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Case Report

Bradycardia secondary to autonomic involvement by small cell lung cancer

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ABSTRACT

We present a case of a male in late 50s with Small Cell Lung Cancer (SCLC) who came with near-fainting episodes and was found to have unexplained bradycardia despite thorough evaluation ruling out common causes. Autonomic testing revealed involvement of both sympathetic and parasympathetic nervous systems, likely due to tumor encasement of cardiac nerve supply. This case illustrates an unusual etiology for bradycardia in SCLC cancer patients, developing from secondary effects due to physical extension of tumor.

Keywords: Bradycardia, Autonomic nervous system, SCLC, Lung hilum, Syncope

INTRODUCTION

Bradycardia is a medical condition characterized by an abnormally slow heart rate, typically less than 60 beats per minute in adults. It is often asymptomatic but can also lead to symptoms such as dizziness, fatigue, confusion, chest pain, nausea, cold skin, and shortness of breath. It may be physiological, as seen in young athletes, aged individuals, during sleep, or due to vagal stimulation, or it may be pathological, as in sick sinus syndrome (SSS), heart block, myocardial infarction, hypothyroidism, electrolyte imbalances, infections, neurological conditions, hypothermia, or certain medications and toxins.[1] Treatment for bradycardia depends on the underlying cause, severity of symptoms, and individual patient factors. Often it can be managed by simply observing, making lifestyle changes, or treating the underlying condition. In other cases, medications such as atropine and epinephrine, or emergency measures such as CPR, cardiac defibrillation, cardioversion, pacemaker, or CRT may be required.[2] Small cell lung cancer (SCLC), also known as oat cell carcinoma, is a centrally located, undifferentiated, and aggressive cancer of neuroendocrine origin (NET). It presents with symptoms such as persistent cough, shortness of breath, hoarseness, and unintentional weight loss, often showing a short duration of symptoms. SCLC is a heterogeneous disease with both chemo sensitive and chemo resistant clones, making the prognosis unpredictable. It is generally divided into two stages limited (LS-SCLC) and extensive (ES-SCLC) with approximately 60-65% of patients presenting with metastatic disease, commonly to the lung, liver, brain, bone (most commonly blasted), adrenal glands, or lymph nodes.[3] Diagnosing SCLC involves a combination of history taking, physical examination, imaging studies, biopsy, and histopathological examination, revealing small dark blue cells in the neoplasm of neuroendocrine Kulchitsky cells. Molecular testing may show amplification of myc oncogenes. Although SCLC does not typically have specific tumor markers, it can be associated with elevated levels of neuron-specific enolase (NSE), progastrin-releasing peptide (ProGRP), chromogranin A, synaptophysin, and lung-cancer specific antigens such as CEA and CA 19-9.[4]

CASE REPORT

A male in his late 50s presented to the ER with recurring episodes of light-headedness and near-fainting over the past two weeks. He had a documented diagnosis of Small Cell Lung Cancer (SCLC), initiated two months prior, undergoing chemotherapy with the CE Regimen. His medical history included well-managed type 2 diabetes mellitus. Physical examination revealed unremarkable findings, with vital signs within normal limits, except for bradycardia (48 bpm). A comprehensive review of the patient's prior medical records, confirming the presence of cancer, was conducted. An ECG revealed sinus bradycardia without any arrhythmias (Figure 1), which was confirmed by holter monitoring. Earlier CT scan reports (Figure 2) showed a heterogeneously enhancing soft tissue density mass measuring 5×4.2 cm in the left suprahilar area. Subsequent transbronchial biopsy with immunohistochemistry confirmed the presence of SCLC. A 2D ECHO indicated mild aortic regurgitation.

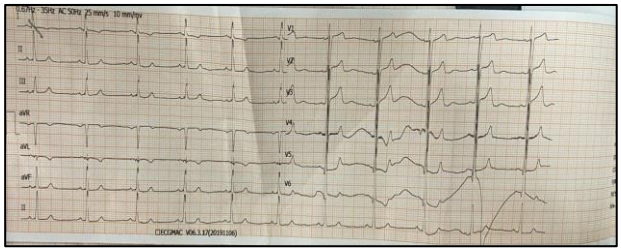

Figure 1: Patient's ECG depicting sinus bradycardia.

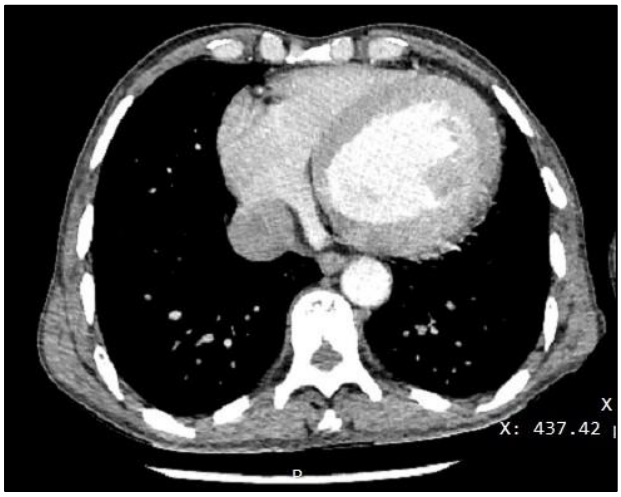

Figure 2: CT scan showing a heterogeneously enhancing soft tissue density mass measuring 5×4.2 cm in the left suprahilar area.

