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Case Report

Multiple Primary Malignancies and Bilateral Vocal Cord Paralysis Confusing the Management of Each Other

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Abstract

Double primary malignancy though uncommon, we often encounter in our clinical practice. The lung malignancy is known to cause left vocal cord paralysis. Bilateral abductor paralysis secondary to adenocarcinoma of the lung with concurrent basal cell carcinoma of the face is not common. Proper counseling and timely management are needed in these cases of multiple primary malignancies. Early evaluation in all cases of hoarseness can help in early diagnosis and management.

Keywords

- adenocarcinoma of lung
- multiple primary
- vocal cord palsy

Introduction

Double primary malignancy is not uncommon.[1–4] In 1934, Bugher was the first to analyze double primary malignancy statistically.[5] The prevalence of multiple primary malignancies ranges from 0.7 to 11.7%.[6] Most diagnosed double primary were metachronous in comparison to synchronous.[7] The increased incidence of double primary is probably due to possible genetic susceptibility and exposure to environmental carcinogens.[8] The mean age for reporting second primary cancer is around 50 years or above.[9–11] Patients with digestive, urogenital, and respiratory tumors are likely to develop multiple primary metachronous tumours.[12] Metastasis of basal cell carcinoma is rare, ranging between 0.0028 and 0.55%.[13] Here, we present a rare case of basal cell carcinoma of the skin along with adenocarcinoma of the lung with bilateral vocal cord palsies.

Case Report

A 44-year-old man, known diabetic, presented with hoarseness of voice for 3 months. He gave a history of pulmonary tuberculosis and completed antitubercular treatment 2 years ago. On examination, we noted a single, nontender, blackish growth measuring about 2 × 1 cm on the left side of the nose, adjacent to the medial canthus of the left eye (►**Fig. 1A**). The patient noticed it but did not seek medical help considering it a normal mole. On indirect laryngoscopy and video laryngoscopy, the bilateral vocal cords were in the paramedian position (►**Fig. 1B**). Contrast-enhanced computed tomography showed mild enhancing wall thickening of the esophagus, with enhancing nodular lesion of the right lobe of the lung and heterogeneously enhancing lesion of the right lobe of the liver (►**Fig. 2A**). Multiple enlarged lymph nodes were noted in the pretracheal, paratracheal, tracheobronchial, and right supraclavicular area, with multiple nodules in both thyroid lobes (►**Fig. 2B**). Flexible gastroesophageal endoscopy was normal. Bronchoalveolar lavage was suggestive of malignant nonsmall cell lung carcinoma. Biopsy from the lateral basal segment of the right lower lobe bronchus mass suggested moderately differentiated adenocarcinoma (►**Fig. 3A**). The molecular study was positive for ALK (D5F3) and negative for ROS1 (D4D6) (►**Fig. 3B**). Magnetic resonance imaging metastasis workup showed marrow signal changes involving multiple vertebrae, pelvic bones, and neck of the left femur, showing diffusion restriction

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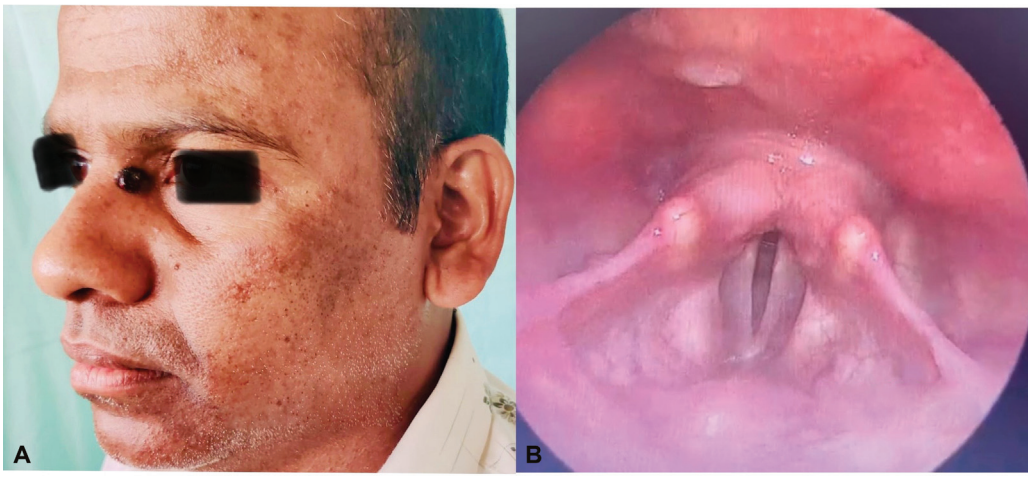

Fig. 1 (A) Blackish growth on the left side of the nose, adjacent to the medial canthus of the left eye. (B) Vocal cords in paramedian position.

