

Content available at: <https://www.ipinnovative.com/open-access-journals>

Journal of Oral Medicine, Oral Surgery, Oral Pathology and Oral Radiology

Journal homepage: www.joooo.org

Review Article

Intricacies of the routes of metastatic lung carcinoma: A review

Varun Rastogi^{1,*}, Nisha Maddheshiya²

¹Dept. of Oral & Maxillofacial Pathology, Universal College of Medical Sciences and Teaching Hospital (UCMS), Bhairahawa, Nepal

²Dept. Oral Medicine & Radiology, Universal College of Medical Sciences and Teaching Hospital (UCMS), Bhairahawa, Nepal



ARTICLE INFO

Article history:

Received 12-11-2020

Accepted 30-11-2020

Available online 02-12-2020

Keywords:

Metastasis

Lung

Oral cavity

Hematogenous

Lymphatic

ABSTRACT

Metastatic malignancies of the oral cavity are a rare phenomenon, accounting for only about 1% of all oral malignancies. The metastatic tumor cells may affect the jaw bones or the oral soft tissues or even both. The primary tumors commonly implicated in oral metastasis are usually from the lungs, breast, kidney and bone. In 25% of cases, oral metastasis indicates the first sign of metastatic spread and in 23% it may be the first evidence of dissemination of malignancy from its primary site. Lung cancer is the most commonly diagnosed major cancer in the world that mainly arises from the epithelial cells such as neuro -endocrine cells, club cells, and neuro – epithelial cells. In this review, we have highlighted the various predisposing factors and propose hypothetical pathways of lung carcinoma metastasizing to the different areas of the body including the oral cavity.

© This is an open access article distributed under the terms of the Creative Commons Attribution License (<https://creativecommons.org/licenses/by/4.0/>) which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

1. Introduction

Metastatic tumors are the commonest malignant neoplasm of the skeleton in general.¹ For the diagnosis of the malignant tumors of the oral cavity, it is necessary to take into account the possibility of both the primary as well as the metastatic tumors.² Metastatic tumors to the jaw are a rare phenomenon, representing about 1–4% of oral malignancies that are metastasis from a distant primary site.³

The most common principal source of metastatic tumors to the oral cavity or maxillofacial area are the breast, lung, prostate, kidney, bone, colon and rectum, thyroid, stomach, testis, bladder, ovary and cervix.^{4,5} The breast forms the commonest primary site for tumors that metastasize to the mandible and lung is the preferred site for tumors that metastasize to the oral soft tissues.⁶ The cervical lymph nodes, mandible and gingiva are the most commonly affected areas by the metastatic tumors.⁷ In the mandible, molar area is the preferred site for metastatic tumors⁸ and

the gingiva is the commonest site for metastatic colonization in oral soft tissues.^{9,10}

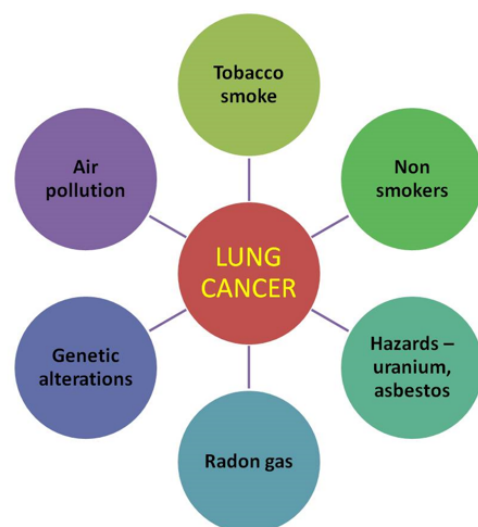


Fig. 1: Predisposing factors for lung cancer

* Corresponding author.

E-mail address: drvarunrastogi@gmail.com (V. Rastogi).

