Vasodepressor syncope and recurrent pharyngeal carcinoma: a form of carotid sinus syndrome?

Introduction

Syncope occurring in the setting of head and neck malignancy may have several possible causes. Local effects of a tumour in the parapharyngeal area may produce a syncopal syndrome similar to carotid sinus hypersensitivity, but with distinctive differentiating features.

This article presents a case of profound vasodepressor syncope in a patient with recurrent pharyngeal malignancy, and discusses the mechanisms by which this occurs and the possible therapeutic options.

Discussion

Carotid sinus syndrome was first described in the 1930s, and although the exact diagnostic criteria remain a subject of debate (Krediet et al, 2011) it is classically manifest as prolonged asystolic pauses and a fall in blood pressure following carotid sinus massage or during day-to-day activities which result in carotid sinus manipulation. The incidence increases with age, and symptoms are usually improved or abolished by pacemaker implant.

Syncope in the setting of pharyngeal malignancy was initially presumed to be analogous to carotid sinus syndrome caused by local tumour effects upon the carotid sinus. Cicogna et al (1985) described three patients with various forms of neck malignancy and recurrent syncope, noting the syncope differed significantly from classical carotid sinus syndrome. The episodes were characterized by a marked vasodepressor response with severe and prolonged hypotension the predominant feature, associated with varying degrees of bradycardia but no prolonged asystolic pauses. As in this patient, right ventricular pacing failed to abolish the episodes in each case, although in two cases symptoms improved following atrioventricular dual chamber pacing.

Cicogna et al (1993) then published a larger case series of eleven patients. The authors confirmed that the syncope seen in relation to parapharyngeal lesions differs markedly from classical carotid sinus syndrome, with more severe and frequent symptoms, a more profound vasodepressor element, failure of pacing to abolish the episodes, and an absence of any apparent triggering factor. Response to pharmacological therapy with anticholinergic and vasopressor agents was limited. Also the authors consistently found that carotid sinus massage failed to reproduce syncopal episodes, and questioned the involvement of the carotid sinus in the process. They hypothesized instead that syncope relates to glossopharyngeal nerve involvement within the parapharyngeal

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Case Report

A 63-year-old man presented with recurrent syncope. He had received radical radiotherapy 2 years previously for localized squamous cell carcinoma of the pharynx which had been successful with no clinical evidence of local tumour recurrence.

Syncopal episodes were initially treated as epilepsy and investigations performed to assess for possible cerebral metastases. Computed tomography of the brain with contrast showed no evidence of metastatic disease and electroencephalogram showed no evidence of epileptiform activity. Magnetic resonance imaging of the brain showed minor changes of white matter ischaemia but no other abnormality. Computed tomography of the pharyngeal region demonstrated thickening of the posterior and lateral pharyngeal wall and loss of clarity of the deep cervical fat surrounding the neck vessels. These changes were felt to be consistent with previous radiotherapy.

Syncopal attacks continued over several months despite increasing doses of sodium valproate. During a witnessed episode of syncope while in hospital it became apparent that the episodes were predominantly hypotensive in origin, characterized by a sudden fall in blood pressure to an initially unrecordable value, associated with mild sinus or junctional bradycardia (heart rate 40–45/min). Hypotension resolved following intravenous fluid and head down positioning, but normalization of blood pressure could take up to 30 minutes. Blood pressure during the admission demonstrated a highly labile pattern with periods of hypertension between the syncopal attacks (*Figure 1*). Short synacthen test was normal. Carotid sinus massage provoked no bradycardia or hypotension.

An initial working diagnosis was made of baroreceptor failure as a result of previous radiotherapy. In view of the associated bradycardia a temporary right ventricular pacing wire was placed, but the syncope continued unchanged. Treatment with midodrine (an alpha-receptor agonist) was therefore initiated, which ameliorated the severity of the attacks but did not abolish them. Dual chamber pacing programmed with a rate drop response algorithm (which paces at higher heart rates of 100–110/min during periods of bradycardia) was then performed, which again lessened the severity of attacks but did not abolish them. Finally, treatment with fludrocortisone was initiated. The combination of all these measures abolished the attacks. During this period the patient also complained of swallowing difficulty, and a barium study demonstrated evidence of aspiration of contrast agent.

Repeat computed tomography imaging of the pharynx performed 6 months after the initial study demonstrated progressive thickening of the soft tissue in the right parapharyngeal space which now displaced the internal jugular vein and engulfed the internal and external carotid arteries, consistent with recurrent malignancy (*Figure 2*). The abnormal soft tissue also involved the path of the glossopharyngeal nerve, suggesting a possible cause for the swallowing difficulty. A final diagnosis of vasodepressor syncope secondary to the local effects of recurrent pharyngeal malignancy was made. The patient was referred for consideration of palliative chemotherapy.

