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Evaluation of Intellectual Function in Patients with Early Bronchogenic Carcinoma in Upper Egypt

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Abstract: ***Background: It's well established that in the course of bronchogenic carcinoma many inflammatory mediators and hypoxemia can affect Intellectual function and cognition through different pathways. This study aims to spotlight the possible cognitive abnormalities in bronchogenic carcinoma patients. Methods: in a case-control study module, twenty-five bronchogenic carcinoma patients and twenty-five age and sex-matched healthy control were enrolled. Mini-mental state examination (MMSE) was used to assess intellectual function in bronchogenic carcinoma patients and the control group. Results: there was significant impairment of the Mini-Mental State Examination questionnaire (MMSE) between the newly diagnosed bronchogenic carcinoma group and normal control. The mean MMSE was (24.52 ± 3.04) in the bronchogenic carcinoma group and (28.12 ± 1.66) in the control group with an observed significant difference between the two groups with a p-value of < 0.0001 emphasizing the early intellectual dysfunction that occurs through the course of early stages of bronchogenic carcinoma. Conclusion: Cognitive dysfunction is observed in the early stages of bronchogenic carcinoma even before any interventional modalities such as chemotherapy, radiotherapy or surgery.***

Keywords: Lung Cancer; Cognitive Function; Mini-Mental State Examination

1. Introduction

Intellectual dysfunction is a common presentation through the course of bronchogenic carcinoma with prevalence ranging from 15 to 90% in different studies.[1] Many studies have assessed the intellectual dysfunction in patients with bronchogenic carcinoma after starting chemotherapy and radiotherapy, however, in the current study we intended to study the intellectual dysfunction in newly discovered bronchogenic carcinoma before starting any interventional modalities such as chemotherapy, radiotherapy, or surgical intervention.

Despite the utmost importance of studying the intellectual impact of bronchogenic carcinoma at the earlier stages of the disease, studies are lacking at that stage. Cognitionis the brain's ability to receive and process different visual and intellectual data. Those functions are classified according to the higher neuronal framework to many levels, In day-to-day activity, cognition is derived from behavior, and is affected by many neuro-psychiatric factors.[2] All those factors are responsible for personal data recognition and analysis.

Neuropsychological tests are a reliable method for the evaluation of cognition and consist of many domains such as verbal, visual, and performances domains with can examinecognitive disorders in the current study we used Mini-mental state examination to assess cognitive function in newly diagnosed bronchogenic carcinoma patients.[3]

2. Patients and Methods

Study Participants and Ethical approval this study enrolled patients attending Chest outpatient clinic in the period between January 2020 and June 2020. Twenty-five newly diagnosed bronchogenic carcinoma and twenty-five matched control groups were enrolled.

Inclusion criteria: All newly diagnosed bronchogenic carcinoma patients attending the chest outpatient clinic and matched healthy volunteers were illegible to participate in the study.

Exclusion criteria were Patients previously diagnosed with any malignancy; Patients already diagnosed with bronchogenic carcinoma and received any interventional modality such as chemotherapy, radiotherapy or surgical intervention, Patients suffering from any end organ failure and Patients with any neurological or psychiatric abnormalities. All patients and healthy volunteers had informed consent to participate in the study.

Demographic, clinical and laboratory data the study group was subjected tocareful history taking, careful physical examination.

1- Pulse oximetry: oxygen saturation was recorded during examination using a pulse oximeter (Fingertip Pulse Oximeter, Beijing Choice Electronic Technology Co., Ltd).

2- Intellectual function evaluation: Mini-Mental State Examination (MMSE) was used which is a 30-point questionnaire that measures various domains of cognitive function including orientation to time and place; registration, concentration, short-term recall, naming familiar items, repeating a common expression, and the ability to read and follow written instructions, write a sentence, construct a diagram, and follow a three-step verbal command.

The MMSE takes approximately 10 minutes to administer. It provides a baseline cognitive function score and pinpoints specific deficits that can aid in forming a diagnosis. Before administering the MMSE, it is important to make the patient comfortable and establish a rapport with them. Praising success may help to maintain rapport and is acceptable. However, persisting on items that the patient finds difficult should be avoided.[4]

Interpretation: A total score of 30 indicates no impairment. Scores between 26 and 30 are considered normal in the general population. Patients who score between 25 and 20 have mild cognitive impairment and will be experiencing problems with the fine use of tools of daily activity, such as shopping, finances, medication use, and meal preparation, but can usually live on their own with support. Those who score between 20 and 10 have a moderate cognitive impairment, usually cannot live independently, and start having problems with basic activities, such as grooming, dressing, and using the toilet. Scores between 9 and 0 denote severe cognitive impairment; patients will have problems with all basic activities, including eating and walking. So a cut-off point of below 25 score is considered a cognitive impairment.

