Primary Neurological Manifestations of Lung Cancer - A Retrospective Analysis of 8 Patients


Abstract

Neurological manifestations are reported in 5 to 10% of cases of lung cancer. We present a series of 216 consecutive patients of lung cancer of which 8 patients presented first with neurological manifestations without overt respiratory symptoms. The present study aimed to identify the number of patients of lung cancer presenting with primary neurological symptoms, the nature of the presentations, and the outcome of these patients among 216 patients who presented over a 2 year period in the Institute of Postgraduate Medical Education and Research, Kolkata. Out of 8 patients, 3 patients presented with seizures, 3 patients with hemiparesis and 2 patients with paraparesis. Thus, 3.7% (8/216) of patients in our series presented with a neurological manifestation. We concluded that primary neurological manifestations are rare in lung cancer. The lungs should be the first site of evaluation in a case of a cerebral metastasis with an unknown primary.

INTRODUCTION

The neurological system is involved in many patients of lung cancer; metastases in general being commonest with small cell cancer. Among patients with non small cell cancer, brain is also the commonest site of metastasis among patients who have extrathoracic disease at presentation. In adults, the most common primary tumor responsible for intracranial metastasis is lung. Although in the majority of patients (80%), brain metastasis developed after the diagnosis of primary tumor, in some patients it manifests before the primary tumor is found. The patients who present with neurological symptoms and imaging studies indicative of metastatic lesions may be investigated for lung cancer. The present study attempts to find the incidence of a primary neurological presentation of lung cancer, the nature of the presentation and the prognosis of these patients as compared to the general population of patients with lung cancer.

We carried out an analysis of 216 patients of lung cancer, who presented in the outpatient departments of General Medicine, Radiotherapy, Chest, Neurology and Neurosurgery. Among them, we found eight patients who had presented with neurological symptoms without any chest symptoms. We analysed the presentation, histology, site of metastasis, and outcome of these patients.

The following eight patients presented with a neurological manifestation without any chest symptoms at the onset of their disease.

CASE 1

A 55 years male patient presented with a generalized tonic clonic seizure, preceded by a history of headache for two weeks. He smoked cigarettes and cannabis.

MRI brain revealed ill-defined nodular lesions in the right cerebral and cerebellar hemispheres with perifocal edema. CT scan thorax showed inhomogeneously enhancing space occupying lesion of 2.7 cm in diameter at the left upper zone, extending into the left hilar zone; multiple nodular areas in both lungs involving all the lobes. This proved on FNAC to be an undifferentiated large cell carcinoma.

Course: The patient received whole brain radiation 30Gy/10 fractions over two weeks followed by chemotherapy with cisplatin 100mg/m² IV on day 1 and oral etoposide 100mg/m² IV from day 1 to day 3. The patient completed six cycles of chemotherapy at three weekly intervals, and is now on follow-up.

CASE 2

A 56 years male patient, known smoker, presented with headache occasional vomiting for two weeks and ataxia for 6 days due to mild weakness on the right side.

CT scan brain showed a contrast enhancing mass on
left frontal region 3.2×2 cm, with peritumoral edema. He underwent craniotomy followed by tumor removal at another institution. Histopathology revealed a small round cell tumor, probably metastatic in origin. He was further investigated with CT scan thorax which showed multiple nodular opacities in the right lower lobe. CT guided FNAC revealed a small cell carcinoma.

**Course:** He was treated symptomatically, with mannitol (100ml IV 8hrly), phenytoin (100 mg PO TDS) and dexamethasone (8mg IV TDS) but the disease gradually progressed with headache, vomiting and recurrent generalized seizures. He died of neurological complications 7 ½ months after diagnosis.

**CASE 3**

A 45 years male patient, smoker, presented with a generalized tonic-clonic seizure. MRI brain revealed ring enhancing lesions in left cerebellar, right cerebral paraventricular regions.

A chest X-ray showed a large parahilar shadow, which proved to be a mass 6.2cm in diameter on CT scan. FNAC from the mass revealed a poorly differentiated adenocarcinoma.

**Course:** After the initial symptomatic therapy, the patient received whole brain radiation 30Gy/10 fractions over two weeks followed by chemotherapy with cisplatin 100mg/m² IV on day 1 and oral etoposide 100mg/m² IV from day 1 to day 3. The patient completed six cycles of chemotherapy at three weekly intervals. Two months after treatment completion, the patient developed progressive chest pain, breathlessness, hemoptysis and died three months after completion of treatment.

**CASE 4**

A 62 years male patient, smoker, presented with sudden onset of paraplegia with bladder and bowel incontinence.

