noted frequent involuntary movements of her eyes, heavily impairing object fixation. Family history was unremarkable. On admission, the patient was anxious, unconcentrated, and restless. She had opsoclonus with the conjugated eyes moving around arrhythmically in all directions with a large amplitude. Movements were also present with the eyes closed. Facial muscles showed diffuse myoclonic jerks, and there was myoclonic speech with dysarthria. No palatal myoclonus was seen; pupillary and the remaining cranial nerve functions were normal. There were no abnormalities in muscle tone and strength. Deep tendon reflexes were briskly elevated, the plantar sign being flexor. No sensory deficit was detected. Voluntary movements were impaired by frequent myoclonic jerking. The jerks increased to severe shivers, spreading out from the cervical region in cranial and caudal directions when the patient tried to sit upright, stand, or walk. Startling had the same effect. Truncal and limb ataxia and intention tremor were also observed. General physical examination revealed a deep tumour in the middle of the abdomen. There was atopic dermatitis of the face and the flexural areas of the extremities.

Laboratory investigations showed an increased ESR of 78 mm/h, a leucocytosis of 12×10^9/l, increased serum activities of γ-glutamyltranspeptidase (26 units/l) and lactic dehydrogenase (250 units/l). Other routine parameters were unremarkable. Carcinoembryonic antigen (5·0 ng/ml) and CA 125 (2161 units/ml) were elevated. Serum antineuronal antibodies anti-Yo, anti-Hu, and anti-Ri were not detected. Search for neurotoxic substances (thallium, neurotoxic drugs such as phenytoin, barbiturates, and benzodiazepines) in blood and urine was negative as were serum and CSF tests of bacterial, viral and fungal infections. CSF contained 3 cells, protein was 23·5 mg/dl. The Link–Tibbling index was 0·62. Isoelectric focusing of the immunoglobulins demonstrated oligoclonal bands in CSF, but not in serum. EEG was normal, without discharges time-locked to the myoclonic jerks. Electro-oculographic analysis (EOG) showed fast conjugated eye movements with amplitudes of 20–30° without intersaccadic interval in horizontal and vertical direction at a frequency of 8/s. MRI of the brain was normal. Further investigations included a radiograph of the chest, ultrasonography of the abdomen, CT scans of the chest and the abdomen, and total body bone scanning. A large cystic tumour was detected with presumed origin in the right ovary. Multiple enlarged lymph nodes were seen around the tumour, along the large vessels of the abdomen, behind the trachea, and in Virchow's node.

Laparotomy revealed a tumour of the left ovary of diameter 35 mm, with widespread lymphogenic metastases within the whole of the abdomen. Surgery was by supracervical abdominal hysterectomy, bilateral salpingo-oophorectomy, and infracolic omentectomy. Pathological diagnosis of the surgical specimens gave a solid ovarian carcinoma, moderately differentiated as an epithelial cell tumour with no oestrogen and progesterone receptors (International Federation of Gynecology and Obstetrics stage IIIc).

With this result, paraneoplastic OMS was diagnosed and treated by intravenous and oral clonazepam (up to 5 mg daily) and diazepam (up to 40 mg daily). The patient was subsequently able to stand and to walk a few steps with support. Two weeks after surgery, intravenous chemotherapy was started with carboplatin (350 mg/m²) and cyclophosphamide (600 mg/m²). Chemotherapy was repeated three times over the following five months, accompanied by a significant improvement in both ocular movements and myoclonic jerks. The patient was able to stand and to walk with aid, and the startle reaction was negative.

Although different aetiologies may cause OMS, its paraneoplastic form cannot be differentiated by signs and symptoms from other origins.[3] As in our case, paraneoplastic OMS usually precedes the detection of the underlying tumour by weeks or months. So far, carcinoma of the ovary is known to be associated with paraneoplastic neurological symptoms of acute or subacute cerebellar degeneration, sensorimotor polyneuropathy, and polymyositis.[7] From our case, this list may be supplemented by paraneoplastic OMS.

In paraneoplastic cerebellar degeneration, an autoimmune pathogenesis has been strongly suggested. Cases with ovarian adenocarcinoma show elevated titres of antibodies mostly against Purkinje cells ("anti-Yo-antibodies").[7] Other antibodies were directed against basket cells, stellate cells, and astrocytes. Antibodies against cerebellar cells were also detected in mixed mesodermal sarcoma of the ovary, oat-cell carcinoma of the lung, ductal carcinoma of the breast, adenocarcinoma and clear cell carcinoma of the uterus, colon carcinoma, and Hodgkin's disease. The antibody "anti-Hu" has been found in paraneoplastic encephalomyelitis together with small cell carcinoma of the lung, and in some cases of paraneoplastic cerebellar degeneration accompanied by encephalopathy and polyneuropathy.[7] The antibody "anti-Ri" directed against neuronal nuclei seems to be more closely related to opsoclonus. It has been found with malignant tumours of the breast, the fallopian tubes, and axillary lymph nodules when opsoclonus was evident clinically.[8 9] These observations may underline earlier suggestions that these antineuronal antibodies show some syndrome specificity. In our patient search for "anti-Yo", "anti-Hu", and "anti-Ri" antibodies were negative in serum. Whether this may be related to the different histological nature of the underlying ovarian tumour compared to those in the literature cannot, at present, be decided. Only oligoclonal banding in CSF gave a weak indication of an intrathecal immunological reaction.

