## The Collet-Sicard syndrome as a complication of cardiovascular surgery

Multiple cranial nerve palsies are a diagnostic challenge as the nerves might be affected at any site along their course. A patient is described with a reversible lesion of the lower four cranial nerves due to cardiac surgery.

A 61 year old woman underwent cardiac surgery for a patent ductus arteriosus with mitral valve insufficiency. She had considerable left-right shunting with elevated pressure in the right side of the heart, resulting in tricuspid valve insufficiency. During surgery, a strongly dilated thoracic aorta, aortic arch, left subclavian artery and ductus arteriosus were discovered. The aortic arch was delivered and clips were placed between the carotid artery and the left subclavian artery as well as on the left subclavian artery. In the postoperative period, she suffered from aspiration pneumonia several times.

Six weeks after surgery, she developed speech and swallowing difficulties. Before surgery, the neurological examination had been unremarkable, but she now showed dysarthria, hoarseness and dysphagia. The function of the first eight cranial nerves was normal on both sides but the pharynx showed asymmetry on the left side with some numbness in that area. The pharyngeal constrictors were displaced to the right on phonation. Considerable tongue atrophy was present on the left side; on protusion the tongue deviated to the left (fig). The left vocal cord showed paresis. The left sternocleidomastoid muscle showed paresis and atrophy. The trapezius muscle had normal function. There was no clinical evidence of autonomic dysfunction. Otherwise the neurological examination was normal.

The clinical diagnosis was the Collet-Sicard syndrome (CSS), a unilateral lesion of the last four cranial nerves, due to ischaemia in the territory of neuromeningeal trunk of the ascending pharyngeal artery (APA). Extensive blood and urinary examinations only showed a slightly elevated erythrocyte sedimentation rate (ESR) and leucocytosis as a result of recurrent pneumonia. CSF examination was normal. CT scans, skull *x*-rays, also of the foramina, especially the jugular foraman, and chest *x*-rays were normal. Electromyography showed denervation and reinnervation activity in the left side of the tongue and the left sternocleidomastoid muscle. The signs and symptoms diminished and after one year, the neurological examination was normal.

A syndrome consisting of a unilateral lesion of the last four cranial nerves was described by Collet[1] and Sicard[2] and is now called the Collet-Sicard syndrome. For the differential diagnosis, a brainstem syndrome, the Villaret syndrome, and the cervical internal carotid artery dissection are relevant. A brainstem syndrome could definitely be excluded by physical examination. The Villaret syndrome consists of a unilateral lesion of the last four cranial nerves together with an ipsilateral incomplete Horner's syndrome with miosis and slight ptosis.[3] This syndrome is generally caused by a mass in the retromandibular space, especially carcinomas and sarcomas behind the parotid gland[4] extending into the parapharyngeal space. Our patient, however, did not have Horner's syndrome. Cervical internal carotid artery dissection might result in multiple cranial nerve dysfunction often accompanied by Horner's syndrome and mostly neck pain; our patient had no pain or autonomic dysfunction.[5 6] A fairly good recovery, as was the case in our patient, has been mentioned before.[7 9]

Lapresle *et al* reported on a patient who had a reversible vascular episode resulting in multiple cranial nerve dysfunction, probably due to catheterisation of the APA during an attempt to reach the distal external carotid artery; nine months later, this patient showed almost complete spontaneous recovery.[7] Devoize *et al* described four patients with paralysis of the lower four cranial nerves due to accidental or therapeutic embolisation in the APA during angiography. All the patients recovered or showed substantial regression of the deficits within six to nine months.[9]

The vascularisation of the distal cranial nerves has been studied by Lasjaunias and Doyan[10] and Lapresle and Lasjaunias.[11] The APA arises from the external carotid artery and supplies the last four cranial nerves. The eleventh nerve receives dual vascularisation from the jugular as well as the musculospinal subdivision of the posterior branch of the APA, which explains why the nerve is sometimes spared in pathological events involving the APA.[11] The trapezius muscle is not often involved in the CSS as was the case in our patient. Sufficient vascularisation is provided by the fact that the APA musculospinal subdivision also forms an anastomosis with the ascending cervical artery which supplies the middle cervical nerves.

