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# Frequent hypotension in nasopharyngeal carcinoma with neck lymph node metastases: A case report

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#### **Abstract**

Neck lymph nodes are one of the common metastatic sites of nasopharyngeal carcinoma, but concurrent unexplained hypotension syncope is rare. We report a case of a 38-year-old male patient who presented with unexplained recurrent syncope and was diagnosed with sick sinus syndrome. Hypotensive syncope persisted even after pacemaker implantation. Nasopharyngeal Carcinoma (NPC) was diagnosed by pathological biopsy and received 5 cycles of gemcitabine + carboplatin chemotherapy and 33 cycles of Intensity Modulated Radiation Therapy (IMRT). The patient had symptoms of hypotensive syncope during each interval of chemotherapy, but after the antineoplastic treatment, the patient's blood pressure was normal, and hypotensive syncope did not recur. This article discusses the pathogenesis, clinical manifestations, diagnosis and treatment of hypotension in patients with primary nasopharyngeal carcinoma and neck lymph node metastasis, and its significance for clinical diagnosis and treatment.

## **Keywords**

Hypotension; Nasopharyngeal carcinoma; Neck lymph node metastasis; Case report.

#### **Abbreviations**

NPC: Nasopharyngeal Carcinoma; IMRT: Intensity Modulated Radiation Therapy; CT: Computerized Tomography; MRI: Magnetic Resonance Imaging.

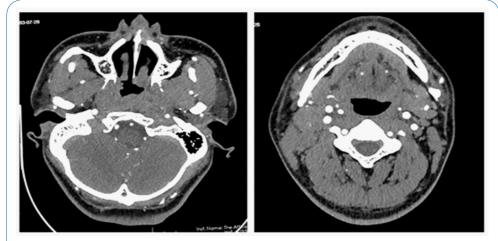
#### Introduction

NPC is one of the most common head and neck malignancies, with a high incidence in East and Southeast Asia [1,2]. The common clinical manifestations of nasopharyngeal carcinoma are nasal congestion, nasal bleeding, tinnitus, hearing loss, headache, etc [3,4]. Hypotension is a state in which systemic arterial pressure is lower than normal. However, there is no uniform standard for the diagnosis of hypoten-

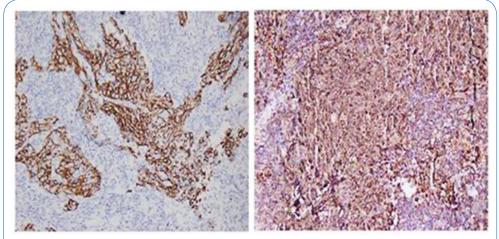
sion. It is generally believed that the upper extremity arterial blood pressure in adults is lower than 12/8 kPa (90/60 mmHg) as hypotension [5,6]. It refers to a decrease in blood pressure caused by a disease of an organ or system in the human body. This kind of low blood pressure can occur rapidly in a short period of time, such as a sharp drop in blood pressure caused by major bleeding, acute myocardial infarction, severe trauma, infection, allergies, etc [7]. In most cases, hypotension occurs slowly and can gradually worsen, such as hypotension secondary to severe pulmonary tuberculosis, malignant tumor, malnutrition, cachexia, etc. [8]. Cardiovascular disease and cancer are the two leading causes of death worldwide [9,10]. Although cardiovascular disease and cancer are two separate disease systems, there are still some tumors that can lead to cardiovascular disease, such as lung cancer, pheochromocytoma and so on [11,12].