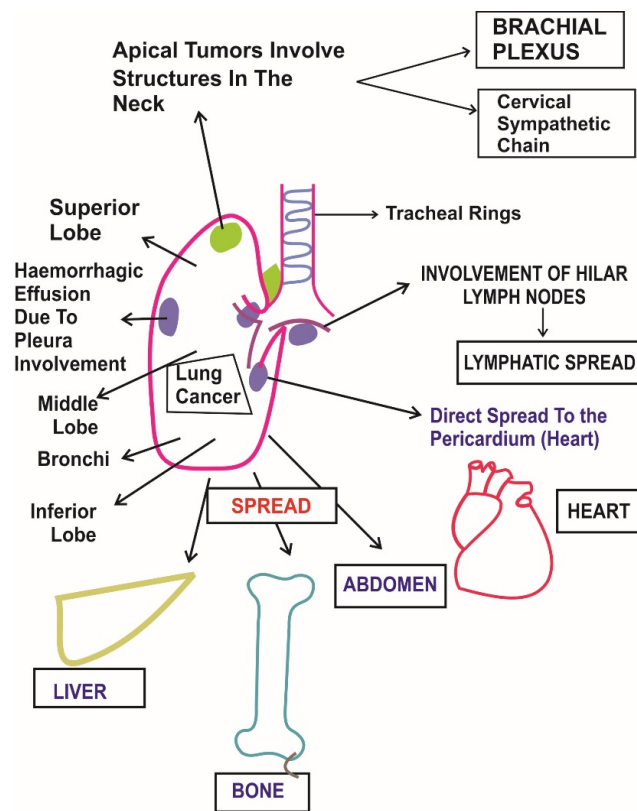


Fig. 2: Spread of lung cancer

In this review, we have highlighted the various predisposing factors and propose hypothetical pathways of lung carcinoma metastasizing to the different areas of the body including the oral cavity.

In considering oral tumors, only 1–3% of oral malignancies are metastatic from a distant primary site, in decreasing order, from the breast, adrenal gland, colorectal system, genital organs and thyroid gland in females and from lung, prostate, bone and adrenal gland in males.^{7,11}

Lung cancer is the most commonly diagnosed major cancer in the world that mainly arises from the epithelial cells. The lung is the most preferred site for the metastasis of tumors from other parts of the body. The 2 most common forms of lung cancer are Non small cell and Small cell lung carcinoma¹² and the major cause is from the carcinogenic effect of cigarette smoke, making it the leading cause of cancer death worldwide.^{12,13} The major symptoms of lung cancer are cough, hemoptysis, weight loss and shortness of breath.¹³

Predisposing factors (Figure 1) that may play a role in lung cancer are tobacco smoke accounting for 80 - 90% of cases^{12,13} and Non - smokers accounting for the remaining 10 -15% of lung cancer.¹⁴ The other factors are industrial hazards such as uranium and asbestos,¹³ radon gas,^{13,15,16} genetic alterations that includes activation of oncogenes such as C- MYC, K - Ras, EGFR and Her 2/ neu^{17,18} and

inactivation of tumor suppressor genes such as p53, RB, p 16 *INK4a*^{19,20} and air pollution.¹³ About 4% of Non-Small Cell lung carcinoma involves EML4 – ALK tyrosine kinase fusion gene and Small Cell lung carcinoma may be derived from neuro -endocrine cells, club cells, and neuro – epithelial cells and these cancers may express CD 44.¹⁷

The cancer that originates in the lung are called primary lung carcinoma and the most common site of metastasis of primary lung cancer are bone, brain, liver and supra – renal glands. Secondary cancers that spread to the lungs are breast, colon, and prostate and bladder cancer.

Metastasis of Lung cancer (Figure 2) occurs by 3 routes namely direct, hematogenous and lymphatogenous spread. In the direct spread of lung cancer, involvement of the phrenic nerve results in paralysis of half of the diaphragm. Apical lung cancers are associated with recurrent laryngeal nerve (branch of vagus nerve) because of its close proximity to the apex of the lung.

Carcinoma arising from the right lung spreads to the heart, inferior and superior vena cava, azygous vein and esophagus and those arising from the left lung spread to the heart, aortic arch, thoracic aorta and esophagus.²¹

Overview of hematogenous spread of lung cancer is outlined in Diagram 1.