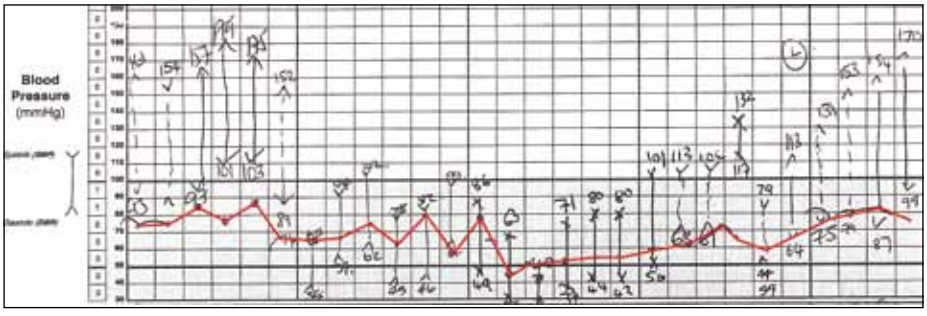

Figure 1. Blood pressure chart demonstrating a highly labile blood pressure with periods of hypertension seen between syncopal episodes characterized by marked hypotension. The initial readings are routine observations taken over approximately 12 hours. The sudden fall in blood pressure and subsequent gradual recovery occur over approximately 90 minutes. Heart rate is shown in red, the mild bradycardia occurring during the nadir of blood pressure is apparent.

space, rather than direct compression or invasion of the carotid sinus.

The glossopharyngeal nerve provides afferent input from mechanoreceptors to the medullary vasomotor centre, with efferent fibres via the vagus nerve. This reflex arc is responsible for vasomotor regulation, and stimulation of the reflex initiates parasympathetic inhibition of sinoatrial and atrioventricular nodal conduction, and reduces noradrenaline-mediated vasoconstriction, reducing peripheral arterial resistance. The involvement of this reflex pathway in syncope is supported by results of surgical intervention in which two of eleven patients underwent carotid sinus denervation, which had no impact on symptoms. However, in six of the eleven patients intracranial resection of the glossopharyngeal nerve (and therefore interruption of the glossopharyngeal–vagal reflex arc) was performed and the clinical features completely resolved. The authors proposed labelling syncope in this setting as 'parapharyngeal space lesion syncope-syndrome'.

Treatment of the primary tumour with radiotherapy or chemotherapy has often already been performed at the time of presentation with syncope, and further treatment may not be possible, although should be considered if appropriate. Ju et al (2009) reported a man with recurrent tonsillar cancer and mixed vasodepressor and cardioinhibitory type syncope which continued following dual chamber pacemaker implant, but resolved following chemotherapy.

The proposed mechanism for syncope fits with the features noted in this patient with profound hypotension but only mild bradycardia, and continued attacks despite pacing. Additionally swallowing difficulty noted is consistent with involvement of the glossopharyngeal nerve by the malignant process. The results of pacing and pharmacological treatment in this setting are highly variable and often disappointing. In this patient a combination of pacing with a high heart rate during episodes of bradycardia combined with midodrine and fludrocortisone controlled the attacks, and surgical intervention was not necessary.

Conclusions

Parapharyngeal pathology is an unusual cause of syncope, but the possibility should be considered, particularly in patients presenting with syncope and a background of head and neck malignancy or in those with associated head and neck symptoms. Syncope in this setting is characterized by a predominant vasodepressor response which may be prolonged and without precipitant, and differs in character from classical carotid sinus syndrome. The syncope is probably mediated via a vagal reaction prompted by compression or invasion of afferent vasomotor fibres of the glossopharyngeal nerve. Although bradycardia may be a feature, pacing is usually ineffective or at best only partially effective. Pharmacological management has unpredictable results. A combination of midodrine (an alpha-receptor agonist) and fludrocortisone were helpful in this case, but surgical transection of the glossopharyngeal nerve may be considered in resistant cases.

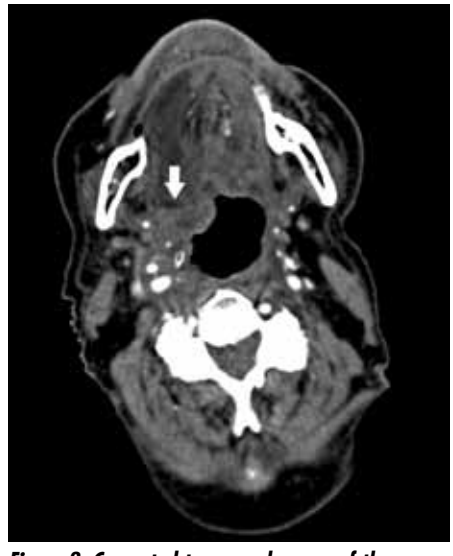

Figure 2. Computed tomography scan of the pharyngeal region showing thickening of the parapharyngeal tissues on the right side around the neck vessels (arrow).

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LEARNING POINTS

- Syncope in head and neck malignancy may be the result of local compressive or invasive effects of the tumour.
- Syncope differs from classical carotid sinus syndrome with a predominant vasodepressor, hypotensive component probably mediated by the glossopharyngeal and vagus nerves.
- Treatment may require a combination of pharmacological therapy and pacing to alleviate or abolish symptoms.
- In resistant cases surgical transection of the glossopharyngeal nerve may be considered.