No agreed treatment exists for OMS. Trials with adrenocorticotrophic hormone, steroids, or even plasmapheresis have not always been successful.[3 4 6 8] In our patient, clonazepam and diazepam reduced eye movements and myoclonic jerks substantially.[3–5] Paraneoplastic OMS has a slowly progressive course determined by successful treatment and the subsequent biological evolution of the underlying neoplasm.[3 5 7]

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Cervical radiculopathy and bilateral internuclear ophthalmoplegia caused by temporal arteritis

A cervical radiculopathy and a bilateral classical internuclear ophthalmoplegia are rarely reported features of temporal arteritis.

A 57 year old man presented with a four day history of diplopia. During the preceding 10 days he had had right and then left sided facial and temporal pain. His medical history included untreated hypertension and mild asthma. He was a heavy smoker.

Examination revealed a painful pupil-sparing left third nerve palsy. Visual fields, fundi, and acuity were normal in both eyes. Tone and power were normal in the limbs and all reflexes were symmetrically present with flexor plantar responses. Blood pressure was 160/100 mmHg.

Blood investigations revealed a normal full blood count, normal urea and electrolytes, ESR 31 mm/hour, normal liver function tests, and a fasting plasma glucose of 7·1 mmol/l; a repeat fasting glucose was 5·6 mmol/l. A Venereal Disease Research Laboratory test was negative. A CT of the brain suggested the presence of an aneurysm of the ophthalmic artery on the left and revealed a pituitary tumour measuring 10 mm by 12 mm without suprasellar or lateral extension. Cerebral angiography confirmed the presence of a small broad based aneurysm at the origin of the left ophthalmic artery but no other abnormalities were found. Subsequent investigations showed that the pituitary tumour was secreting follicle stimulating hormone and that other aspects of pituitary function were normal.

Five weeks after presentation he developed weakness in both arms with discomfort around the neck and shoulders. He had also noticed some shortness of breath on exertion but did not complain of orthopnoea. Clinical examination revealed a residual left ptosis and a bilateral classical internuclear ophthalmoplegia with ataxic nystagmus in the abducting eye; convergence was preserved. In the upper limbs

there was wasting and weakness of deltoid, biceps, and brachioradialis bilaterally; biceps and supinator reflexes were absent bilaterally but the triceps reflexes were present and there were no sensory symptoms or signs. Tone, power, and reflexes in the lower limbs were normal and both plantars were flexor. Abdominal wall movements with respiration were paradoxical and vital capacity fell from 3·2 litres sitting to 1·9 litres lying. The ESR was now 90 mm/hour. Electrical studies showed normal nerve conduction with evidence of acute C5 and C6 denervation bilaterally. An MRI scan of the cervical region and cerebrospinal fluid examination were normal.

A gradual improvement in the patient's condition occurred but the ESR remained high and he continued to complain of occasional headaches. Eleven weeks after presentation a temporal artery biopsy was performed. Microscopy showed features typical of temporal arteritis with numerous giant cells within the wall of the artery, intimal fibrosis, and fragmentation of the internal elastic lamina. Steroid treatment was started immediately with prompt relief of the remaining headache and malaise; the strength in both arms and the exertional dyspnoea continued to improve.

Observation over the next 12 months failed to find any other cause for his symptoms and signs. MRI (including MR angiography) of the brain showed that the pituitary tumour and the aneurysm of the ophthalmic artery had not increased in size; both are being managed conservatively. He remains well on a gradually reducing course of steroids and clinical examination of the eyes and upper limbs is now normal.

In this case temporal arteritis was associated with a third nerve palsy, a bilateral classical internuclear ophthalmoplegia, and a radiculopathy affecting the fifth and sixth anterior cervical roots bilaterally. On clinical grounds it seemed that the patient had associated impairment of diaphragm function but this was not assessed formally by transdiaphragmatic pressure measurements. Although other vascular risk factors were present, and a pituitary tumour, these could not be implicated in the pathogenesis of all the neurological deficits seen.

