Carotid Sinus Syndrome as a Manifestation of Head and Neck Cancer - Case Report and Literature Review

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Abstract

Head and neck cancers rarely manifest as Carotid Sinus Syndrome (CSS). CSS is a rare complex of symptoms found in 1% of all patients who experience syncope, the pathophysiology of which is yet to be fully understood. Common trigger mechanisms for CSS include neck movement, shaving, constricting neck wear, coughing, sneezing and straining to lift heavy objects. The left carotid sinus mainly causes AV block while the right carotid sinus mainly causes sinus bradycardia. The incidence of AV block in CSS is very low (4.9 to 16.7%) as reported in many case series. In case of head and neck cancers, treatment is by surgical removal of the cancer, chemotherapy or radiation.

We present an interesting case where a patient with head and neck cancer developed bradycardia and second degree heart block due to compression of the carotid sinus on neck movement. Whenever the patient turned his neck to the right, telemetry showed prolongation of the PR interval and 2:1 conduction across the AV node (Wenckebach) which resolved on moving his neck back to the midline.

In conclusion, unexplained abrupt episodes of bradycardia and intermittent heart block should alert the physician of the possibility of carotid sinus compression by a neck mass in patients with head and neck cancer.

Keywords
Carotid sinus syndrome, Carotid sinus hypersensitivity, Head and neck cancer, Wenckebach heart block

Introduction

The carotid sinus is a bulb like enlargement of the internal carotid artery at its origin. It can be palpated just below the angle of the jaw by tilting the neck slightly backwards and away, at the level of the thyroid cartilage [1]. The Carotid Sinus Reflex serves as a regulatory mechanism in maintaining arterial blood pressure. Receptors for this reflex are located in the tunica adventitia of the carotid sinus and they generate impulses by stretch of the arterial wall, transmitted by the nerve of Hering (via Glossopharyngeal Nerve) to the Medulla. Efferent fibers transmit impulses through sympathetic adrenergic nerves and the Vagus nerve, affecting the sinus node (of the heart), AV node and other blood vessels in the body [2].

In 1799, Parry noticed that the heart rate can be slowed by applying pressure over one of the carotid sinuses [3]. An exaggerated response to this maneuver is called Carotid Sinus Hypersensitivity (CSH). Most patients with CSH are asymptomatic [4,5]. However, sometimes CSH can manifest with hypotension, cerebral ischemia, spontaneous dizziness or syncope, and this is termed Carotid Sinus Syndrome (CSS). The incidence of CSS increases with advancing age [2,6]. Spontaneous CSS is a rare phenomenon, found in 1 percent of all cases of syncope [4]. Induced CSS is much more common, found in 14% syncope cases in one study and diagnosed by carotid sinus massage or compression [7].

Rarely, head and neck tumors can cause Carotid Sinus Syndrome [8], and this often resolves with treatment of the underlying malignancy [9]. The first case of Carotid Sinus Syndrome with head and neck malignancy was described by Weiss and Baker in 1933 [10]. A strong carotid sinus reflex in neck tumors is attributed to either pressure by the tumor on the carotid body, or invasion of the carotid sinus or glossopharyngeal nerve by the tumor itself [1,8].

A hypersensitive carotid sinus can cause an abnormally strong efferent vagal discharge, which could result in marked sinus bradycardia, sinus arrest or impaired Atrio Ventricular (AV) conduction [2,11,12]. Herein, we describe a case where a recurrent tonsillar carcinoma in a left submandibular lymph node caused a patient with baseline first degree heart block to have intermittent episodes of bradycardia with second degree Mobitz type 1 heart block (Wenckebach phenomenon). These episodes were brought on by neck turning and carotid massage, evidenced by the telemetry.

Case

A 70 year old hispanic male with a history of hypertension, gout and left sided squamous cell tonsillar carcinoma (treated with neck dissection and brachytherapy 6 months ago) came in for examination in a local clinic. He presented with symptoms of severe pleuritic chest pain, a decreased appetite with 15 pounds weight loss over 2 weeks, fever of 40°C and productive cough. A chest X-ray showed consolidation and the patient was treated with Piperacillin/Tazobactum and Doxycycline for pneumonia. On further evaluation he was found to have an elevated WBC count at 22,000/mm³ with left shift, an elevated ESR of 126 and a serum Calcium level of 15.2 mg/dl for which he was subsequently referred to our institution.

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The patient’s baseline ECG (Figure 1) showed a first degree heart block with prolonged PR intervals, regular rhythm and a normal QRS complex. The QT interval was significantly shortened due to the hypercalcemia. On examination of his radial pulse, there were transient episodes of bradycardia which could not be explained. For close monitoring of the patients condition, he was transferred to the medical ICU and kept on a 24 hour telemetry.

The patient’s only other significant history was hypertension in both his parents and Marfan’s syndrome in his mother and 2 siblings. An echocardiogram was completely normal. He smoked 1 pack per day for 35 years, and quit 5 years ago. His current medications included Amlodipine for hypertension and Allopurinol+Indomethacin for gout.

