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

Authors
Dr Joydeep Singh Vasant1, Dr Ashok Kumar Chauhan2, Dr Paramjeet Kaur3, Dr Jyoti Pannu4, Dr Roshani Vyas5, Dr Shashank Joshi6, Dr Anjali Bhol6, Dr Anil Khurana8
1,4,5 3rd year post graduate student, Department of Radiotherapy, PGIMS, Rohtak, India
2Senior Professor, Department of Radiotherapy, PGIMS, Rohtak, India
3Professor, Department of Radiotherapy, PGIMS, Rohtak, India
6,7 2nd year post graduate student, Department of Radiotherapy, PGIMS, Rohtak, India
8Senior medical officer, Department of Radiotherapy, PGIMS, Rohtak, India

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. 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 (Image 2). 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
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). 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. 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.

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.

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, and for patients with locally advanced disease (stage IIIA and IIIB) who cannot tolerate any chemotherapy due to comorbid conditions or poor performance status. 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.

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. Sequential chemotherapy and radiotherapy could potentially result in clinical benefits. 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 subclones; 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).\textsuperscript{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.\textsuperscript{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.\textsuperscript{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**

12. Paik PK, Varghese AM, Sima CS, Moreira


