Prevalence of Neurological Manifestations of Lung Cancer among Adult Sudanese Patients
Abbashar Hussein, Mohammed OH Gadour, Yasir Osman ALI, A Sidig.

Abstract:
The objective: is to study the prevalence of neurological manifestations among adults Sudanese patients with lung cancer seen in the Radiation and Isotope Centre in Khartoum.

Methods: This is a prospective cross sectional hospital based study, conducted at Radiation and Isotope Centre in Khartoum. Sample of 52 adults Sudanese patients with lung cancer were included in the study. The period of the study was from February 2006 to July 2006. Data were collected by self administered questionnaire; this was constructed in sections to address the different aspects of the study as follows: personal data, presentation, physical examination, and investigations.

The results: showed that 41 patients were males. Most of the patients were above 50 years of age. Fifty percent of our patients were from Khartoum state. All of our patients had chest findings except one. The most common symptoms observed were of cranial nerves involvement, headache, limb weakness, numbness, and sphincteric disturbance. More than half of the patients were smokers. Other extrapulmonary manifestations noticed include: clubbing, lymph node enlargement, bone metastasis or fracture, gynaecomastia, superior vena cava obstruction, hepatomegaly, and ascites. Chest X-ray abnormalities showed pleural effusion, consolidation, hilar lymphadenopathy, collapsed lung, and fibrosis in the majority of patients. Most of our patients had adenocarcinoma, followed by squamous cell carcinoma, poorly differentiated carcinoma, and small cell carcinoma.

Conclusion: The common neurological manifestations of lung cancer were found to be cranial nerves palsies, followed by lower limbs weakness, numbness, and sphincteric disturbances.

Key words: Cerebellar, numbness, neuropathy, convulsion.
secondary or part of manifestations of paraneoplastic syndrome\textsuperscript{5, 6}.

**Objectives:** To study the prevalence of neurological manifestations among adult Sudanese patients with lung cancer, seen in Radiation and Isotope Centre- Khartoum, Sudan.

**Methods:** This a prospective cross sectional hospital based study, conducted in Radiation and Isotope Centre (Khartoum), which is a tertiary hospital located in the centre of Khartoum. Samples of 52 adult Sudanese patients with lung cancer were included in the study after taking informed consent. The period of the study was from February 2006 to July 2008.

**Inclusion criteria:** 1) Sudanese nationality 2) Age 18 years and above.

**Data collection:** Data were collected by self administered questionnaire. It was constructed in sections to address the different aspects of the study as follows: 1) Personal data 2) Presentation 3) Physical examination 4) Investigations.

**Patients' assessment:** This was done in classical manner by history, examination and investigations. Investigations included: Urinalysis, FBC, Chest-X-R (CXR), blood urea and electrolytes, chest CT scan, bronchoscopy and biopsy, nerve conduction study, EMG, MRI brain, and CT brain when they were needed.

**Data Entry and Analysis:** All collected data were analyzed using statistical package program for social science (SPSS). The results were expressed as figures, tables and graphs.

**Results:** The study showed that out of 52 patients with lung cancer, 41 (78.8%) were males. The age distribution ranged between 27–76 years with a mean 56.27 ± 12.18. Maximum number [18 (34.61%)] were found between 50–59, and the least number [1 (1.92%)] between 19 – 29 years of age.

The highest number of patients [27(51.92%)] were from Khartoum state, followed by Western states [10 (19.23%)], 4 (7.6%) from Eastern states, 4 (7.6%) from Northern states, and 1(1.92%) from White Nile state. The main non neurological symptoms related to the chest were cough which was observed in 40 (76.9%) patients, dyspnoea in 32 (61.5%), chest pain in 29 (55.8%), haemoptysis in 29 (55.8%), 16 (30.8%) patients had GIT symptoms in form of, nausea, vomiting, weight loss, and poor appetite. (Fig. 1)
Figure 5 shows Neurological symptoms in 52 adult Sudanese patients with lung cancer seen in Radiation and Isotope centre-Khartoum (from Feb – Jul 2006).

7.70% 0.00% 1.90% 13.50% 1.90% 5.80% 5.80% 5.80% 1.90% 0%

Regarding the neurological symptoms four patients (7.7%) had headache, loss of consciousness was seen in one patient (1.9%). Fig 2. It was found that twenty nine patients (55.8%) were smokers. Almost all patients had findings on examining the chest, forty two (80.8%) had impaired tactile vocal fermitus Table 1.

Table (1) shows chest examination findings in patients with lung cancer.

| Chest Examination Findings         | No. of Patients (%) |
|------------------------------------|---------------------|
| Chest contour                      | 15 (28.8)           |
| Scars or swelling                  | 9 (17.3)            |
| Dilated veins                      | 3 (5.8)             |
| Abnormal movement                  | 35 (67.3)           |
| Abnormal position of the trachea   | 12 (23.1)           |
| Impaired TVF                       | 42 (80.8)           |
| Impaired percussion                | 38 (73)             |
| Abnormal breath sounds             | 41 (78.9)           |
| P = 0.177                          |                     |

Extra-pulmonary examination findings were shown in table 2. Clubbing was the commonest one.