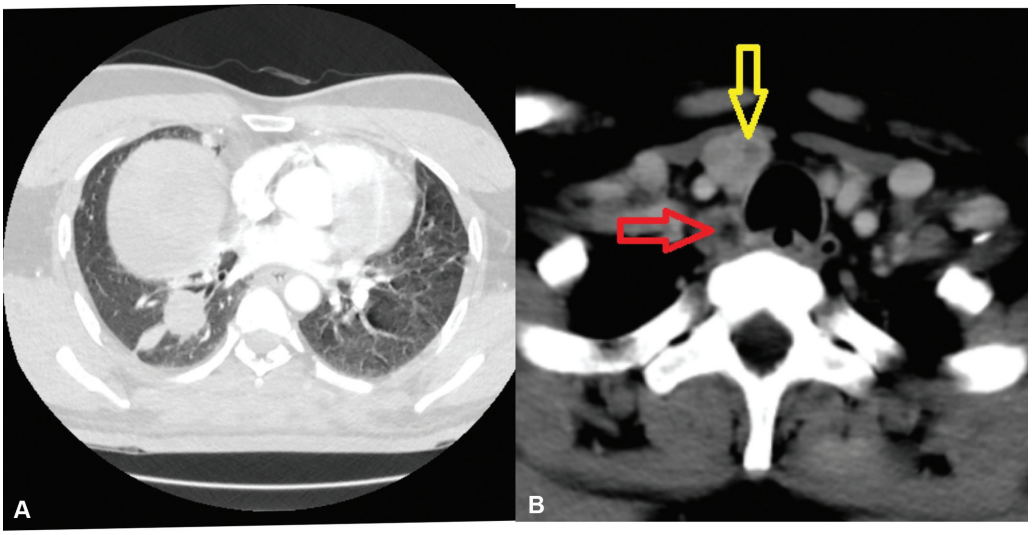

Fig. 2 (A) Contrast-enhanced computed tomography (CECT) neck with thorax showing enlarged nodular lesion of right lower lobe. (B) CECT neck, red arrow showing enlarged right paratracheal lymph node, yellow arrow showing nodule in the right lobe of thyroid.

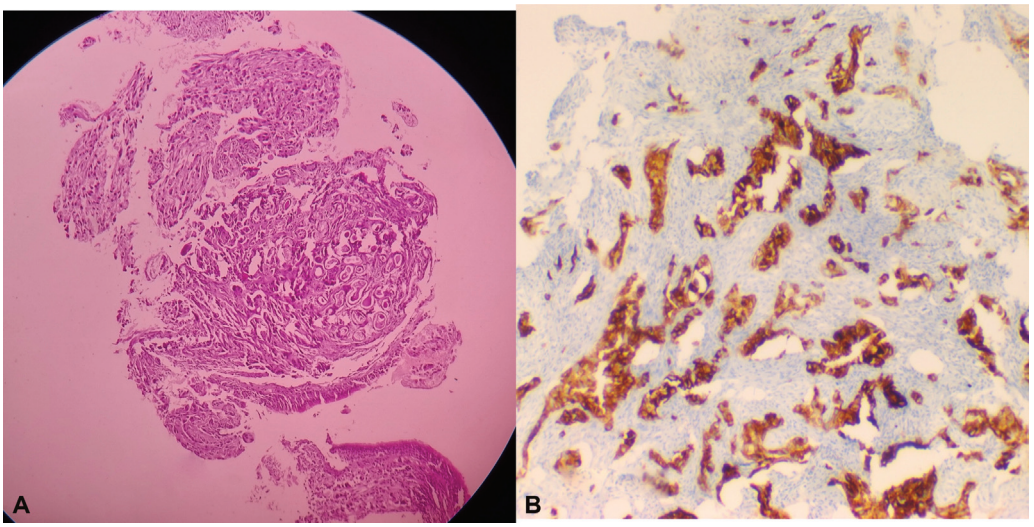

Fig. 3 (A) Microscopic picture of adenocarcinoma showing tumor cells arranged in acinar formation with high nuclear-to-cytoplasmic ratio (10× magnification). (B) Immunohistochemistry suggestive of positive ALK (D5F3) marker (10× magnification).

suggestive of metastasis, without any intracranial metastasis. The biopsy from the nasal lesion was suggestive of basal cell carcinoma (►**Fig. 4**). Fine-needle aspiration cytology of the pretracheal lymph node was suggestive of metastatic adenocarcinoma, whereas in thyroid it was suggestive of colloid nodular goiter. Considering the metastatic spread of the adenocarcinoma, the patient was started on chemotherapy meanwhile kept under close observation for the progression of basal cell carcinoma and development of respiratory stridor. The patient underwent six cycles of chemotherapy (pemetrexed/carboplatin $\times 6$ cycles $+$ GCSF $\times 4$ cycles and crizotinib). Positron emission tomography after six cycles of chemotherapy was suggestive of a partial response to chemotherapy. The basal cell carcinoma of the nose responded to the chemotherapy with significant reduction in its size. Currently, the patient is on crizotinib maintenance therapy on a compassionate basis due to his poor socioeconomic status until a complete response will be obtained. The patient refused to undergo surgical excision of basal cell carcinoma as there was a significant reduction in the size of the tumor and he wants to get it done later. At present, there is no stridor and the patient is kept on close observation.

