. This titre increased two weeks after plasmapheresis, indicative of rebound overproduction of the antibody. After tumour resection and subsequent anticancer chemotherapy, the patient's anti-Yo antibody titre gradually decreased. Her neurological symptoms showed mild improvement, suggesting that early tumour resection ameliorates neurological symptoms. Increases in antibody titre indicate the immunological state of the host, indirect evidence of tumour antigen stimulation. Therefore it is very important to follow up changes in specific antibodies in patients with PCD.

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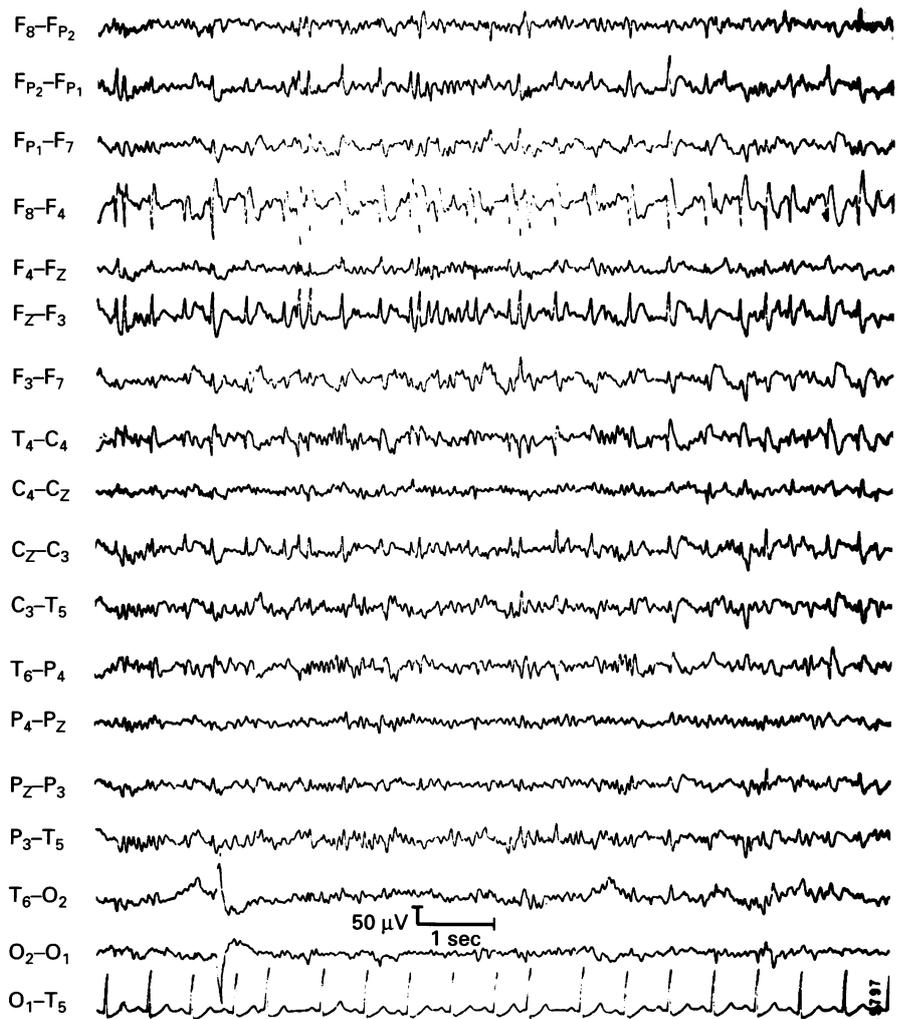
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### Painful paroxysmal dystonia associated with focal epileptic activity

Painful paroxysmal dystonia, a rare movement disorder, is characterised by recurrent episodes of brief, intensely painful unilateral abnormal posturing of one or two limbs unassociated with clonic movements or impairment of consciousness.<sup>1</sup> The mechanism remains obscure, and most cases with identifiable causes have subcortical lesions, particularly in the brain stem, as in multiple sclerosis. Our patient had typical painful paroxysmal dystonia associated with cortical epileptic activity in the EEG.