MRI spine revealed multiple osteolytic lesions in D12, L1, L3 vertebrae with compression of L3, narrowing of spinal canal at L3, L4, and cord edema above the region. FNAC from the spine showed a metastatic carcinoma. Subsequently an X-ray chest was done revealing a right hilar opacity. FNAC from the lung mass showed a poorly differentiated adenocarcinoma.

**Course:** The patient received radiotherapy to the dorsolumbar spine (from D10 to L5) with 20 Gy in 5 fractions over one week followed by chemotherapy with cisplatin 75 mg /m² IV on day 1 and etoposide 100mg/m² from day1 to day 3 at three weekly intervals. The patient has completed the cycles of systemic therapy and is clinically stable after 4 months from diagnosis.

**CASE 5**

A 65 years male patient, hypertensive, smoker, with a past history of pulmonary tuberculosis 23 years back, presented with progressive right upper limb monoparesis for two weeks along with right sided Horner’s syndrome and mild headache.

CT scan brain showed a homogeneous opacity in the left frontal lobe with contrast enhancement. Craniotomy and tumor decompression was planned. During routine anaesthetic checkup the CXR showed a small soft tissue mass extending from C6 to D4, destruction of the neck of the 1st rib, destruction of D1 and D2 vertebrae with involvement of spinal canal. CT scan brain was normal. CT scan thorax revealed a mass arising from the right apex of the lung. CT guided FNAC showed a poorly differentiated adenocarcinoma. Bone scan showed multiple sites of increased uptake in C6 to D4 and also on L1, L3, and L4.

**Course:** The patient received radiation 20 Gy / 5 fractions to both cervico-dorsal and lumbar spines in two separate fields. Now, he is on chemotherapy with cisplatin 75 mg / m² IV on day 1 and etoposide 100mg/m² from day1 to day 3 at three weekly intervals. The patient has completed the cycles of systemic therapy and is clinically stable after 4 months from diagnosis.
30Gy/10 fractions over two weeks followed by chemotherapy with cisplatin 100mg/m² IV on day 1 and oral etoposide 100mg/m² IV from day 1 to day 3 for two cycles at three-week intervals. After receiving the second cycle, the patient developed progressive intracranial metastases with right sided hemiplegia and urinary incontinence. He died after coma had ensued, 3 months after diagnosis.

**CASE 8**

A 58 years male smoker presented with a sudden onset generalized tonic clonic seizure, followed by a progressive hemiparesis.

CT scan brain showed a nodular opacity in the right paraventricular region. Chest x-ray showed a mass in the left lower zone. CT scan thorax showed a mass in the left apical lobe. Bronchoscopic biopsy of the mass showed a squamous cell carcinoma.

**Course:** The patient received whole brain radiation 30Gy/10 fractions over two weeks followed by chemotherapy with cisplatin 100mg/m² IV on day 1 and oral etoposide 100mg/m² IV from day 1 to day 3. He received only one cycle and died due to progressive neurological disorder 3 months after diagnosis.

### RESULTS

Eight out of 216 patients (3.7%) of lung cancer presented primarily with neurological complications. The patient characteristics, treatment opted and the outcome are shown in Table 1. Three out of 216 patients (1.3%) presented with seizures, 2 patients (0.9%) presented with hemiplegia, 2 patients (0.9%) with paraplegia and one patient with right upper limb monoparesis and Horner’s syndrome. The histology of 3 out of 8 cases was adenocarcinoma, 2 cases of squamous cell carcinoma, 2 cases of large cell carcinoma and 1 case of small cell carcinoma. The average duration of survival after diagnosis among those who died is 4 months. The median survival time was 11 months (with a range of 8 to 13 months) in the rest of the 216 patients of lung cancer with or without neurological sites of metastasis.

### DISCUSSION

Lung cancer is a major health problem and a leading cause of death both in developed and developing countries. In India, its incidence exceeds 70/100,000 males. Behera and Kashyap analyzed the pattern of malignancy in patients admitted to PGIMER, Chandigarh, from 1973 to 1982. They found that of the 223930 hospital admissions, there were 863 lung cancer cases (0.38%). Lung cancer was the fifth most common cancer. The total number of lung cancer patients steadily rose from 1973. Jindal and Behera (1990) in a series of 1009 lung cancer cases reported that both the mean and the peak ages of lung cancer were lower compared to the West (54.3 years). The smoker to nonsmoker ratio was 2.7:1. Most of the patients had advanced disease and 51.8% had evidence of metastasis. The commonest presentation was mass lesion with or without collapse in 68%, 25% had pleural effusion and 16.7% superior vena cava compression syndrome. Squamous cell carcinoma was found in 34.3%, anaplastic in 27.6%, adenocarcinoma in 25.9% and unclassified in 12.2%.

