**Short report**

**Neck tumour with syncope due to paroxysmal sympathetic withdrawal**

JACK ONROT, RONALD G WILEY, AGNES FOGO, ITALO BIAGGIONI, DAVID ROBERTSON, ALAN S HOLLISTER

*From the Autonomic Dysfunction Clinic, Departments of Pharmacology, Medicine, Neurology and Pathology, Vanderbilt University School of Medicine, and VAMC, Nashville, TN*

**Summary**  A patient with recurrent squamous carcinoma metastatic to the neck after radical neck dissection and high dose radiation therapy developed paroxysmal hypotensive episodes that were severe, spontaneous and characterised by suppressed sympathetic but not enhanced parasympathetic activity. Intravenous pressors were successful in treating acute episodes but neither drug therapy nor surgical neck exploration reliably prevented syncopal attacks. Glossopharyngeal and/or vagal nerve infiltration by tumour with episodic activation of the afferent limb of the baroreflex arc producing vasodilatation primarily due to sympathetic withdrawal is the likely mechanism of life threatening syncope in this patient.

Macdonald, et al. recently called attention to the association of neck tumours and syncope and suggested it was more common than previously realised. However, specific data on the underlying pathophysiology and management of syncope in this setting are very limited. We present here a patient with neck tumour and syncope who underwent detailed autonomic testing.

**Case report**

This 73 year old white male underwent resection of a squamous carcinoma of the left anterior tonsillar pillar in April 1983 followed by left radical neck dissection for lymph node metastases in November 1983 and by 6100 rads external beam radiation in February 1984. Syncopal spells began in August, 1984 shortly after the onset of dysphagia, hoarseness, and left sided deafness. Syncopal attacks were preceded by left occipital head pain and associated with excessive salivation. Indomethacin, fluorocortisone, phenylpropanolamine and salt tablets produced only transient benefit. By November 1984, the syncopal attacks were occurring even while supine.

On admission (November 1984), supine blood pressure (BP) was 165/75 mm Hg and heart rate was 92/min. Cardiovascular examination was normal. Neurological evaluation was remarkable for left lower facial weakness, sensorineural deafness on the left, hoarseness with poor cough, left tongue wasting and weakness, and a left Horner's syndrome. Admission blood tests, EKG, echocardiogram and radionuclide ventriculogram were unremarkable. Arteriography showed a 50% smooth narrowing of the left common carotid. EEG revealed mild, diffuse slowing without focal features. Head CT scan revealed mild cerebral atrophy and a soft tissue mass encasing the left internal carotid artery. Cr51-labelled RBC mass and T131-labelled albumin plasma volume were normal.

Numerous attacks were observed even while supine with precipitous decline of BP to 50/? and syncope which did not respond to volume expansion but did respond to intravenous dopamine or norepinephrine. Untreated, the attacks spontaneously resolved in 10–15 min. Central venous pressure fell from 10 to 3 mm Hg during one attack. After partial success with local anaesthetic injections, an attempt was made surgically to denervate the left carotid sinus. Post-operatively, syncopal attacks recurred despite drug and fluid therapy (fig 1). Weight loss and dysphagia progressed, gastrointestinal bleeding developed along with aspiration pneumonia, hypoxaemia, confusion and fluctuating level of consciousness. He succumbed to hypotension and cardiac arrest 3½ weeks after operation.

Necropsy confirmed the presence of bilateral bronchopneumonia. Residual tumour was present in the neck with involvement of the left temporal bone, left mastoid sinuses and inner ear. Fibrosis and tumour infiltration of peripheral nerves was present in a fibrotic mass removed en bloc with the distal left internal carotid artery just beneath the base of...
the skull (fig 2). Careful gross and microscopic examination failed to reveal any evidence of intracranial pathology.

**Autonomic nervous system testing**

Testing was performed after a 2 day period free of attacks. Respiratory variation with heart rate and response to right carotid massage were normal. There was no response to left carotid massage. Intra-arterial BP monitoring revealed normal responses² to Valsalva's manoeuvre, ice water immersion of the hand and isometric hand grip. The patient exhibited a normal pressor response to IV phenylephrine and normal chronotropic and depressor responses to IV isoproterenol³.

**Catecholamines**

During a catecholamine study, blood levels (supine) of noradrenaline (NE) were 500 and 525 pg/ml and epinephrine (E) 53 and 48 pg/ml while BP was 180/80 mmHg and heart rate was 96/min respectively, consistent with the physiological and psychological stress of the ICU setting. Fortuitously, an attack occurred 5 mins later; the patient felt syncopal with BP = 60/? and HR = 96. Norepinephrine in blood drawn immediately was 410 pg/ml and epinephrine was 57 pg/ml. On another occasion during recovery from an attack, NE = 634 and E = 262 pg/ml. Tyramine, 3000 µg raised mean BP by 25 mm Hg and NE increased from 700 to 847 pg/ml. Ice water immersion of the hand increased NE from 707 to 802 mm Hg and yohimbine, 2-5 mg, raised BP from 180/85 to 203/96 mm Hg, NE from 598 to 770 pg/ml and E from 60 to 85 pg/ml.