The tumor cells enter the systemic circulation by invading the wall of vessel of the lung which is then

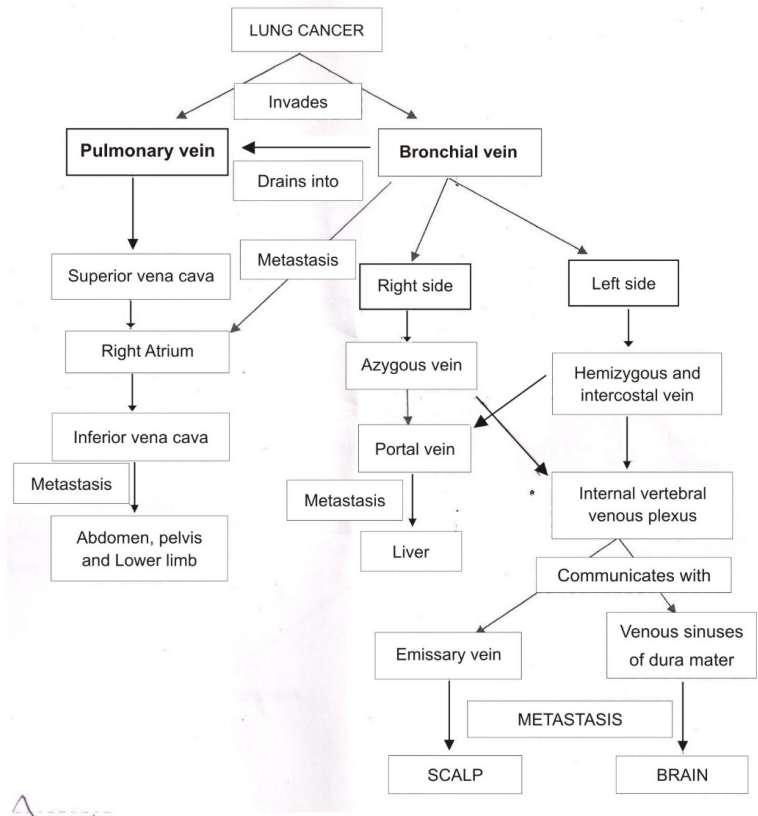


Fig. 3: Venous spread of lung cancer

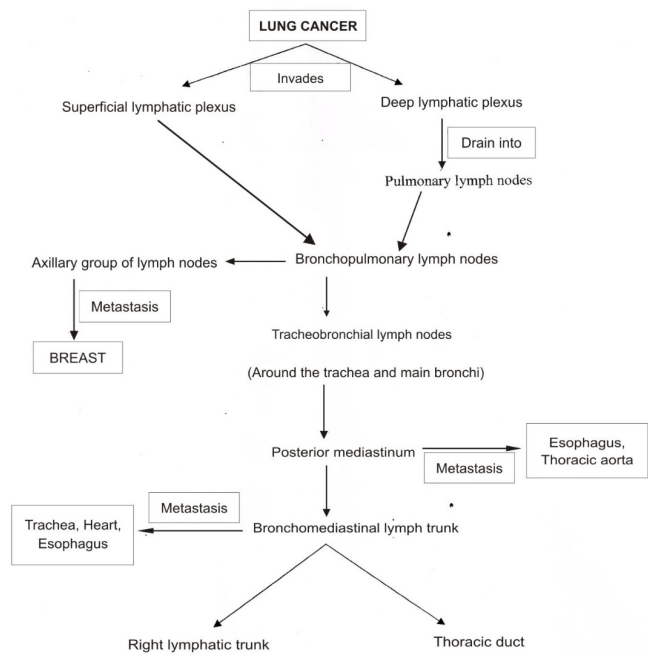


Fig. 4: Lymphatic spread of lung cancer

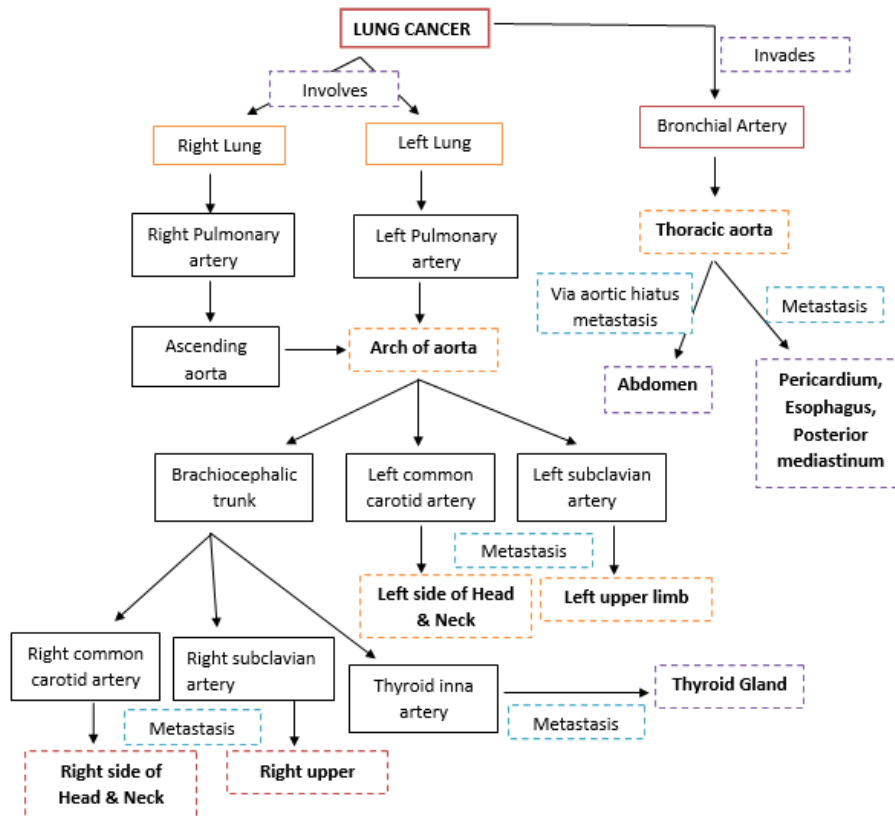


Diagram 1: Hematogenous spread of lung cancer

transported via the pulmonary veins, left heart and aorta. This constitutes the venous drainage (Figure 3) which forms another route for the metastasis of lung cancer. The route of metastasis of lung cancer occurs via lymphatic spread is outlined in Figure 4.

This lymph thus carries the cancer cells into the venous system and right atrium of heart. The cancer cells after passing through the pulmonary circulation are carried back into the heart, from where they are distributed to the entire body.

Lung cancer is mostly detected on the chest radiographs and CT scans can also be used as a diagnostic modality to detect lung cancer. These lung cancers are confirmed by biopsy, which is usually performed by either bronchoscopy or under CT – guidance. The various treatment modalities that can be used for these lung carcinomas include surgery, chemotherapy and radiotherapy.

2. Conclusion

Oral cavity has been described as a reflection or mirror of systemic diseases. Oral manifestations are often the sole indication of the disease and also the first indicator for the presence of malignant tumors. With the advent of Immuno – histochemical markers and advancement in molecular techniques, the diagnosis becomes easier and a better

understanding of the biology of the tumors can be achieved, so that the newer therapies targeting the molecular level may be introduced to halt the tumor proliferation, thereby improving the quality of life as well as life expectancy of the patients.

3. Source of Funding

None.

4. Conflict of Interest

The author(s) declare(s) that there is no conflict of interest regarding the publication of this article.