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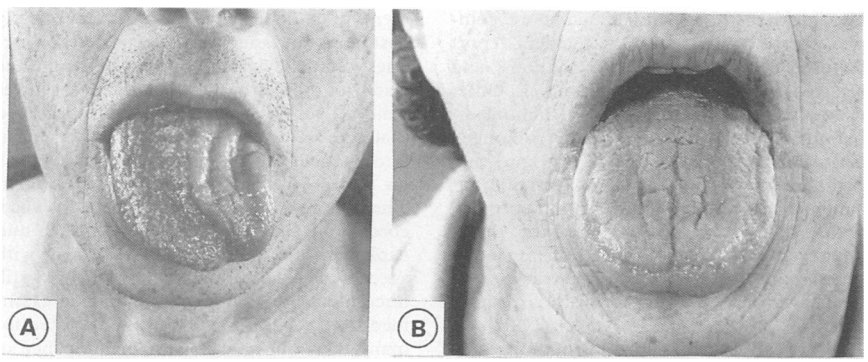


*Figure Six weeks after surgery the patient showed considerable tongue atrophy on the left side with deviation to the left on protrusion (A); after one year, the neurological examination was unremarkable (B).*

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## Late onset radiation-induced motor neuron syndrome

Radiation-induced lumbosacral lower motor neuron syndrome is a rare complication of radiotherapy to lumbar fields,[1] and previous reports have described its onset from four months possibly up to 13 years following irradiation, though detailed clinical information was not provided.[2] We report a case where symptoms began 23 years after irradiation for testicular neoplasia.

In December 1964 a 26 year old electrician had excision biopsy of a mass in the right testicle which had been present for two months. Histology revealed testicular teratoma and he received cobalt irradiation to pelvis, para-aortic nodes and scrotum in thirty six fractions over seven weeks to a maximum dose of 4500 rads (estimated total dose to lower end of spinal cord and cauda equina—4920 rads). Chest *x* ray and abdominal examination remained normal thereafter, but he developed a dusky skin reaction at the site of radiotherapy which was treated with topical emollients. He was followed up for nine years with no sign of recurrence. In 1973 he developed hypertension which was controlled on aldactide.

In April 1988 he developed a slowly progressive predominantly distal leg weakness more marked on the left. Examination revealed coarse fasciculations in both calves and right quadriceps. In the left leg there was mild weakness of knee flexion and extension and moderate weakness of all movements at the ankle. Power in the right leg was normal. Knee jerks were bilaterally brisk, but ankle jerks were depressed on the right and absent on the left. Sensation was normal and general

examination unremarkable except for some skin changes in the previously irradiated area.

Chest *x* ray and bone scan were normal. Myelography revealed minor posterior protrusion of L5/S1 disc on flexion of the back. Cerebrospinal fluid contained normal cellular constituents but elevated protein at 0·8 g/litre. Motor conduction velocities in left posterior tibial and both lateral popliteal nerves were normal as were sensory conduction velocities in superficial peroneal nerves. Electromyography of left gastrocnemius and peroneus longus revealed fasciculations, complex repetitive discharges and positive sharp waves with reduced voluntary activity suggesting denervation in the territory of L5 and S1 myotomes. Surface electromyography showed profuse fasciculations in the legs below the knee bilaterally, fewer in the right upper leg and none in the left upper leg or arms.

By June 1990 movements of both feet were weaker and fasciculations were also visible in the hamstrings bilaterally. Both ankle jerks were absent. Nerve conduction studies again showed normal motor and sensory conduction times and amplitudes in the upper and lower limbs. Proximal conduction assessed by F-waves was also normal. Central motor conduction time measured by magnetic cortical stimulation was normal in both upper and lower limbs. Electromyography from right tibialis anterior showed fasciculations, motor units of prolonged duration and high amplitude, and a discrete interference pattern. Electromyography from the right vastus lateralis showed fasciculations, recurrent trains of motor unit potentials, some large motor unit potentials and a moderate interference pattern. Electromyography of the arms was normal. Motor unit counting revealed reduction in number and increase in size of motor units from the extensor digitorum brevis bilaterally, consistent with anterior horn cell loss.

Following lumbar field irradiation a slowly evolving painless amyotrophy may develop, with lower motor neuron paresis and absent or depressed tendon reflexes.[3] Fasciculation of affected muscles is variable, but absence of pain or sensory signs and normal sensory nerve conduction velocities are characteristic. Myokymic discharges on electromyography are also a typical feature.[4]

In this case the onset of symptoms was 23 years following radiotherapy. Despite this, the characteristic clinical picture and electrophysiological evidence favour x-irradiation as the cause. Lumbar root infiltration may be excluded by the absence of pain and sensory features, the very slow rate of deterioration and normal radiographic studies whilst the localisation of abnormalities to the irradiated area of the nervous system distinguishes this condition from amyotrophic lateral sclerosis.