5-10% of patients of lung cancer present with neurological symptoms, irrespective of whether they have chest symptoms or not at presentation. In the present study, we have found that only 3.7% of patients present with neurological symptoms without any index

<table>
<thead>
<tr>
<th>No</th>
<th>Age (yrs)</th>
<th>Presentation</th>
<th>Histology</th>
<th>Site of metastasis</th>
<th>Outcome (after chemoradiotherapy)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>55</td>
<td>GTCs*</td>
<td>Undifferentiated large cell carcinoma</td>
<td>Right cerebral and cerebellar hemisphere</td>
<td>Stable; 3 months follow up after chemotherapy</td>
</tr>
<tr>
<td>2.</td>
<td>56</td>
<td>Hemiparesis, preceded by headache</td>
<td>Small cell carcinoma</td>
<td>Left frontal cerebral hemisphere</td>
<td>Expired 7½ months after diagnosis</td>
</tr>
<tr>
<td>3.</td>
<td>45</td>
<td>GTCs*</td>
<td>Poorly differentiated adenocarcinoma</td>
<td>Left cerebellar, right cerebral paraventricular regions.</td>
<td>Expired 7½ months after diagnosis, 3 months after treatment completion</td>
</tr>
<tr>
<td>4.</td>
<td>62</td>
<td>Paraparesis</td>
<td>Adenocarcinoma</td>
<td>Osteolytic lesions in D12, L1, L3 vertebrae, narrowing of spinal canal at L3, L4</td>
<td>Expired 3 months after diagnosis</td>
</tr>
<tr>
<td>5.</td>
<td>27</td>
<td>Paraparesis</td>
<td>Anaplastic large cell carcinoma</td>
<td>Demyelination involving D4, D7, D10, L1, L2</td>
<td>Expired 4 months after diagnosis</td>
</tr>
<tr>
<td>6.</td>
<td>72</td>
<td>Hemiparesis</td>
<td>Poorly differentiated adenocarcinoma</td>
<td>Paraspinal soft tissue mass extending from C6 to T4</td>
<td>Stable 3 months after diagnosis</td>
</tr>
<tr>
<td>7.</td>
<td>67</td>
<td>Monoparesis, Horner’s syndrome</td>
<td>Poorly differentiated adenocarcinoma</td>
<td>Left frontal lobe</td>
<td>Expired 3 months after diagnosis</td>
</tr>
<tr>
<td>8.</td>
<td>58</td>
<td>GTCs, followed by hemiparesis</td>
<td>Squamous cell CA</td>
<td>Right paraventricular region</td>
<td>Expired 3 months after diagnosis</td>
</tr>
</tbody>
</table>

*Generalised tonic-clonic seizures; **All patients were male.
of suspicion to the primary site. Brain metastases are the initial manifestation of an underlying tumor in 10 to 30% of cases. Of these, two-thirds are from the lung; of these, two thirds are from non small cell lung cancer. Therefore, primary neurological manifestations of lung cancer are limited to a very small subset of these patients. In the study of Sculier JP, et al 641 patients had been evaluated, of which 29.5% had at least one neurologic disorder, either at the time of presentation or during the subsequent clinical course of the disease. The total number of neurologic disorders was 210, which included brain metastases (75.7%), meningeal carcinomatosis (6.7%), intramedullary metastases (2.4%), epidural metastases (11.0%), hyponatremia producing CNS symptoms (3.3%), and Eaton-Lambert syndrome (1.0%). When a neurologic disorder related to cancer occurred, the survival time from the date of that diagnosis was usually short. The neurologic disorder was the immediate cause of death in the majority of cases. In our study, 8 out of 216 patients (3.7%) had a primary neurological presentation, of which 5 patients (62.5%) had brain metastases and 3 patients (37.5%) had spinal metastases with cord compression. In the series of Goldman et al 610 patients were evaluated and 24 cases (4%) of spinal cord compression were detected. Cerebral metastases occurred in 45% of patients with cord compression (13).

For patients who present with brain metastasis without a known primary, the lung should be the primary focus of evaluation. Sixty percent of these patients will have a primary lesion in the lung. Among the symptoms, headache occurs in 40-50% of patients with brain metastasis, 10-20% present acutely with seizures, another 5-10% as a result of stroke caused by embolisation. Focal neurological dysfunction is the presenting feature in 40% of cases; hemiparesis is most common.