On general examination the patient was found to have a palpable 1.0 cm mass in the left submandibular region that was firm, fixed and non-tender (Figure 2). Fine Needle Aspiration Cytology (FNAC) of the mass, along with Computerized tomography (CT) (Figure 3) and Positron Emission Tomography (PET) imaging (Figure 4) confirmed the presence of squamous cell carcinoma with atypical squamous cells, most probably a recurrence of his tonsillar cancer. The patient’s PTHrP was elevated and was considered the cause of his hypercalcemia. His calcium levels normalized in response to IV normal saline over the next few days along with Calcitonin and Pamidronate.

The patient’s telemetry (Figure 5) was very remarkable. It showed intermittent periods of asymptomatic bradycardia - a heart rate reaching 35/min with a second degree type 1 heart block (Wenckebach pattern). The QRS complex was not widened during these episodes. We noticed that whenever the patient turned his neck to the right, he developed bradycardia and 2:1 conduction across the AV node. On turning his neck back to the midline, heart rate returned to normal and the AV conduction defect resolved. Palpation over the left sided neck mass also at times could induce episodes of bradycardia and second degree heart block.

The treatment plan was focused on surgical removal of the tumor with anticipated resolution of the patient’s asymptomatic bradycardia and heart block. If bradycardia episodes persisted, a permanent pacemaker would be implanted. However during the course of hospitalization, the patient had ongoing fevers and lung consolidation showed enlargement despite the use of antibiotics. Tumor associated fever was suspected and a bronchoscopy was

**Figure 1:** Baseline electrocardiogram showing first degree heart block (PR interval = 236 msec) indicated by red arrows and a shortened QT interval (324 msec).

**Figure 2:** Mass with soft tissue swelling in the left submandibular region indicated by a black arrow.
performed which showed metastasis of the primary tonsillar cancer in the left side along with a CT scan that showed impingement of the tumor on the left main bronchus and left pulmonary artery causing necrotizing post-obstructive pneumonia.

In conclusion, the patient had recurrence of his tonsillar cancer in the left submandibular region (confirmed by FNAC) that caused compression of his carotid sinus resulting in progressive AV block. Further, metastatic lesions were also found in the lungs causing paraneoplastic hypercalcemia. Due to the extensive nature of his tumor spread, he transferred to our cancer center for comfort care. We prescribed NSAIDs to help with his tumor fever. After being discharged on home hospice, he unfortunately succumbed to his illness 2 weeks after.

**Discussion**

The carotid sinus syndrome (CSS) is a complex of symptoms resulting from excitation of the hyperactive carotid sinus reflex. It can be classified into three types: (1) The cardioinhibitory response (70-75% of cases) - bradycardia or asystole lasting more than 3 seconds, mediated by the Vagus nerve. (2) The vasodepressor response (5-10% of cases) - fall in systolic pressure greater than 50 mm Hg. (3) The mixed type - a combination of the cardioinhibitory and vasodepressor type (20-25% of cases). A “fourth” type, noted previously in the literature as the “cerebral response” is due to direct compression of the carotid artery causing ipsilateral cerebral ischemia and not a true “reflex”, hence excluded as a component of the carotid sinus syndrome [13]. McIntosh et al. studied the characteristics of each type of CSS in elderly patients (>65yrs) and found 29% patients to have cardioinhibitory CSS, 37% to have vasodepressor CSS and 34% to have mixed CSS [14].

In most cases of CSS, no obvious precipitating cause can be identified. Earlier stated trigger mechanisms include head and neck movement, hyperextension of the neck, constricting neckwear (such as collars) and shaving to name a few [15,16]. Any pathology close to the carotid sinus such as carotid body tumors, local tumors such as thyroid cancers, cervical lymphadenopathy, and internal carotid artery aneurysms can also cause CSS [4,8,17]. Triggering actions such as coughing, sneezing, straining for stool, and lifting of heavy objects are also known to cause CSS [5,10,18]. The clinical features of people diagnosed with any type of CSS are the same - dizziness, unexplained
The different responses to stimulation of the right versus left carotid sinus are both interesting and clinically relevant. Sigler in the early half of the 20th century studied the carotid reflex in 345 individuals and found that both the right and the left carotid sinuses caused slowing of the heart [19]. However, the left showed more frequent response to stimulation than the right. Sino-atrial asystole, or complete stoppage of the heart occurred twice more often with pressure on the right. Mild degrees of atioventricular (AV) block (First degree and Mobitz type 1) occurred equally between the right and the left, but high degrees of AV block (Mobitz type 2 and third degree) occurred twice more often with pressure over the left, especially complete heart block.