**Discussion**

Detailed autonomic nervous system testing in this patient failed to reveal a significant sympathetic or parasympathetic nervous system defect in the basal state. Adequate BP and heart rate responses to cold pressor, handgrip and Valsalva tests indicated an intact capacity of the sympathetic nervous system to respond to stimuli.² In addition, there was normal sensitivity to exogenous sympathomimetic amines (phenylephrine, isoproterenol) which is consistent with intact sympathetic vasomotor innervation. Autonomic failure patients generally exhibit marked hypersensitivity to these agents.³

Plasma NE levels reflect the balance between release, spillover and clearance, and are considered a reliable index of sympathetic activity.⁴ Plasma NE

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**Fig 1  Schematic diagram of hospital course. The four major drug therapies attempted are indicated as shaded areas. Daily dose scales are given on vertical axes at left. Each hypotensive attack witnessed in hospital is indicated by a vertical slash. Neck surgery with skeletonisation of the carotid bifurcation is indicated by the arrow, ‘operation.’ Self-limited episodes of atrial fibrillation are indicated by arrows beneath ‘a fib.’ Date is indicated along horizontal axis. Parasympathetic blockade with atropine 2 mg raised resting HR but failed to reverse hypotension. Carbamazepine has been used to treat syncope in association with glossopharyngeal neuralgia.⁸ ¹⁰ Yohimbine is a centrally active alpha-2-adrenoceptor antagonist that acts presynaptically to enhance sympathetic vasomotor outflow.¹⁵ Methscopolamine and yohimbine together produced limited improvement presumably by blocking all cholinergic depressor mechanisms and stimulating sympathetic outflow.**
Fig 2 Photomicrographs of tumour involving nerves adjacent to the left internal carotid artery 1–2 cm below the styloid process; tissue obtained at necropsy. Top: low magnification image of a medium sized nerve embedded in dense fibrosis and surrounded by rim of tumour cells. At higher magnification and with special stains, this nerve and others contain decreased numbers of axons and increased numbers of Schwann cell nuclei consistent with damage to axons and myelin sheaths. Bottom: higher magnification image of a small nerve fascicle in same tissue block with a thick layer of tumour cells encasing a nerve segment that is devoid of axons. In both photos, arrowheads indicate tumour cells, stain is H and E and magnification bars in right lower corner indicate 200 µm. Note: these specimens were obtained from the carotid sheath just beneath the base of the skull after the last surgical procedure and demonstrate longitudinal infiltration of tumour along the nerves. No tumour was found intracranially at necropsy suggesting that intracranial nerve section might have been successful in stopping syncopal attacks.
rose in response to cold pressor, tyramine and yohimbine challenges indicating intact sympathetic responses. However, during an attack of hypotension to 60/7 mm Hg with presyncope, NE fell from 500 to 410 pg/ml. This was the lowest NE level measured in this patient on any occasion. This apparent sympathetic withdrawal is even more striking in the context of the profound fall in blood pressure. Syncope should have produced an increase in NE, not a decline.\(^5\) The elevated E and NE during recovery from an attack probably indicates an appropriate adrenomedullary response which contributed to eventual recovery of BP. Some parasympathetic activation was also involved as supported by the excessive salivation that accompanied the pain and hypotension attacks.

Glossopharyngeal neuralgia with syncope may occur in patients with\(^1\) -\(^7\) or without\(^8\) -\(^10\) neck tumours. A patient similar to ours with this entity also had normal BP and NE responses to orthostasis and showed a fall in NE with a delayed rise in E in association with a hypotensive episode.\(^6\) Although pure vasodepressor syncope is thought to account for 5–10\% of cases of idiopathic carotid sinus syncope,\(^11\) 10/17 (59\%) neck tumour patients with syncope had episodes that appeared to be purely vasodepressor and/or persisted after pacemaker therapy.\(^1\) Syncope persisting after pacemaker therapy in similar patients has also been reported by others.\(^6\) -\(^8\) -\(^12\) -\(^14\) Thus, pure vasodepressor syncope or a significant vasodepressor contribution to syncope seems more common in association with neck tumours than in idiopathic carotid sinus syncope. We propose therefore that paroxysmal activation of baroreceptor afferent discharge due to infiltration of the ninth and/or tenth cranial nerves by tumour resulted in profound hypotension primarily due to withdrawal of sympathetic tone and that this is a common mechanism of syncope in patients with recurrent neck tumours. Intracranial transection of the ninth and rostral portion of the tenth cranial nerves is indicated in similar patients with severe, recurrent hypotensive episodes.\(^1\) -\(^7\)

### References

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