The third nerve palsy was probably due to involvement of branches of the intraorbital ophthalmic artery as there were no features to suggest a nuclear or a fascicular third nerve palsy. A bilateral classical internuclear ophthalmoplegia is a rarely reported complication of temporal arteritis[1 2] and is probably due to emboli from the vertebral artery occluding perforating branches of the basilar artery. Both the vertebral and ophthalmic arteries are recognised as being frequently and severely affected in temporal arteritis.[3]

A cervical radiculopathy is an unusual feature of temporal arteritis and the aetiology is less clear. Five cases have been reported[4-7] and in all cases the fifth anterior cervical root has been involved, unilaterally or bilaterally, and in only one case were there sensory signs; in one case there was also evidence of unilateral involvement of the sixth and seventh anterior cervical roots. Constitutional symptoms but no other neurological signs were present in the four cases for which details are available and in all of these patients considerable improvement occurred with prednisolone treatment. Two other cases of upper limb paresis occuring in patients with temporal arteritis have been reported but the aetiology of the weakness was not established.[8]

A review of the blood supply of the cervical spinal cord and roots provides a possible explanation for the pattern of root involvement seen. The main supply comes from the anterior and posterior spinal arteries, branches of the vertebral arteries. These vessels anastomose with anterior and posterior radicular arteries that enter the spinal canal alongside their corresponding roots. There is great variation in the number, size, and location of the radicular arteries,[9] but if present those to the upper six cervical roots also originate from the vertebral arteries whereas those for C7, C8, and T1 originate from other vessels in the vicinity including the thyrocervical trunk and the costocervical trunk. Therefore the first six cervical segments and roots are dependent solely on a blood supply originating from the vertebral arteries.

We think that the most likely explanation for the radiculopathy is arteritic or embolic occlusion of the relevant radicular artery due to involvement of the parent vertebral artery. A myelopathy has not been seen in association with the radiculopathies suggesting that essential downwards flow in the spinal arteries is maintained. This downwards flow may be able to compensate via anastomotic channels for involvement of radicular arteries to the upper cervical roots but not to the lowest "vertebral artery dependent" roots, C5 and C6; this may explain why these roots are so commonly affected. It has been suggested that the impairments seen are due to damage to the cords of the brachial plexus caused by a vasculitis in the neighbouring subclavian and axillary arteries[7] but this seems unlikely as sensory involvement has been a feature in only one case and was restricted to a single dermatome.

This case serves as a reminder of the many neurological signs that may occur in temporal arteritis and of their natural history. The diagnosis of temporal arteritis should always be considered in patients with multiple or fluctuating neurological signs involving the vertebrobasilar circulation, even if the ESR is not grossly raised at presentation.

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Methylenetetrahydrofolate reductase deficiency revealed by a neuropathy in a psychotic adult

5,10-Methylenetetrahydrofolate reductase (MTHFR; EC 1.1.1.68) deficiency, although rare, may be suspected when homocystinuria is detected. Homocystinuria is also present in other inherited disorders such as cystathionine β synthase deficiency or some inborn errors of cobalamin metabolism.[1] Deficiency of MTHFR, an autosomal recessively inherited error of folate metabolism, leads to an inability to synthesise 5-methyltetrahydrofolate, the major form of folate in fluids and tissues, in amounts sufficient for remethylation of homocysteine to methionine. Therefore homocysteine accumulates in plasma whereas methionine concentrations are normal or decreased. Deficiency of MTHFR is associated with a wide spectrum of neurological abnormalities, most often convulsions and mental retardation[1]; rarely psychotic symptoms.[2] Age of diagnosis has ranged from the first days of life to adolescence.[2] Recently MTHFR deficiency was detected in a young adult of a family with premature vascular disease.[3] We report a case of MTHFR deficiency diagnosed in a psychotic adult with neuropathy.

A 45 year old Chinese woman was referred to the hospital for a gait disturbance over a week. She had lived in France for 15 years but spoke very poor French. The first of four siblings of unrelated healthy parents, her early growth and development had been normal. A schizophreniform disorder appeared at age 19. She had four children and no abortions. No relapse occurred during her pregnancies, but several psychotic episodes happened 10 years later and were treated with perphenazine enanthate. Since then, she was almost socially adapted despite probable progressive cognitive impairment with increasing difficulties in speaking and writing French and eventually speaking Chinese. Withdrawal, hallucinations, delusions, and anorexia led to psychiatric consultation. She was treated with chlorpromazine. Paranoid symptoms decreased in three weeks, and then she developed a weakness of the lower limbs with dysaesthesia.

On admission she had a flaccid symmetrical paraplegia and severely reduced sensation, predominant distally. Tendon reflexes were absent in the legs and weak in the arms. Cranial nerves were normal. She had no sphincter problems. She had a mild bilateral genu recurvatum but no noteworthy morphological abnormalities. She was oriented in space and time but was very slow, and timid. She refused food, had difficulties in sleeping, collected food wastes, and was suspicious. Cognitive evaluation was impossible and only part of the investigations required were done because of the patient's negative attitude.