The development of radiation-induced neuropathy is only partially dependent on radiation dose and fractionation, and there is marked individual variation in susceptibility. Nothing is known of the factors influencing the latency of the onset of symptoms, and once established the disease is often slowly progressive, though some patients appear to stabilise.[5] The electromyographic features place the likely site of the lesion at the anterior horn cell or most proximal parts of the lower motor neuron.[6] The development of purely lower motor neuron damage after irradiation of the entire neuraxis of some patients[1] demonstrates the particular vulnerability of these cells to radiation-induced damage. Primary injury to the highly metabolically active anterior horn cell body is a possible pathology, and lumbosacral motor neurons with their very long axonal processes may be particularly susceptible.

This case illustrates that the latent period before the onset of radiation-induced lower motor neuron damage may be more prolonged than previously realised. The delay before symptoms become manifest suggests that the direct effects of radiation may become lethal to neurons only with the additive effects of cellular ageing. Vascular endothelium is very sensitive to injury from ionising radiation and ischaemic damage from radiation-induced microvascular disease is an alternative possible cause of delayed neuronal injury.

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## Delusions and cyclosporine toxicity

Since the introduction of cyclosporine there have been a small number of case reports of side effects that might be attributed to some action on the cerebral grey matter. These have included myoclonus and epilepsy but also incidents suggesting much more complex cortical activation. One incident report featured complex visual hallucinations[1] and referred to three previous examples. Other examples have included cortical blindness,[2] hemiplegia and focal convulsions,[3] prolonged confusion of possible epileptic origin[4] and complex movement disorders, akinetic mutism and dysphasia.[5] These often occurred with cyclosporine levels within the therapeutic range. Delusions have not previously been reported and we describe a case in which we believe cyclosporine was responsible.

A 63 year old man with a history of treated hypertension from 1979 had a myocardial infarction complicated by a left ventricular aneurysm and cardiac failure in 1981. In the early months of 1991 he had episodes of intermittent mild confusion and bifrontal headaches. These were felt to be related to low cardiac output related to his now end stage heart failure and he received cardiac transplantation in May 1991 at which he was started on prednisolone, azathioprine (10 mg daily) and cyclosporine (initially given intravenously but changed postoperatively to 3 mg/Kg/day orally, a low dose being used because of his slightly impaired renal function), nystatin, ranitidine, thiamine and aspirin. There was some early post operative confusion without localising features which progressively increased. A CT brain scan one month postoperatively showed deep white matter changes and a small left parietal infarct. Two days after this he began to have episodes of dysphasia and right sided weakness lasting from 30 minutes to several hours with full recovery between episodes. He was transferred to Charing Cross Hospital for further assessment. On arrival he was unresponsive and exhibited version of head and eyes to the right with shaking of the right arm and facial grimacing. He was treated with intravenous diazepam which abolished his focal fitting, allowing him to recover consciousness and speak when he was immediately orientated, able to give his name, the place and date of cardiac transplantation and obey three step commands. There were no focal neurological signs. The cyclosporine dose was reduced to 2 mg/Kg, he was given a phenytoin load and the diazepam maintained as an infusion for 18 hours. Carbamazepine was introduced 12 hours after admission because of persisting focal fitting.

Full blood count revealed a haemoglobin of 11·0 g/dl with normal indices, a white count of 11·8 $\times$ $10^9$/l and a platelet count of 273 $\times$ $10^9$/l. Biochemical evaluation showed normal sodium, potassium and glucose, a urea of 9·9 mmol/l, creatinine 145 $\mu$mol/l, bilirubin 1·3 $\mu$mol/l and alkaline phosphatase 276 U/l but urate, proteins, aspartate aminotransferase, calcium and phosphate were all normal. Magnesium in serum was 0·74 mmol/l and in red cells 2·21 mmol/l (normal range in red cells 1·8 to 2·7 mmol/l). The CSF contained no cells, a protein of 0·5 g/l and glucose of 4·8 mmol/l. Repeat CT scan revealed no new abnormalities. Serum cyclosporine levels were 59 ng/ml on admission and 105 ng/ml three days later (therapeutic range 75–150 ng/ml in serum) despite the dose reduction.

As the focal fitting abated at 24 hours post admission frequent bilateral myoclonic jerks became apparent which persisted for a day after the fitting ceased. At this stage his higher intracranial functions were rapidly returning to normal except for the development of a delusion. This was very clearly described and accurately repeated on requestioning days later. On first hearing it the clarity of the description was such that it was believed for several minutes. He reported that a piece of a cork ceiling tile had fallen into his open mouth while lying on his back on a trolley on the way to the CT scanner. The cork had lodged behind one of his vocal cords and had caused a sore throat and explained the difficulty he had had with speech. He felt that his throat was still uncomfortable and that it should be examined for the cork. This delusion persisted for many days but abated with maintenance of his cyclosporine at the lower dose. On follow up one month later he recalled the delusions