A 72 year old woman was admitted for the evaluation of recurrent painful dystonic posturing of her left extremities. These attacks were characterised by sudden unprovoked torsion of the head leftward, adduction of the left arm at the shoulder with flexion at the elbow and at the wrist and extension of the fingers, extension of the left knee, and plantar flexion of the left



Almost continuous epileptic activity apparent in the right frontal-frontal sagittal region during drowsiness.

foot and toes. During an episode, which lasted for one to five seconds, the patient complained of sharp pain in the left extremities that could not be explained solely by the muscle contraction causing the dystonic posturing. There were no alteration of consciousness, loss of sphincter control, or clonic movements in the limbs. The attacks had started without obvious precipitating factors 10 days before admission and occurred with a frequency of 5–10 per day.

The patient reported that at the age of 23 she had experienced a single similar attack of "painful spasm" in her left extremities that had not been treated and had not recurred.

Mild depressive symptoms had been present since the age of 60, being treated with fluvoxamine and benzodiazepines intermittently. There was no family history of epilepsy or other neurological diseases.

Her interictal general and neurological examination was unremarkable. Blood counts and serum biochemistry were normal. The routine EEG recording was normal. After sleep deprivation the awake EEG disclosed no abnormalities; during drowsiness and sleep an almost continuous focal epileptic activity was apparent in the right frontal-frontal sagittal region (figure). Computed tomography with and without contrast and MRI of the brain were performed and showed mild symmetric brain atrophy without any evidence of focal structural lesions or changes suggestive of a demyelinating disease. Treatment with carbamazepine (200 mg three times daily) led to dramatic cessation of attacks and disappearance of the epileptic activity on the EEG.

Painful paroxysmal dystonia was previously described by different terms, such as painful tonic seizures and painful tonic spasm.<sup>1</sup> It represents one of the distinct paroxysmal features of multiple sclerosis.<sup>1</sup> Ephaptic activation of axons within demyelinated plaques or other structural lesion may be responsible for both motor and sensory components of the paroxysms.<sup>1</sup>

Bennett<sup>2</sup> attributed painful paroxysmal dystonia to the heterogeneous group of paroxysmal dyskinesias, stressing their non-epileptic character and emphasising their important place in the differential diagnosis of epilepsy. The most characteristic features of these fits are their painful nature and typical pattern of unilateral limb posturing.<sup>1,2</sup> Both ictal and interictal EEGs were reported to be normal or showed non-specific changes<sup>1,2</sup> supporting the non-epileptic origin of painful paroxysmal dystonia. By contrast, dystonic posturing may occur in epilepsy, albeit it is usually not painful.<sup>3</sup>

Paroxysmal pain associated with motor phenomena may also be a rare manifestation of epilepsy.<sup>4,5</sup> It has been suggested that epileptic pain originates from the contralateral rolandic area<sup>4</sup> or superior and medial parts of the parietal lobe.<sup>5</sup> The motor component of painful epileptic seizures was reported to be represented by unilateral clonic or tonic-clonic convulsions with or without march, tonic deviation of the head and eyes, bilateral clonic movements of the extremities, generalised tonic-clonic convulsions, transient motor weakness without tonic or clonic phenomena, and "stiffness" of the arm or leg.<sup>4,5</sup> Painful epileptic seizures with a characteristic pattern of unilateral posturing of the extremities meeting the criteria of painful paroxysmal dystonia

to our knowledge have apparently never been described.

Our patient had typical unprovoked painful paroxysmal dystonia associated with focal cortical epileptic activity in the contralateral frontal-frontal sagittal region. This approximates to the premotor and supplementary motor region that, when activated, may result in postural changes.<sup>2</sup>

Although we have not obtained an ictal recording, the association of the clinical events with a very active epileptic focus in the EEG and the disappearance of both after carbamazepine treatment, suggest a causal relation between the electrographic phenomena and the bouts supporting their epileptic nature. They may represent a distinct type of painful paroxysmal dystonia of cortical epileptic origin.