Routine blood investigations, including biomarkers, revealed notable findings such as low haemoglobin (7.7 g/dl, normal range: 12-18 g/dl), elevated pro-GRP (125 pg/ml, normal range: <50 pg/ml), and elevated NSE levels (43 ng/ml, normal range: ≤15 ng/ml). Multiple differentials were considered for the patient's bradycardia, including sick sinus syndrome, hypothyroidism, infectious etiology, electrolyte imbalances, and kidney dysfunction. However, no prominent reason could be found despite normal ECG, Holter monitoring, and absence of medications known to cause bradycardia. Given the suprahilar location of the tumor and the proximity to nerves supplying the heart, autonomic involvement was hypothesized. The patient underwent autonomic testing, which suggested both cardiac sympathetic and parasympathetic involvement, potentially due to the tumor affecting the nervous supply of the heart. However, determining the exact nerves involved would have required invasive exploration, which was not advisable in the patient's current situation. The patient was referred to the oncology department for revaluation of tumor staging, treatment planning, and prognosis. Additionally, he was referred to the cardiology department for management of sinus bradycardia. The patient underwent chemotherapy and subsequently received a pacemaker placement by the cardiology department. Following this intervention, the patient reported no new episodes of near-fainting.

Table 1: Results of tests for parasympathetic function.

	Observed value	Normal value
Deep breathing test: E/I Ratio	1:11	>1.21
Supine to standing test: 30:15 ratio	0.97	>1.01
Valsalva Manoeuver: valsalva ratio	1.12	>1.21

Table 2: Results of tests for sympathetic function.

	Blood pressure (mmHg)	Pulse rate (per minute)
In response to standing		
Resting supine	155/108	71
Immediate after standing	124/53	80
1 Minute after standing	127/51	86
3 Minutes after standing	134/54	87
5 Minutes after standing	130/54	87
In response to sustained hand grip		
Baseline	133/56	84
At 30 Seconds	149/55	85
At 1 Minute	143/53	88
At 2 Minute	139/50	82
At 4 Minutes	147/53	82
At 2 Minutes after release of grip	115/51	49

For reference, fall in systolic BP, Normal<10 mmHg, Abnormal>30 mmHg, for reference, rise in diastolic BP: Normal: >16 mmHg, Abnormal<10 mmHg.

DISCUSSION

The patient’s clinical presentation is particularly intriguing as, despite thorough evaluation, the etiology of bradycardia remained elusive. The patient had a normal

ECG and holter monitoring, ruling out any cardiac causes such as sick sinus syndrome and heart block. Normal WBC count ruled out infection, normal thyroid levels ruled out hypothyroidism, normal electrolyte levels and kidney function ruled out any electrolyte imbalances and toxicities, normal liver enzymes, and the patient was not on any medication at that time, ruling out any medication-induced causes. Small cell lung cancer (SCLC) is known to cause many paraneoplastic syndromes, such as Lambert-Eaton myasthenic syndrome, paraneoplastic myelitis, encephalitis, encephalomyelitis, subacute cerebellar degeneration, and endocrine paraneoplastic syndromes like Cushing syndrome and SIADH, but they are not regularly associated with bradycardia. Previous literature has reported paraneoplastic encephalomyelitis leading to dysautonomia, as seen in a report by Winkler et al, although patients had no symptoms suggestive of encephalomyelitis, thus anti-Hu and anti-Yo antibody testing wasn't conducted.[5]

Further research revealed reports of cisplatin-induced bradycardia.[6] However, since this manifestation occurred independently of cisplatin administration in our patient, no temporal relation was observed and the cause was ruled out. Considering the tumour's suprahilar location, we hypothesized that it might be encasing or obstructing either or both of the cardiac sympathetic (superficial and deep cardiac plexuses) and parasympathetic nerve supply (vagal cardiac nerves). Autonomic function testing was conducted, revealing both sympathetic and parasympathetic involvement, thereby reinforcing our hypothesis and offering a plausible explanation for the patient's sinus bradycardia.

In a review by Jiang et al, similar cases were found but overall, it is a rare manifestation. Notable differences in age and tumor location were seen. Our patient was significantly younger, as the mean age in earlier cases was 60+ years while our patient was 47 years old. There were 4 cases with a similar location of the tumor as ours located in hilum of left lung. Relapse of syncope was observed in 2 earlier cases. While syncope was seen 2 months after diagnosis of carcinoma in our case, all earlier cases had a very varied time of onset between cancer and syncope, thus no direct relationship could be established between diagnosis of cancer and onset of symptoms.[7]

All of these cases suggested a neurally mediated mechanism behind bradycardia induced by the tumor's physical growth onto neural structures. Martin et al, proposed explanations such as intermittent great-vessel obstruction and baroreceptor failure as well, but imaging ruled out both possibilities in our case.[8] In a report by Campagna et al, physical excision of the tumor was conducted, revealing the encasement of vagus and laryngeal nerves by the tumor.[9] Although definitive identification of the specific nerve structures affected would have required invasive exploration, the potential risks outweighed the benefits in the patient's clinical context.

CONCLUSION

In conclusion, this case highlights a rare presentation of bradycardia in a patient with Small Cell Lung Cancer (SCLC), attributed to autonomic nervous system involvement. The physical encasement of nerves supplying the heart by the tumor underscores the importance of considering secondary effects of tumor growth in SCLC patients presenting with cardiovascular abnormalities. Unlike more commonly known paraneoplastic syndromes associated with SCLC, this case suggests a unique mechanism where direct neural involvement can result in severe dysautonomia, manifesting as unexplained bradycardia and near-syncope episodes.

Clinicians should be vigilant for such unusual presentations, as early recognition and multidisciplinary management can lead to timely interventions, such as the eventual pacemaker placement in our patient, improving quality of life and potentially preventing further complications. This case adds to the limited literature on SCLC-induced dysautonomia and underlines the importance of autonomic testing in similar unexplained cardiac presentations. Further research is warranted to better understand the mechanisms of neural encasement by SCLC and optimize care for affected patients.

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