References

1. de Padua Bertelli A, Costa FQ, Mizziara JEA. Metastatic tumors of the mandible. *Oral Surg, Oral Med, Oral Pathol.* 1970;30(1):21–8. doi:10.1016/0030-4220(70)90005-8.
2. Oba T, Nakagawa E, Nakada E. Metastatic tumor of the gum. *Jpn J Cancer Clin.* 1974;20:692–6.
3. Kim JS, Kim JD. Metastatic hepatocellular carcinoma on the mandible: A case report. *Korean J Oral Maxillofac Radiol.* 2005;35:215–9.
4. Buchner A, Ramon Y. Distant metastases to the jaws. *J Oral Surg.* 1967;25:246–50.
5. Meyer I, Shklar G. Malignant tumors metastatic to mouth and jaws. *Oral Surg, Oral Med, Oral Pathol.* 1965;20(3):350–62.

- doi:10.1016/0030-4220(65)90167-2.
6. Uchiyama Y, Murakami S, Kakimoto N. Diagnostic imaging findings for mandibular metastasis from Gastric adenocarcinoma. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod.* 2009;107:49–53.
 7. Hirshberg A, Leibovich P, Buchner A. Metastases to the oral mucosa: analysis of 157 cases. *J Oral Pathol Med.* 1993;22(9):385–90. doi:10.1111/j.1600-0714.1993.tb00128.x.
 8. Hirshberg A, Buchner A. Metastatic tumours to the oral region. An overview. *Eur J Cancer Part B: Oral Oncol.* 1995;31(6):355–60. doi:10.1016/0964-1955(95)00031-3.
 9. Lim SY, Kim SA, Ahn SG. Metastatic tumors to the jaws and oral soft tissues: A retrospective analysis of 41 Korean patients. *Int J Oral Maxillofac Surg.* 2006;35:412–5.
 10. Nishimura Y, Yakata H, Kawasaki T. Metastatic tumors of the mouth and jaws: A review of the Japanese literature. *J Maxillofac Surg.* 1982;10:253–60.
 11. Kwast WVD, Van der Waal I. Jaw metastases. *Oral Surg Oral Med. Oral Pathol.* 1974;37:850–7.
 12. Longo DL, Fauci AS. Lung neoplasms. *Harrison's Principles of Internal Medicine.* 18th ed. McGraw Hill; 2011.
 13. Robert J, Mason MD. Murray and Nadel's textbook of Internal medicine. 5th ed. Saunders, Elsevier; 2011.
 14. Thun MJ, Hannan LM. Lung cancer occurrence in never smokers: an analysis of 13 cohorts and 22 cancer registry studies. *PLoS Med.* 2008;5:185–91.
 15. Marchevsky A. Pathogenesis and experimental models of lung cancer. *Surgical Pathology of Lung neoplasm.* New York: Marcel Dekker; 1990.
 16. Pershagen G, Akerblom G, Axelson O, Clavensjo B, Damber L, Desai G. Residential Radon Exposure and Lung Cancer in Sweden. *New Engl J Med.* 1994;330(3):159–64. doi:10.1056/nejm199401203300302.
 17. Herbst RS, Heymach JV, Lippman SM. Lung Cancer. *New Engl J Med.* 2008;359(13):1367–80. doi:10.1056/nejmra0802714.
 18. Ronen SA, Blackhall FH, Shepherd FA, Tsao MS. K - ras mutations in small cell lung carcinoma: a review. *Clin Lung Cancer.* 2006;8:30–8.
 19. Sheer CJ, McCormick F. The RB and p53 pathway in cancer. *Cancer Cell.* 2002;2:103–10.
 20. Liu MC, Gelmann EP. P53 gene mutations: Case study of a clinical marker for solid tumors. *Semin Oncol.* 2002;29(3):246–57. doi:10.1053/sonc.2002.32900.
 21. Drake RL, Vogl W, Mitchell A, Gray. *Anatomy for Students.* 2005;p. 140–147.

Author biography

Varun Rastogi, Professor & HOD

Cite this article: Rastogi V, Maddheshiya N. Intricacies of the routes of metastatic lung carcinoma: A review. *J Oral Med, Oral Surg, Oral Pathol, Oral Radiol* 2020;6(4):177-181.