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#### Treatment of spasmodic torticollis with intramuscular phenol injection

Phenol is a caustic agent that produces tissue destruction and has been used to weaken muscle in patients with spasticity by either nerve block, motor point block, or intramuscular neurolysis.<sup>1–5</sup> Local muscle pain and tenderness but no systemic or long term side effects have been reported after such use. There is no report of the use of intramuscular phenol in the treatment of spasmodic torticollis. I have used this agent in patients with spasmodic torticollis who have not responded well to intramuscular injections of botulinum toxin A (BTX). Both patients gave informed consent to participate in the trial with the approval of the Duke University Investigational Review Board.

The muscles responsible for abnormal head movements were determined by clinical examination and by EMG recordings made with a concentric EMG needle in the sternomastoid, splenius capitis, or other neck muscles involved in head turning. Phenol solution (1% weight/volume USP phenol crystals in sterile aqueous solution) was injected into the involved muscles with a recording monopolar injection electrode to determine that injections were made in muscle active in the abnormal movement. Injections were made at two to six sites in each muscle, in sites where motor unit action potentials with sharply rising components were recorded, indicating that the needle tip was close to muscle fibres that were activated during the abnormal move-

ment. Areas near major vessels or nerves were avoided. After 18 hours or more, subsequent injections were given if improvement was incomplete as determined by the patient's symptoms and by examination. At each visit, examination of strength in the involved muscles and functional assessment of the patient's torticollis were recorded on videotape for comparison with examinations made before phenol treatment.

Patient 1 is a 53 year old man who has had torticollis since the age of 43. Medical treatment had produced no improvement. At the age of 48, he had shown moderate improvement with BTX injections but, after 18 months, the response to repeated injections diminished despite increasing doses. Muscles no longer developed weakness, atrophy, or denervation changes on EMG testing after BTX was injected. Antibody to botulinum could not be detected in the serum. He underwent selective peripheral denervation surgery when aged 50 and 51, with only mild improvement. Several months later, BTX injections were repeated without benefit.

He had tonic, uncontrollable turning of the head to the left with a phasic component and mild retrocollis before phenol injection. He maintained his head in the midline with great difficulty while sitting. Standing and any attempt to talk, walk, or use his hands produced immediate uncontrollable head turning. He had constant posterior neck and intrascapular pain.

Within 18 hours after the initial injection of 100 mg phenol into the left splenius capitis, splenius cervicis, and longissimus capitis muscles, he noted a fuller range of motion in the neck and mild improved head control while walking. The injected muscles were tender and oedematous but the neck and intrascapular pain was considerably less. After subsequent injections he noted progressive improvement. After receiving a total dose of 500 mg of phenol over one month, he could walk, drive, or sit to eat even in public with only occasional involuntary head turning. Manoeuvres that previously had exacerbated the abnormal head movements now were performed with little or no difficulty. He estimated that pain was reduced by 90%. His only side effects were mild erythema and tenderness over the injected muscles lasting one to two days after each injection. The improvement was sustained for five months after the initial injection. He then experienced gradual worsening of head control and some return of pain. He has subsequently received phenol injections at intervals of six months to maintain improvement.

Patient 2 is a 43 year old white male physician who had onset of involuntary head turning to the left at the age of 33. Medical treatment produced intolerable side effects and no appreciable improvement. At the age of 41, he received BTX injections every three to four months with moderate improvement but symptoms of head turning and pain returned four to six weeks after each injection. After each BTX injection, he developed severe dysphagia that persisted for two weeks. Before phenol was injected, he had moderately severe torticollis that was greatly exacerbated by public speaking and manual activities.

Eighteen hours after the initial injection of 120 mg phenol into the left splenius capitis, splenius cervicis, and longissimus capitis muscles, he noted improvement in neck