Table (2) shows extra-pulmonary examination findings.

| Extra-pulmonary Findings            | No. (%) |
|-------------------------------------|---------|
| Clubbing                            | 9 (17.3)|
| Gynaecomastia                       | 1 (1.9)|
| Lymph nodes enlargement             | 7 (13.5)|
| Bone tenderness & fracture          | 7 (12.9)|
| Superior vena caval obstruction     | 1 (1.9)|
| Jaundice                            | 1 (1.95)|
| Hepatomegally                       | 5 (9.6)|
| Ascites                             | 4 (7.7)|

CNS examination showed that two patients (3.85%) had higher function impairment. Table 3.

Table (3) shows CNS findings

| CNS Examination Findings             | No. (%) |
|--------------------------------------|---------|
| Higher functions impairment          | 2 (3.85)|
| Cranial nerves involvement           | 7 (13.5)|
| Motor signs                          | 3 (5.8) |
| Sensory signs                        | 4 (7.7) |
| Cerebellar signs                     | 1 (1.9) |
Chest x–ray abnormal findings were detected in 48 patients (92.3%) it included: pleural effusion in 26 (50%) patients, consolidation in 20 (38.5%), hilar lymphadenopathy in 3 (5.8%), collapsed lung in 2 (3.8%), and fibrosis in one patient (1.9%). Histological classification showed that 19 patients(36.5%) were diagnosed as having adenocarcinoma, 9 (17.3%) as squamous cell carcinoma, 7 (13.3%) as poorly differentiated, 4 (7.7%) as small cell carcinoma, 3 (5.8%) as malignant cell, 1 (1.9%) as synovial, 1 (1.9%) anaplastic and 1 (1.9%) as mucus secretary carcinoma.

Discussion:
The study showed that 55% of our patients were smokers, most of them were males(78.8%). This differs from the study done by Scagliotti G. The difference is due to the fact that smoking is the most common risk factor, and in our community- unlike the developed countries- incidence of smoking among males is far more common than among females. Like other cancers the incidence increases with age, which explains prolonged exposure to carcinogenic materials. Most of our patients were from Khartoum state where the study had been conducted. The non-neurological symptoms in this population was found to be similar to what was mentioned in the literature. Symptoms of cranial nerves involvement were similar to that reported by Dellatre et al. but it differs from Adams and Victors findings. Cranial nerves involvement are either part of false localizing signs as in case of six nerve palsy or may be due to increased intracranial pressure (ICP) as in case of papilloedema resulting from metastasis to the brain. Other neurological symptoms including headache, lower limbs weakness, numbness, and sphincteric disturbance were similar to the observation of Grippi MA and different from that of Hyde. Limbs weakness and numbness can occur as a manifestation of cord lesion secondary to metastasis or as a part of paraneoplastic syndrome. Very rare manifestations include muscle pain as a part of clinical picture of dermatomyositis. Neck stiffness was detected in one patient (1.9%) and it was due to meningeal irritation secondary to opportunistic infections, which is a well known complication that tends to occur in immunocompromised patients. Loss of consciousness can occur in patients with lung cancer either due to brain metastasis, paraneoplastic manifestations of the tumor, associated hyponatraemia as a manifestation of SIADH or may be due to opportunistic infections like Cryptococcus neoformans. Most of our patients showed abnormal findings on examination of the chest, the most common was pleural effusion, followed by consolidation and collapse, this can be explained by the late presentation of our patients, and it was supported by the increased incidence of abnormal findings on extrapulmonary examination like clubbing, lymphadenopathy, bone tenderness and fractures, hepatomegaly, and ascites. There is strong relation between abnormal chest findings, extrapulmonary findings, and CNS findings most of the patients who had cranial nerves involvement showed abnormal findings either in form of consolidation, collapse or pleural effusion. Upper and lower limb weakness were detected in 5.8% of our patients, this is similar to what was mentioned in the literature, it is either due to cord compression, nerve damage or muscle disease. Sensory disturbances were detected in 7.7% of our patients, this is similar to what was mentioned by Wilkinson and it differed from what was reported by Parker, it is either part of manifestations of cord compression or paraneoplastic manifestations. Out of the seven patients who had cranial nerves palsies, three had adenocarcinoma. Sensory and motor signs were detected in patients with squamous cell carcinoma. In spite of delay in presentation of our patients only 6.8% had an element of higher function impairment which is similar to what was reported by Feinstein AR but differed from what was mentioned by Merchut. Only one patient had cerebellar sign as apart of manifestation of paraneoplastic syndrome similar to the finding of Brain WR.
The histological type of lung cancer in our patients agreed with what was mentioned in the literature.\textsuperscript{31-32}

**Conclusions:** Most of our patients were from Khartoum state. Males dominated our studied population as the adenocarcinoma. As expected there is a strong relationship between smoking and lung cancer and also between abnormal chest findings, extrapulmonary findings, and CNS findings. A variety of neurological manifestations were observed among our patients including, cranial nerves palsies, lower limbs weakness, numbness,cerebellar lesion,and sphincteric disturbances. Half of the patients with cranial nerves involvement had adenocarcinoma, while sensory and motor signs were detected in patients with squamous cell carcinoma.

