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Miraculous response to sequential therapy in a case of squamous cell lung carcinoma

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Abstract
Lung cancer has been the most common cancer in the world for several decades.
As majority of the patients of non-small cell lung cancer present in locally advanced stage along with poor general condition, therefore they cannot tolerate conventional radical regimes and doses of radiotherapy and chemotherapy. Such patients require urgent symptomatic relief and reduction in tumor burden. Therefore for such patients an individualized treatment approach has to be crafted. We are reporting a case of locally advanced non-small cell lung cancer which showed a miraculous response to an individualized approach of sequential therapy comprising of Radiotherapy, chemotherapy and metronomic Cyclophosphamide.

Introduction

About a hundred years ago, lung cancer was a reportable disease, and now it has the highest incidence and highest mortality amongst cancers in the world. The disease has no distinguishing signs or symptoms for early detection, therefore most patients present in locally advanced stage. Majority of the patients who report to the department of Radiotherapy, PGIMS Rohtak are bidi smokers, which poses a 6-fold higher risk of lung cancer as compared to cigarette.[1] In developing countries like India, most of the patients present with locally advanced as well as metastatic disease, which could be due to lack of awareness, economic constraints and asymptomatic early stages of the disease. Locally advanced stages, along with poor general condition and symptomatic distress of the patient presents a unique kind of challenge about its management as in majority of the cases the patients are unfit for any sort of conventional radical treatment. Therefore, there is a need for tailoring out treatment for such patients which can give them symptomatic relief and local control of disease.

Case Presentation

A 50 year old male with a history of smoking bidi since 30 years presented to the Department of Radiotherapy with the chief complaints of cough

and breathlessness since 6 months, which were insidious in onset and gradually progressive. There was also history of moderate intensity chest pain, generalized weakness, and loss of weight & appetite. As per contrast enhanced computed tomography the patient was stage IIIB and histologically squamous cell carcinoma. Keeping in view the general condition and symptomatic distress of the patient palliative Radiotherapy 30 Gy/10 fractions/ 2 weeks was given and after 1 month follow up, the patient had good symptomatic relief as well as partial response on x-ray chest as per the RECIST criteria version 1 (Image2). Taking into account the improved general condition of the patient and no symptomatic distress, 6 cycles of chemotherapy with inj. Paclitaxel 260 mg i/v and Carboplatin 450 mg i/v were given at an interval of 3 weeks. After 6 cycles of chemotherapy the tumor response was good (Image 3)and the patient was started on metronomic chemotherapy with Tab Cyclophosphamide 50 mg OD and the patient was kept on 1 month follow up. After 7 months on metronomic chemotherapy there is a miraculous complete response on x-ray chest as per the RECIST criteria version 1 (Image 4). The total time period for which the patient was studied and observed is 17 months (from the day of presentation to last follow up), the patient is still on follow up without any symptomatic distress.