3-Histopathology: All patients had a confirmed histopathological report of bronchogenic carcinoma before participating in the study.

Radiological Evaluation using a Computed tomography scan of the Brain done for all patients to exclude neurological abnormalities or brain Metastasis before participation in the study

Sample size: according to recent studies the incidence of lung cancer was estimated in the total Egyptian population in 2018 to be nearly 56,000 new cases; the sample size was calculated to be 25 using Open Epi V.3.01 computer program.[5]

Statistical Analysis: Data was recorded to SPSS statistical software computer program version 24 (Statistical Package for Social Science), Medcalc v.11.6.and Open Epi V.3.01. Data were described using mean ± standard deviation (SD) and frequencies according if they are quantitative or qualitative respectively. Mann-Whitney Test is used to estimate the mean difference in the study group; the Chi-Square test is used to estimate the difference between categorical data of the study groups. A P-value below 0.05 was accepted as significant.

3. Results

In the current study, twenty-five patients with a confirmed diagnosis of bronchogenic carcinoma and twenty-five matched healthy controls were enrolled. Demographic data and patient characteristics were recorded, oxygen saturation was measured and MMSE was performed for both groups.

It was important to establish a matched case-control module especially as the main aim of the study was to evaluate intellectual dysfunction it was of utmost importance for both groups to be matched regarding age, education level, and residence all such factors that if not establishing a suitable matching would alter the result of the study.

From that perspective, the demographic data of both the bronchogenic carcinoma group and control group as demonstrated in table 1 show that the mean age of the bronchogenic carcinoma group and control group was (61.76 ± 9.18) and (58.6 ± 8.49) respectively with the non-significant difference between the two groups and p-value of 0.18. There were 22 males& 3 females in bronchogenic carcinoma and 21 male & 4 females in the control group with a p-value of 0.291. The results showed a non-significant difference between the two groups regarding smoking state with a p-value of 0.146. Regarding the education level of the bronchogenic carcinoma group, there were 17 literate patients and 8 illiterate patients. Inthe control groups, there were 15 literate subjects and 10 illiterate subjects with t non-significant difference between the two groups with a p-value of 0.22. There was no significant difference between both groups in the aspect of residence with a p-value of 0.158.

The data of comorbidities and oxygen saturation among the bronchogenic carcinoma group and control group was demonstrated in table 3. Six patients in the bronchogenic carcinoma group were diabetic and four in the control group, with no significant difference, witha p-value of 0.218. In the bronchogenic carcinoma group, there were 6 patients with mild cardiac disease and 2 in the control group with no significant difference, witha p-value of 0.099. There were 5 hypertensive patients in the case group and 7 in the control group with no significant difference between the two groups and p-value of 0.21. The mean oxygen saturation in the bronchogenic carcinoma group was 96.2 ± 2.29versus 98.16 ± 0.987in the control group with an observed significant difference between the two groups with a p-value of 0.001.

Table 3 shows the results of MMSE in both groups. The mean MMSE was (24.52 ± 3.04) in the bronchogenic carcinoma group and (28.12 ± 1.66) in the control group with an observed significant difference between the two groups with a p-value of < 0.0001 demonstrating a significant difference in the intellectual and cognitive function in the early stage of bronchogenic carcinoma than in control subjects.

Figure 1 shows the distribution of histopathology of the bronchogenic carcinoma in the case group. There were 22 patients with confirmed histopathology of non-small cell lung cancer (NSCLC) constituting 88% of the case group and Three patients with small lung cell cancer (SLCC) constituting 12% of the case group.

Table 1: Demographic data of bronchogenic carcinoma and control groups

	Bronchogenic carcinoma Group (n= 25)	Control Group (n= 25)	p-value
Sex:			
Male	22	21	0.291
Female	3	4	
Age: (years)			
Mean ± SD	61.76 ± 9.18	58.6 ± 8.49	0.18
Smoking:			
Smoker	10	9	0.146
Ex-smoker	9	11	
Non-smoker	6	5	
Residence:			
Urban	12	9	0.158
Rural	13	16	
Education:			
Literate	17	15	0.22
Illiterate	8	10	

Table 2: Comorbidities and oxygen saturation of bronchogenic carcinoma and control group

	Bronchogenic carcinoma Group (n= 25)	Control Group (n= 25)	p-value
Diabetes:			
Non-diabetic	19	21	0.218
Diabetic	6	4	
Hypertension:			
Not hypertensive	20	18	0.21
Hypertensive	5	7	
Cardiac disease:			
Without cardiac diseases	19	23	0.099
With cardiac diseases	6	2	
Oxygen saturation:			
Mean ± SD	96.2 ± 2.29	98.16 ± 0.987	0.001*