There are many theories to explain CSS in patients with head and neck cancer. Muntz and Smith postulated that a tumor located near the Carotid Sinus or its nerve could cause a permanent depolarization of its axons with an increased tendency of adjacent uninjured axons to fire impulses causing signs and symptoms of CSS [20]. Radiation therapy of the carotid sinus has often been used to treat malignancies of the head and neck region, but some case series have described it as a cause of CSH (by post-irradiation fibrosis) by a mechanism similar to the one just described [8,21]. Our patient had received Brachytherapy for his primary tonsillar carcinoma, which could be the cause of the CSH he developed. We suspect that either of these theories could explain CSH in our patient. Wallin and Westerberg suggested that syncope in these patients is caused by abnormal impulses that are rerouted via the pharynx to the dorsal motor nucleus of vagus, causing excitation of the vagus [22]. Dyskman and Montgomery postulated that catecholamine levels decreased during CSS attacks and therefore caused a decrease in adrenergic response, but the adrenomedullary response was intact [23]. Glossopharyngeal nerve invasion by a tumor can also cause neuralgia without any disease in the carotid sinus area, termed glossopharyngeal neuralgia [9]. Lesions at the cerebellopontine angle can cause cardiovascular symptoms similar to CSS. In spite of these theories, the pathophysiology of CSS due to head and neck cancer is yet to be fully understood.

Our patient had a left sided neck mass and documented a 2nd degree heart block, which as noted earlier and explained by Sigler, is more common with left sided carotid sinus stimulation. Similar results were also shown by Purks in his study, where the right carotid sinus had greater influence on the SA node while the left had a greater influence on the AV node [24]. However McIntosh et al, in their study of 55 CSH patients, found the overall cardioinhibitory response to be more frequent on the right (54%) as opposed to the left (27%) [14]. In another study by Sigler, males showed a greater frequency of response to carotid sinus stimulation than females as well as a greater degree of slowing [6]. Out of a total of 426 patients, 193/246 males (79.4%) showed response to carotid sinus pressure versus 116/183 females (63.3%). The study also showed that a greater response to carotid sinus stimulation was seen in patients having hypertension and/or underlying atherosclerotic heart disease.

Our patient with CSS had a Mobitz type I heart block, since the telemetry showed prolongation of the P-R interval in successive beats followed by dropped beats with a narrow QRS complex. His sinuses rate was not slowed (Figure 5). Case series describing cardioinhibitory CSS show the effector response is mainly by inhibition of the SA node and less often by the AV node. Sigler when studying the EKGs of 345 patients, observed AV block in only 25 of them (7.25%) and high degrees of AV block in 17 of them (4.93%) [19], while Purks out of 67 patients observed AV block in only 7 (10.45%) [24]. Walter et al described 21 cases of his own out of which 3 cases showed AV block (14.3%) [12], while Maggi et al in 2007 described 18 cases of which again only 3 showed AV block (16.7%) [25].

Treatment of CSS depends on the frequency and severity of symptoms. For immediate treatment of CSS, anticholinergic drugs and cardiac pacing are useful [23]. Anticholinergic drugs include Atropine, Propantheline and longer acting formulations like Hyoscine. However due to larger doses, issues of long term tolerance and anticholinergic side effects, they are less favored over pacemakers. If the patient has cardioinhibitory CSS, like in our case, it is best treated with dual chamber cardiac pacing [7]. Other surgical methods of treatment include surgical denervation of the carotid sinus by sectioning the nerve of hering, arterectomy with adventitial stripping and intracranial sectioning of the glossopharyngeal nerve and upper 2 rootlets of the vagus nerve [26]. But there is limited data regarding the effectiveness of these therapies. Treatment of the vasodepressor or the mixed type of CSS is unsatisfactory and remains to be established. Cardiac pacing is ineffective in pure vasodepressor CSS since it can only control the bradycardia component that is found in cardioinhibitory CSS and not the low blood pressure [9]. Limited success has been achieved with beta-blockade (to block the reflex) either alone or in combination with ephedrine, however there is always the risk of supine hypertension and aggravation of the bradycardia itself [27]. Mild cases could be treated with mineralocorticoids to increase blood volume. Severe cases again, could be treated with surgical denervation of the carotid sinus.

In patients with head and neck cancers, definitive treatment is by eliminating the cause, that is the tumor itself. This is either by surgical removal of the tumor or induction chemotherapy to help with regression of the tumor [28]. Chemotherapy agents include Cisplatin, Paclitaxel, Docetaxel, 5-Fluourouracil and Cetuximab. Monotherapy with Docetaxel showed a 27-42% response rate [29]. Docetaxel with Cisplatin, which is the most common combination regimen showed a greater response rate of 42-80% among several studies [30,31]. Therefore multiple agents should be preferred over monotherapy. Radiation therapy, although having lesser efficacy is also a treatment option.

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References
3. Parry CH (1799) An inquiry into the symptoms and causes of the syncope anginosa commonly called angina pectoris.
27. Task Force for the Diagnosis and Management of Syncope; European Society of Cardiology (ESC); European Heart Rhythm Association (EHRA); Heart Failure Association (HFA); Heart Rhythm Society (HRS), Moya A, Sutton R, Ammirati F, Blanc JJ, et al. (2009) Guidelines for the diagnosis and management of syncope (version 2009). Eur Heart J 30: 2631-2671.