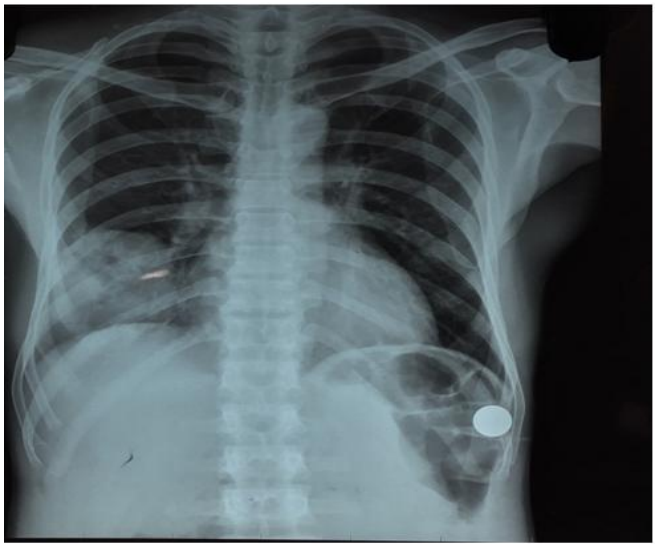

Image 1 – tumor status at presentation, tumor in right lower lobe

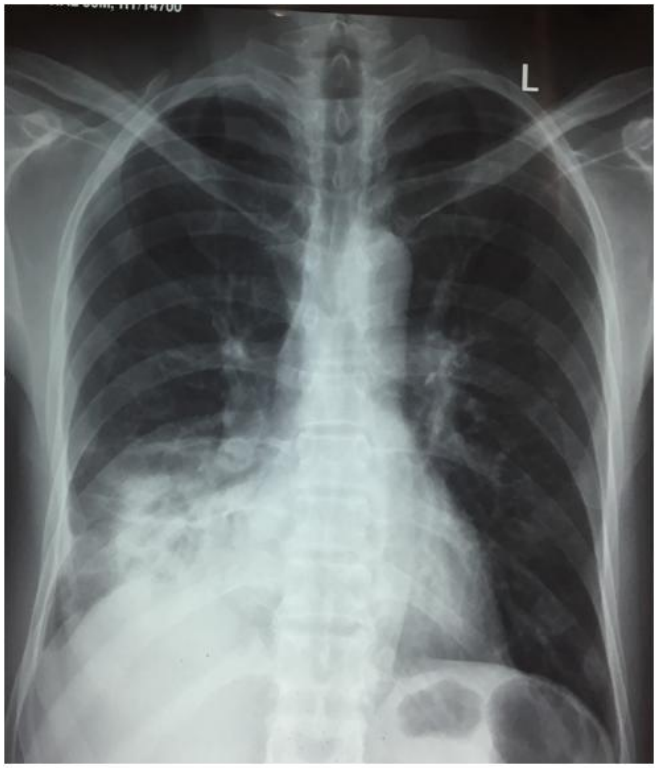

Image 2 partial response after palliative Radiotherapy

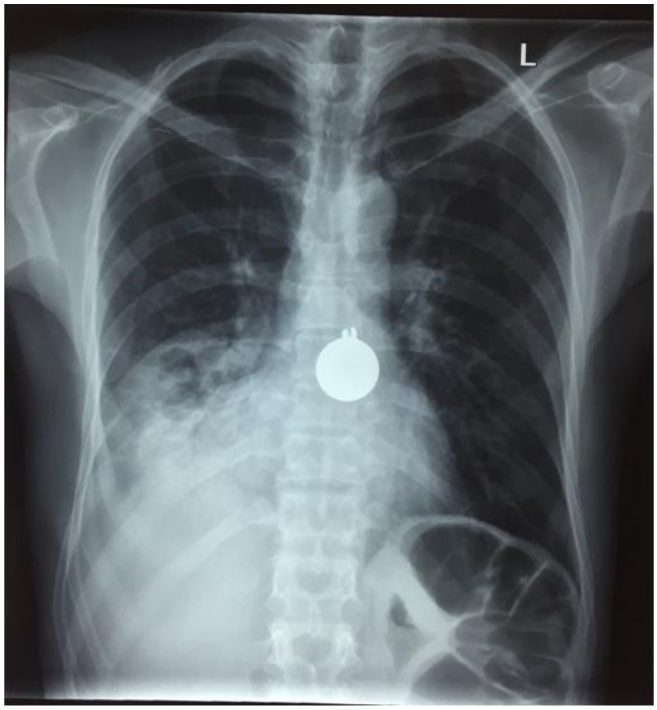

Image 3 Response after 6 cycles of chemotherapy

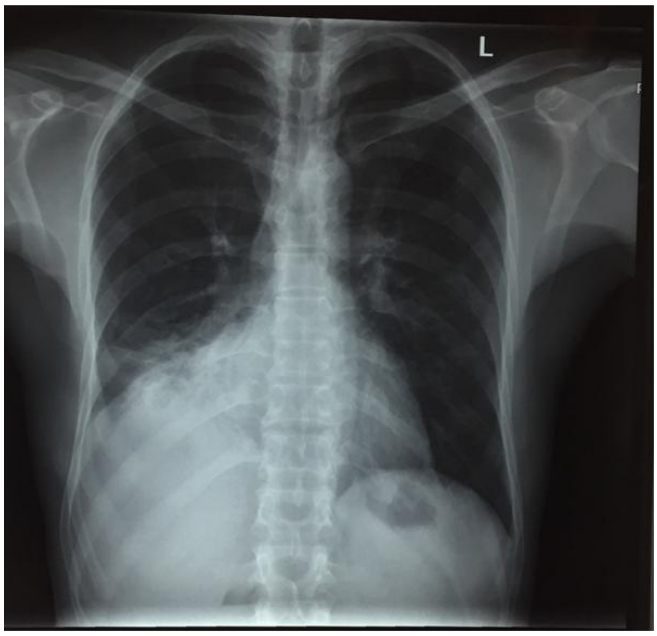

Image 4 Complete response after 7 months of metronomic Cyclophosphamide

Discussion

Lung cancer has been the most common cancer in the world for several decades. There were estimated 2.094 million new cases in 2018 (11.6% of the total), 58% of which occurred in the less developed regions. In India, the estimated number of new cases in 2012 were 67,795 (5.9% of the total).[2] In India, lung cancer has constituted 5.9 per cent of all new cancer cases and 9.3 percent of all cancer related deaths in both sexes as per GLOBOCAN 2018.[2] It is the commonest cancer and cause of cancer related mortality in men, with the highest reported incidences from Mizoram in both males and females.[3]

In patients of non-small cell lung carcinoma, the most important prognostic factor is tumor stage, which largely determines treatment. Surgery is the standard mode of treatment of patients with stage I and II tumors and for selective patients with stage III tumors. But only 20% of all the patients presenting with lung cancer are suitable for surgery.[4]

In general, the nonsurgical treatment of NSCLC can be divided into four broad categories. Radiation therapy alone in conventional regimes is used primarily for early-stage (stage I and II) patients, who are not candidates for surgery,[5] and for patients with locally advanced disease (stage IIIA and IIIB) who cannot tolerate any chemotherapy due to comorbid conditions or poor performance status.[6] Concurrent chemotherapy and radiation therapy is the standard of care for fit patients with locally advanced disease. Sequential chemotherapy followed by radiation therapy is reserved for patients with locally advanced disease who are unable to tolerate concurrent chemotherapy and radiation therapy. Endobronchial brachytherapy is considered for patients with obstructing endobronchial lesions. Palliative radiation therapy is for patients with very poor performance status in locally advanced and metastatic disease.[7]