Table 3: Results of MMSE in Bronchogenic carcinoma and control group

Groups	Bronchogenic carcinoma group	Control Group	P-value
	Mean ± SD	Mean ± SD	
MMSE	24.52 ± 3.04	28.12 ± 1.66	< 0.0001*

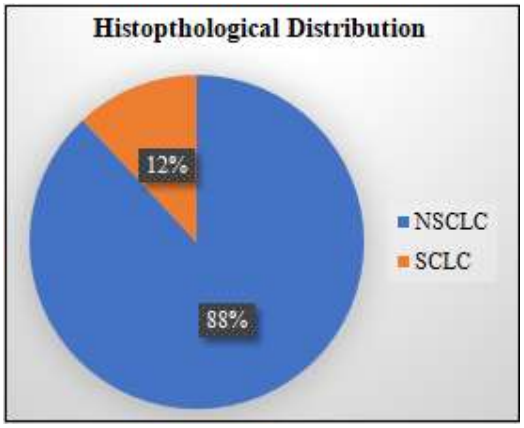

Figure 1: Showing the histopathological distribution of bronchogenic carcinoma group

4. Discussion

In our study we observed significant cognitive dysfunction in patients with early bronchogenic carcinoma even before starting chemotherapy and radiotherapy or presence of brain metastasis.

Brown et al. used MMSE to evaluate cognitive decline in patients with low grade glioma.[6] Intellectual dysfunction early in the course of bronchogenic carcinoma even before the start of prophylactic cranial radiation therapy is multifactorial due to use of various chemotherapies, use of steroid and even as a part of Para neoplastic syndrome. This was observed in patients with several types of malignancy.[7-9]

The exact etiology of these impairments is still unknown, this may be due to immunological abnormalities, microscopic brain metastasis or release of many

inflammatory mediators, and tissue necrosis factors.[10] another important etiology is a neurotoxic effect of chemotherapy used for treatment of different types of lung cancer including vincristine, etoposide and cisplatin.[11]

Limbic encephalopathy has been observed in a group of patients of small cell lung cancer which may attribute to cognitive dysfunction in those patients.[12] Minor cognitive deficit was observed In small cell lung cancer patients even before chemotherapy and prophylactic cranial irradiation.[9]

In up to 10% of small cell lung cancer patients para neoplastic syndrome occurs[13]; as a part several polypeptide hormones, inflammatory mediators and immune complexes is released[14], Which may attribute to cognitive impairment in lung cancer patients.

Small cell lung cancer is commonly associated with auto immune neurological syndromes with production of anti-neuronal antibodies (anti-Hu).[15, 16]

Bartels et al. found that among 167 patients with lung cancer; Brain-directed autoantibodies 36.5% of patients; 33 patients (19.8%) had known autoantibodies and 28 patients (16.8%) had autoantibodies against currently unknown antigens that were detected through immunohistochemical analysis. Cognitive impairment was found in 67% of patients.[17]

There also were several changes in magnetic resonance spectroscopy in neurotransmitters, especially in the amygdaloid nucleus and Para hippocampal gyrus which may attribute to intellectual dysfunction in those patients.[18]

Wessel and colleagues observed the occurrence of cerebellar signs in 26% of their study group of bronchogenic carcinoma patients not complicated by brain metastasis or other comorbidities, their results showed no significant results in different histological types of bronchogenic carcinoma.[19]

In a study by Simó and colleagues, 28 SCLC patients and 20 NSCLC were studied for neurocognitive abnormalities; revealed verbal memory abnormalities in 39% and 30% respectively.[20]

Consistent with our study 96 SCLC patients were studied for cognitive impairment before undergoing prophylactic cranial radiation, cognitive dysfunction was observed in 47% of patients.[21] Komaki and his colleagues reported 97% of SCLC patients (29 patients out of 30 patients enrolled in his study) had intellectual dysfunction using various evaluation tests and batteries (before Prophylactic Cranial radiation).[22]

Like our results, Meyers and colleagues observed cognitive disorders in the SCLC patient Group, before and after chemotherapy.[9]

5. Conclusion

In this prospective, case-control study, patients with lung cancer early in the course of illness showed cognitive impairment. Mini mental state examination is simple and effective tool that can be used to evaluate cognitive dysfunction in lung cancer patients.

These findings signify that intellectual dysfunction represent a potentially under estimated and major comorbidity among patients with lung cancer that need early diagnosis and management.

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