Discussion

Multiple primary cancers are classified as synchronous and metachronous. Those malignancies observed at the same time or within 6 months are termed synchronous, and those cancers that develop at more than a 6-month interval are termed metachronous.[14] Synchronous multiple primary cancers were first reported by Beyreuther.[15] Second primary cancers have been increasing in recent years. This is probably due to an increased survival rate and improved imaging technology.

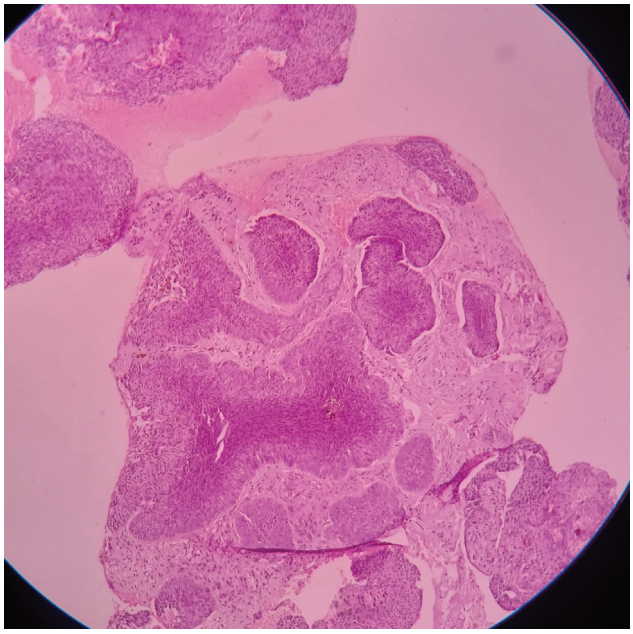

Fig. 4 Microscopic picture of basal cell carcinoma showing basaloid cells seen in island arrangements, peripheral palisading pattern noted (10× magnification).

Basal cell carcinoma is the most common low-grade skin carcinoma. The usual site for basal cell carcinoma is exposed head and neck areas. Metastatic basal cell carcinoma is rare. Metastasis usually occurs in regional lymph nodes, lungs, and bones.[16] The primary treatment is surgical excision. In metastatic cases of basal cell carcinoma, wide surgical excision along with chemoradiation is the treatment modality.[13]

Lung adenocarcinoma is a fatal disease, despite significant progression in management, such as surgical resection, ablation, and targeted therapy.[16] In the recent 5 years, the survival rate of lung cancer has been 22%.[17] Ventana anti-ALK (D5F3) CDX assay is an Food and Drug Administration-approved method for the qualitative detection of ALK (anaplastic lymphoma kinase protein) in formalin-fixed paraffin-embedded nonsmall cell lung carcinoma tissue stained with Benchmark XT, or Benchmark Ultra automated staining instrument. The presence of strong granular cytoplasmic staining in tumor cells (any percentage of tumor cells) is considered as positive.[18,19] It helps identify patients who may benefit from crizotinib, ceritinib, and alectinib treatment.

Bilateral abductor palsy was probably due to the involvement of pretracheal, paratracheal, and mediastinal lymph nodes in this case. The malignant infiltration of the upper lobe of the lung can be the cause for recurrent laryngeal nerve palsy. But lung malignancies mainly involve the left recurrent laryngeal nerve. Other differential diagnoses are malignant conditions of the thyroid. Our patient had benign thyroid nodules, unlikely to cause bilateral recurrent laryngeal nerve palsy. Fibrotic changes following tuberculosis could also be a possible differential diagnosis in our patient, as this patient had tuberculosis in the past. Preexisting undiagnosed unilateral vocal cord palsy could be one of the causes. The patient could now be symptomatic due to the involvement of the other recurrent laryngeal nerve. Early evaluation and management may prevent the extensive spread in this case. Our patient was not on stridor, so he was kept on observation and close follow-up.

In the case of dual malignancy, the priority is for the management of advanced malignancy. Both can be dealt with simultaneously if amenable to surgical resection.[20] The multidisciplinary team approach is required in multiple primaries. The proper counseling of the patient regarding the therapeutic challenges and uncertainty about the prognosis is a must.

Systemic chemotherapy is preferred if both tumors are likely to respond to the same chemotherapeutic drugs, for example, squamous cell carcinoma of the head and neck and squamous noncell carcinoma of the lungs.[21] Though chemotherapy does not play a significant role in basal cell carcinoma, surprisingly, in this case response was good. Unfortunately, dual malignancies are less understood. This probably is due to most of the clinical trials exclude multiple primaries.

In this case, the management of lung adenocarcinoma was prioritized due to its metastatic spread and aggressive nature. Subsequently, the basal cell carcinoma and vocal

cord palsy will be managed depending on the patient's response to chemotherapy. Counseling the patient and providing adequate information regarding their condition plays a crucial role in managing multiple primary malignancies.

Conclusion

Malignancy is the most common extralaryngeal cause of vocal cord palsy. Surgical resection is the best modality of management for basal cell carcinoma unless it is in the advanced stage. Chemoradiation would be the ideal modality of management in dual malignancies. In conclusion, a thorough evaluation is a must while evaluating any malignancy to rule out the presence of a second primary.

Consent

Patient's consent is taken.

Funding

None.

Conflict of Interest

None declared.

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