As majority of the patients of non-small cell lung cancer present in locally advanced stage along with poor general condition, therefore they cannot tolerate conventional radical regimes and doses of radiotherapy and chemotherapy.[8] Such patients require urgent symptomatic relief and reduction in tumor burden.[9]

Sequential chemotherapy and radiotherapy could potentially result in clinical benefits.[10,11,12] While radiotherapy is intended to act on the main tumor bulk at the primary tumor site, chemotherapy has an effect on systemic micro-metastases. Therefore, there is a strong rationale for implementing both modalities. Chemotherapy and Radiotherapy may modify different tumor sub-clones; combining both regimens should therefore lead to an increased tumor cell death.

Metronomic chemotherapy is the chronic administration of low, non-toxic doses of chemotherapy on a frequent schedule of administration. While conventional doses of chemotherapy aim solely towards killing of malignant cells, the metronomic approach owes its efficacy to numerous additional effect. These subtle effects which are probably marked at routinely used higher doses, include anti-angiogenic effects and immunomodulatory effects. The antiangiogenic effect has been experimentally observed in that metronomic chemotherapy could reduce angiogenic factors

such as thrombospondin and vascular endothelial growth factor (VEGF).[13,14] The use of such a non-toxic and effect regime can be particularly useful in developing and low – middle income nations like India, as most patients present in locally advanced stage.[15]

Watanabe et al achieved good results in the treatment of elderly (> 60 years) patients of locally advanced non-small cell lung cancer in terms of symptomatic relief and recurrence rates with oral Cyclophosphamide and palliative radiotherapy, and they recommended that radiation and low-dose chemotherapy as useful treatments for the advanced non-small lung cancer in elderly patients.[16]

Conclusion

In our patient, palliative Radiotherapy on presentation was given considering the general condition and symptomatic distress of the patient. Due to good objective and subjective response after Radiotherapy and improvement in general condition 6 cycles of chemotherapy were administered and then the patient was kept on metronomic chemotherapy. To our surprise this sequential therapy provided a miraculous tumor response and symptomatic control along with relatively minimal toxicity.