Patients with untreated brain metastasis have a survival of one month as a whole. Medical decompression by steroids increases the survival to 2 months, while Whole Brain Radiotherapy (WBRT), increases survival to 3-6 months. Patients with single brain metastases may be treated with surgery and WBRT with a median survival of 10-16 months. Cranial irradiation can effectively improve the features of neurodeficit in about 50-85% of patients; however the potential for improvement is directly related to the time from diagnosis to treatment. Paraneoplastic manifestations are rare at presentation.

In the present series, 1 out of 8 patients has completed radiotherapy and chemotherapy and is surviving without any neurologic symptoms for eight months. Another patient is now on treatment and clinically stable. One patient completed full course of treatment and died three months after completion. In one patient, we could not start any specific therapy and he died of disease progression. The remaining for patients could not complete the full course of therapy and died during treatment. The overall survival time is short in the present series which is consistent with the studies mentioned above.

Regarding the pathology, frequency of CNS involvement in 407 non-resected and 227 resected cases of lung cancer were 29 and 5% in small cell, 26 and 10% in adenocarcinoma, 23 and 18% in large cell, and 10 and 5% in squamous cell carcinoma in an autopsy series. In resected adenocarcinoma, frequency was highest in poorly differentiated type.

Primary neurological manifestations are a rare event in the spectrum of the clinical features of lung cancer. On the other hand, in any elderly patient with a new-onset seizure, the possibility of a cerebral metastasis from a lung cancer is to be considered. The lungs should be the first site of evaluation in a case of a cerebral metastasis with an unknown primary. We also noted that seizures followed by hemiparesis were the most common presentation and adenocarcinoma was the most common histology. The survival time of lung cancer patients with primary neurological manifestations is short. WBRT is effective in controlling the neurological symptoms but without any significant change in the overall survival rate.

References

13. Goldman JM, Ash CM, Souhami RL, Geddes DM, Harper...
Announcement

Society for Free Radical Research - India
Affiliated to SFRR-Asia and SFRR-International
(C/o Cell Biology Division, Bhabha Atomic Research Centre Mumbai-400085)
(Registration No. M.S./Mumbai 64/2001)

Appeal for Enrolling As a Member in SFRR-India

The Society for Free Radical Research-India (SFRR-India) has been formed in 2001. The major aims and objectives of SFRR-India are to promote research on free radicals and antioxidants with particular reference to medical and industrial importance. ‘Free radicals’ are short-lived and highly reactive and cause serious damage in the human body, if kept unchecked. Antioxidants are the natural defenses that can neutralize these free radicals. Our society organizes conferences and workshops at national and international levels. The society also helps in promoting interaction between clinicians and scientists working in related areas within and outside the country. In the last five years the society has organized four international conferences with sizable participation from both India and abroad. Another important activity of our society is to publish ‘SFRR-India bulletin’, as its official organ. This contains research papers and related articles that will be of use to both clinicians and basic scientists. The executive committee of the society, headed by highly honoured Padmabhushan Dr. R.D. Lele, has many representatives from the medical fraternity. We appeal to all, especially physicians and other medical professionals, interested in the above areas of research to enroll themselves as members. Membership forms, giving details, are available from one of the following members. Dr. T.P.A. Devasagayam, present Secretary-General (tpad@apsara.barc.ernet.in); Dr. S. Adhikari, Secretary-General-Elect (tihai35@yahoo.com); Dr. Shashank R. Joshi, Executive Committee member (srjoshi@vsnl.com). Membership fee: Life members – Rs. 3000 or US$60; Corporate membership – Rs. 10000; Annual membership – Rs. 200 + entrance fee of Rs. 50; Student membership (annual) – Rs. 100 + entrance fee of Rs. 50 or US$10.

Book Review

Geriatric Care
A Textbook of Geriatrics and Gerontology
O. P. Sharma

Geriatric Care is a compilation of carefully chosen topics pertaining to Clinical Geriatrics and Gerontology. The chapters have been written by authors and wide ranging experience in treating the elderly, especially in India. This approach has been rendered necessary by the fact that the problems of the Indian elderly differ from their American or European contemporaries due to differences in race, nutrition, socio-economic factors and climatic conditions. Since this book provides a comprehensive account of the care needed for the Indian elderly, it will be an asset for family physicians also who treat elderly patients. Geriatrics is a multi-discipline speciality that is being added to the academic curricula of Medical Colleges. This book will therefore prove a competent guide for Medical Students in general, and students of Geriatrics in particular, who will find everything they need to know within the cover of a single volume.

Published by
Viva Books Private Limited

For Further Details Contact
Dr. O. P. Sharma
K-49, Green Park Main, New Delhi – 110 016
Telefax: 91-11-26863916 Email: opsharma@geriatricindia.com