#### **Case Presentation**

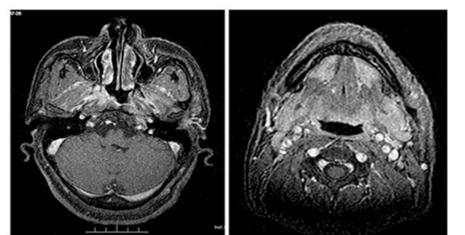
A 38-year-old man was admitted to the emergency department on December 31, 2020 due to «recurrent syncope for 1+ months». The patient suffered from syncope without obvious cause, mainly manifested as sudden dizziness, headache, then black eyes, fainting on the ground, loss of consciousness after fainting lasting about 10-20 seconds. Without vomiting, limb twitching, and binocular staring. The above symptoms occured repeatedly, and on 2021-1-3, he went to the Cardiology Department, and the dynamic electrocardiogram showed: Sick sinus syndrome was finally considered, and on 2021-1-7, after permanent pacemaker was implanted, the heart rate was normal under pacemaker protection, but blood pressure still decreased up to 54/42 mmHg leading to severe hypotension. A Computerized Tomography (CT) scan of the head showed a nasopharyngeal mass with enlargement of the neck lymph nodes (Figure 1). A nasopharyngeal mass was found by CT scan of the head, and the results of pathological biopsy of the nasopharyngeal mass suggested that the nasopharyngeal mass was considered as non-keratinizing undifferentiated carcinoma (T3N2M0) (Figure 2). During the admission period, the patient still experienced repeated hypotension, the lowest was 60+/40+ mmHg. After dopamine + norepinephrine, the blood pressure rises to about 100+/60+ mmHg. On 2021-1-18, the blood pressure will be transferred to the Cardiology Department for further blood pressure control. After the blood pressure is slightly stabilized, the patient will be transferred to the Oncology Department on 2021-1-25 for tumor radiotherapy and induction chemotherapy (gemcitabine + carboplatin) will be given on 2021-1-28, 2021-2-23, 2021-3-16, 2021-4-8, 2021-4-28. Blood pressure could be controlled during chemotherapy, but blood pressure dropped significantly during each chemotherapy period. Therefore, treatment was performed after admission due to hypotension, and the next chemotherapy was performed after blood pressure was stabilized. And on 2021-5-11 IMRT+ carboplatin (33 times) was performed for cancer. After 33 concurrent chemoradiotherapy (IMRT+ carboplatin), the nasopharyngeal mass and cervical enlarged lymph nodes were significantly reduced after treatment (Figure 3)(2021-5-7) compared with the MRI images before radiotherapy (Figure 4) (2021-7-29). After the end of radiotherapy, the patient had no recurrence of hypotensive syncope, and regular blood pressure examination showed normal results.



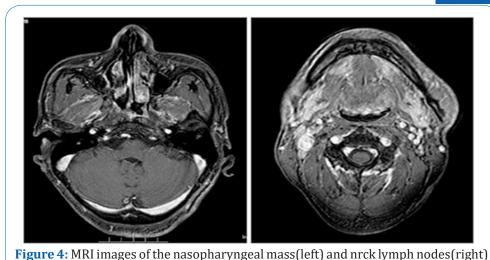
**Figure 1:** CT image of the patient with the first nasopharyngeal tumor(left) and neck lymph node(right) metastasis on December 31, 2020.



**Figure 2:** Pathological picture of a patient with a nasopharyngeal mass undergoing pathological biopsy for definite diagnosis.



**Figure 3:** MRI images of the nasopharyngeal mass(left) and neck lymph nodes(right) after concurrent chemoradiotherapy.



before concurrent chemoradiotherapy.

#### **Discussion**

Cases of hypotension in patients with nasopharyngeal carcinoma are very rare, and no cases of hypotension in patients with nasopharyngeal carcinoma have been reported so far. This case has an obvious feature: Before tumor treatment, The patient often have unexplained hypotension. After the diagnosis of sick sinus syndrome, a temporary pacemaker was installed to correct the heart rate, but the blood pressure continued to drop. After the beginning of antitumor therapy, the blood pressure fluctuated occasionally during chemotherapy, but the blood pressure decreased significantly during each interval of chemotherapy, and obvious hypotension occurred outside the hospital. However, when the patient underwent chemotherapy again, the blood pressure returned to normal. After the patient finished the course of anti-tumor treatment, the patient's symptoms of hypotension did not recur. Therefore, it is believed that the blood pressure of the patient remains stable when the anti-tumor treatment is effective, while the blood pressure decreases when the tumor progresses, so the symptoms of hypotension in this patient were accompanied by the occurrence of tumor. At the same time, during hospitalization, we excluded all possible causes of hypotension except tumors. The reasons for the exclusion are as follows: 1. From the perspective of imaging, the patient has completed head and neck CT and Magnetic Resonance Imaging (MRI) examinations, considering the origin of the two branches of the left vertebral artery In the aortic arch, the V4 segment was slightly slender locally, and the vascular problem was not enough to cause syncope; the rest of the brain parenchyma showed no obvious abnormality. 2. Explanation from the endocrine aspect: the patient has repeated episodes of hypotension. If the level of hormones affects blood pressure, it generally affects not only blood pressure, but also changes in blood sodium and blood sugar. Combined with the patient's examination results: seven pituitary glands, catecholamine determination, No obvious abnormality was found in blood glucose, thyroid function, and electrolytes, so endocrine diseases could not explain the cause of hypotension and syncope.