Thus we conclude that such a sequential combination of Radiotherapy, chemotherapy and metronomic therapy which had been specifically been tailored out for this patient keeping in view the patients general condition, symptomatic distress and response to subsequent therapies is a very useful and good tool for locally advanced non-small cell lung cancer.

References

1. Prasad R, Singhal S, Garg R. Bidi smoking and lung cancer. Biosci Trends. 2009 Apr;3(2):41-3.
2. Ferlay J, Soeriomataram I, Ervik M, Dikshit R, Eser S, Mathers C, et al. GLOBOCAN 2018 v1.0, Cancer Incidence and Mortality Worldwide: IARC Cancer Base No. 11. Lyon, France International Agency for Research on Cancer; 2018.
3. Indian Council of Medical research; 2013. [accessed on June, 2016]. National Cancer Registry Programme. Three year report of population based cancer registries: 2009-2011. Available from: http://www.nrcpindia.org
4. Pearson FG. Current status of surgical resection for lung cancer. Chest 1997;106:337.
5. Zimmermann FB, Bamberg M, Molls M, Jeremic B. Radiation therapy alone in earlystage non-small cell lung cancer. Semin Surg Oncol. 2003;21(2):91-7. Review.
6. Sigel K, Lurslurchachai L, Bonomi M, Mhango G, Bergamo C, Kale M, et al. Effectiveness of radiation therapy alone for elderly patients with unresected stage III non-small cell lung cancer. Lung Cancer. 2013 Nov;82(2):266-70.
7. Nieder C, Tollali T, Yobuta R, Reigstad A, Flatoy LR, Pawinski A. Palliative Thoracic Radiotherapy for Lung Cancer: What Is the Impact of Total Radiation Dose on Survival? J Clin Med Res. 2017 Jun;9(6):482-487.
8. Fojo T, Grady C. How much is life worth: cetuximab, non-small cell lung cancer, and the $440 billion question. J Natl Cancer Inst. 2009 Aug 5;101(15):1044-8.
9. Kelly M, O'Brien KM, Lucey M, Clough-Gorr K, Hannigan A. Indicators for early assessment of palliative care in lung cancer patients: a population study usinglinked health data. BMC Palliat Care. 2018 Feb 26;17(1):37.
10. Tannock IF. Treatment of cancer with radiation and drugs. J ClinOncol. 1996;52:3156- 74
11. Vokes, Everett E. Combined modality therapy of solid tumours. Lancet. 1997;349(2 Suppl):4-6.
12. Paik PK, Varghese AM, Sima CS, Moreira

AL, Ladanyi M, Kris MG, et al. Response to erlotinib in patients with EGFR mutant advanced non-small cell lung cancers with a squamous or squamous-like component. Mol Cancer Ther. 2012;11:2535-40.

13. Montagna E, Cancello G, Dellapasque S, et al. Metronomic therapy and Breast cancer: a systemic review. Cancer Treat Rev 2014;40:942-50.
14. Miller KD, Sweeney CJ, Sledge GW Jr. Redefining the target: chemotherapeutics as antiangiogenics. J ClinOncol. 2001 Feb 15;19(4):1195-206.
15. André N, Banavali S, Snihur Y, Pasquier E. Has the time come for metronomics in low-income and middle-income countries? Lancet Oncol. 2013 May;14(6):e239-48.
16. Watanabe Y, Ogo E, Kaida H, Suzuki G, Eto H, Suefuji H, et al. Treatment with low-dose cyclophosphamide and radiation therapy for advanced non-small lung cancer in elderly patient. GanTo Kagaku Ryoho. 2011 Sep;38(9):1503-5.