**References:**
1- Jemal A, Siegel R, Ward E, et al. Cancer statistics. CA Cancer J Clin 2006; 56:106-130.  
2-Parkin DM, Pisani P, Ferlay J. Global cancer statistics. CA Cancer J Clin 1999; 49: 33-64.  
3-Jackman DM, Johnson BE. Small-cell lung cancer. Lancet 2005; 366:1385-1396.  
4-Mountain CF. Revisions in the International System for Staging Lung Cancer. Chest 1997; 111: 1710-1717.  
5-Strauss GM, Kwiatkowski DJ, Harpole DH,. Molecular and pathologic markers in stage I non-small-cell carcinoma of the lung. Journal of Clinical Oncology 1995; 13: 1265-1279.  
6-Slebos RJ, Kibbelaar RE, Dalesio O. K-RAS oncogene activation as a prognostic marker in adenocarcinoma of the lung. New England Journal of Medicine 1990; 323: 561-565.  
7-Scagliotti G. Symptoms, signs and staging of lung cancer. Eur Respir Mon 2001; 17: 86-119.  
8-Doll R. Mortality from cancer in relation to smoking: 50 years observations on British doctors. British journal of cancer 2005; 92:426-9.  
9-Grippi MA. Clinical aspects of lung cancer. Semin Roentgenol1990;25:12-24.  
10- Hyde L, Hyde CI. Clinical manifestations of lung cancer. Chest 1974; 65: 299-306.  
11- Cromartie RS, Parker EF, May JE. Carcinoma of the lung. Ann Thorac Surg 1980; 30: 30-35.  
12-Dellatre JY, Krol G, Thiler HT. Distribution of brain metastasis. Arch Neurology 1988; 45: 741-744.  
13- Adams and Victors. Principles of Neurology 7th ed. NewYork, McGrow-Hill 2001; 3: 1457-1459.

**Neurological Manifestations of Lung Cancer.**

14-Tai P, Yu E, Battista J, Van Dyk J. Radiation treatment of lung cancer-patterns of practice in Canada. Radiother Oncol 2004; 71: 167-74.  
15-Swash M, Schwartz MS. Paraneoplastic syndromes. Current Therapy in neurological diseases 1990; 3: 236-243.  
16-Grippi MA. Clinical aspects of lung cancer. Semin Roentgenol 1990; 25: 12-24.  
17- Hyde L, Hyde CI. Clinical manifestations of lung cancer. Chest 1974; 65: 299-306.  
18-Patel AM, Davila DG, Peters SG. Paraneoplastic syndromes associated with lung cancer. Mayo Clin Proc 1993; 68: 278 –287.  
19-Anderson Ne, Rosenblum MK, Graus F. Auto antibodies in paraneoplastic syndromes associated with small -cell lung cancer. Neurology 1988; 38:1391-1398.  
20-Grover FL, Piantadosi S. Recurrence and survival following resection of bronchioloalveolar carcinoma of the lung: the Lung Cancer Study Group experience. Annals of Surgery 1989; 209: 779-790.  
21- Feinstein AR. Symptomatic patterns, biologic behavior, and prognosis in cancer of the lung. Ann Intern Med 1964; 61: 27-43.  
22-Pass HI. Malignant pleural and pericardial effusions. Cancer Principles and Practice of Oncology 5th ed 1997; 2586-2598.  
23-Bulzebruck H, Bopp R, Drings P. New aspects in the staging of lung cancer: prospective validation of the International Union against Cancer TNM classification. Cancer 1992; 70: 1102-1110.  
24-Hyde L, Hyde CI. Clinical manifestations of lung cancer. Chest 1974; 65: 299-306.  
25-Cromartie RS, Parker EF, May JE. Carcinoma of the lung. Ann Thorac Surg 1980; 30: 30-35.  
26- Karsell PR, McDougall JC. Diagnostic tests for lung cancer. Mayo Clin Proc 1993; 68:288-296.  
27- Croft PB, Wilkinson M. The incidence of carcinomatous neuromyopathy in patients with various types of carcinoma. Brain 1965; 88: 427-434.  
28-Feinstein AR. Symptomatic patterns, biologic behavior, and prognosis in cancer of the lung. Ann Intern Med 1964; 61: 27-43.  
29- Merchut MP. Brain metastases from undiagnosed systemic neoplasms. Arch Intern Med 1989; 149: 1076-1080.  
30-Brain WR, Wilkinson M. Subacute cerebellar degeneration associated with neoplasms. Brain 1965; 88: 465.  
31-Davis J, Mills KR. Favorable prognosis in Lambert – Eaton myasthenic syndrome and small cell carcinoma. Lancet 1999; 353: 117 – 118.  
32-Nussbaum ES, Djallilian HR, Cho KH, Hall WA. Brain metastases. Histology, multiplicity, surgery, and survival. Cancer 1996; 78:1781-8.