A common metastatic site of nasopharyngeal carcinoma is the neck lymph nodes, which leads to the enlargement of the neck lymph nodes. The patient's head and neck imaging results showed that the carotid sheath was severely compressed by enlarged lymph nodes on the right side of the neck. The carotid sheath

consists of the common carotid artery, external carotid artery, internal carotid artery, internal jugular vein and vagus nerve [13]. Therefore, Other factors that cause hypotension are excluded, the following two possible conditions are consistent with the clinical symptom interpretation of this patient:

### Hypotension caused by vagus nerve compression

The patient was considered for nasopharyngeal carcinoma, and imaging showed multiple enlarged lymph nodes adjacent to the bilateral carotid sheaths, mainly on the right side. Therefore, the patient had definite neck lymph node metastases, and the enlarged lymph nodes can compress and stimulate the vagus nerve, resulting in a decrease in blood pressure.

#### Damaged carotid sinus baroreceptors

The carotid sinus is a bulge at the origin of the internal carotid artery with special sensory nerve endings (baroreceptors) in the wall [14,15], with damage to the carotid sinus being a major cause of baroreflex failure. Considering the intimate relationship between enlarged lymph nodes and great vessels, it is reasonable to believe that tumor invasion or mechanical compression of receptors can lead to failure of the baroreflex and ultimately hypotension in the patient.

Vagus nerve stimulation can reduce blood pressure by promoting acetylcholine release and inhibiting sympathetic nerve. The reasons are as follows: On the one hand, when the vagus nerve is stimulated, acetylcholine can be released. Thereby it has the effect of dilating blood vessels, slowing down heart rate, weakening Purkinje fibers, slowing down atrioventricular conduction, myocardial contractility, and shortening atrial refractory period. Vasodilation can delay the automatic depolarization of the sinus node during diastole, slow down the heart rate, and thus achieve the effect of lowering blood pressure. On the other hand, when the vagus nerve is stimulated, the sympathetic nerve is inhibited (while the sympathetic nerve is excited, the  $\alpha$  and  $\beta$  receptors are excited, the blood vessels contract, the heart rate increases, and the blood pressure increases), and the blood pressure decreases.

Tumors affecting the vagus nerve include schwannoma, paraganglioma, branchial cleft cyst, malignant lymphoma, and metastatic neck lymph nodes. There has also been a case report showing that a mass in the carotid space caused asystole and syncope due to its proximity to the vagus nerve [16]. It is further suggested that our mass in the neck may stimulate the patient's vagus nerve and produce hypotensive syncope.

When the arterial pressure rises, it causes the sinus wall to expand, stimulates the nerve endings, and sends nerve impulses to the center, reflexively causes the heartbeat to slow down, and the peripheral blood vessels expand, thereby reducing blood pressure [17]. Baroreceptors and related reflexes respond to changes in arterial pressure to buffer excessive blood pressure fluctuations. The carotid sinus has receptors that respond to dilation of the vessel wall and communicates with the brainstem via the glossopharyngeal nerve. Low-pressure receptors also communicate with the central nervous system via the vagus nerve. Both the vagus and glossopharyngeal afferents enter the nucleus of the solitary tract [18]. Lesions

anywhere along these pathways can lead to baroreceptor damage, with damage to the carotid sinus being a major cause of baroreflex failure. The main feature of baroreflex failure is instability in blood pressure and heart rate because of the loss of the buffering mechanism provided by the induction reflex. Previous studies have reported stimulation of carotid baroreceptors as a therapeutic target for hypertension and other cardiovascular diseases [19,20]. At the same time, similar cases have been reported in NPC patients with hypotensive syncope due to baroreceptor damage, resulting in failure of the barorereflex. It is further confirmed that the damage of carotid sinus baroreceptor can cause the blood pressure to drop in patients.

#### Conclusion

To sum up, in view of the lack of reasonable alternative explanations for the symptoms in the patient, and at the same time, the hypotensive symptoms occurred with the development of the patient's tumor and were relieved with the effective antitumor therapy. The reason is that after antitumor treatment, the neck lymph nodes shrink, reducing the compression and damage to the carotid sinus and vagus nerve. Therefore, we excluded other causes of hypotension and concluded that the patient's hypotension was caused by the tumor. Through further examination to exclude other causes of hypotension and review relevant information, Finally, we have reason to believe that the hypotension of this patient was caused by abnormal blood pressure regulation caused by the vagus nerve compression of the enlarged neck lymph nodes, and the damage of baroreceptors in the carotid sinus caused by the compression or invasion of the enlarged metastatic lymph nodes. Therefore, in clinical nasopharyngeal carcinoma patients or other types of tumor patients with neck lymph node metastasis, or primary neck lymph node enlargement, if the patient is complicated with unexplained hypotension, we should be vigilant whether the presence of enlarged lymph nodes compression of the patient's neck blood vessels and nerves. Therefore, when patients develop unexplained hypotension, it is necessary to be aware of the concomitant vagal nerve compression by neck lymphadenopathy and the injury of carotid sinus baroreceptors.

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