Brain, Behavior, & Immunity - Health 25 (2022) 100507

Contents lists available at ScienceDirect

Brain, Behavior, & Immunity - Health

journal homepage: www.editorialmanager.com/bbih/default.aspx

The role of psychiatry in quality of life in young patients with non-small cell lung cancer

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A B S T R A C T

Background: Lung cancer is often seen in geriatric patients, with an age of onset of approximately 60 years. Non-small cell lung cancer (NSCLC) remains the leading cause of cancer-related mortality in the United States and around the world. Young patients are rarely diagnosed with lung cancer, with less than 3.5% of patients presenting with this tumor at an age less than 45. In this paper, we examine NSCLC in young patients, between 18 and 35 years of age, which most commonly occurs in non-smokers and is characterized by a higher proportion of adenocarcinoma histology and advanced disease at presentation. These patients often present with metastasis involving one organ and they test positive for driver gene mutations including, but not limited to, epidermal growth factor receptor (EGFR), tyrosine kinase inhibitor (TKI) sensitive mutation and anaplastic lymphoma kinase (ALK). We addressed depression and anxiety and their effect on quality of life (QOL) and attempted to examine how improvement in QOL in these young patients could affect their course of illness and prognosis.

Methods: We conducted a literature review using PubMed, Cochrane, and Google search. We concentrated our search on two elements, reviewing approximately 50 articles focusing on the driver mutations EGFR and ALK as well as genetic mapping of lung adenocarcinoma in patients aged 18–35 years old. We also conducted a review of approximately 30 articles focusing on quality of life in the context of anxiety and depression within this patient population.

Results: We have described a case of a 28-year-old male with new-onset metastatic lung adenocarcinoma that we had treated in our hospital. He was found to have mutations in EGFR and ALK rearrangement. We aimed to address his depression, anxiety, and poor QOL in the context of his diagnosis. Due to his presenting symptoms leading to the diagnosis of adjustment disorder, he was treated with pharmacotherapy as well as conventional therapy to improve his QOL. Due to the time required to identify mutations, our patient passed away before a more targeted treatment could be offered.

Conclusion: It is important to fully explore the nature of the cancer, including mutation types. Our case demonstrates that the detection of the driver gene mutation EGFR and/or ALK rearrangement could affect treatment and prognosis in this patient population. There are many studies available that highlight targeted therapies for these mutations as well as chemotherapy and radiation. Psychiatry has a significant role in improving quality of life in these patients, which could enhance their response to treatment and survival. Involving psychiatry early in the course results in lower rates of depression, anxiety and premature death.

1. Introduction

Lung cancer is the first leading cause of tumor–related mortality with approximately 1.38 million deaths occurring worldwide every year (Chapman et al., 2016). In the United States, the number of deaths from lung cancer annually is 131,880 in both sexes (Siegel et al., 2021), pointing to poor prognosis. The majority of lung cancers in the United States are associated with smoking, while 10–15% of lung cancers occurring in the United States are not associated with smoking (Chapman et al., 2016; Chen et al., 2019). Lung cancer is often seen in geriatric patients with an age of onset of approximately 60 years (Chen et al., 2019). Young patients are rarely diagnosed with lung cancer, with less than 3.5% of patients presenting with this tumor at age 45 years and younger (Chen et al., 2019).

Lung cancers are divided into 2 groups, small cell lung cancer (SCLC) and non-small cell lung cancer (NSCLC). NSCLC are divided into large cell carcinoma (LCC), squamous cell carcinoma (SC) and adenocarcinoma (AC) (Chapman et al., 2016). About 65% of patients who are diagnosed with AC are non-smokers. NSCLC remains the leading cause of cancer-related mortality in the United States and around the world (Garrana et al., 2021). This cancer type is usually diagnosed in patients in the 6th and 7th decades of life, with less than 5% seen in patients below age 50 and even fewer below age 40 (Sacher et al., 2016; Piccirillo et al., 2004; Jorgensen et al., 2012). NSCLC is extremely rare in young adults, who we defined developmentally between 18 and 35 years of age. Other cancers such as lymphoma, melanoma, sarcoma, breast and testicular cancers occur more frequently in this age group and are the leading cause of mortality in the young adult age group (Garrana et al., 2021).

Studies have shown that young patients with NSCLC have different

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https://doi.org/10.1016/j.bbih.2022.100507
Received 13 June 2022; Received in revised form 23 August 2022; Accepted 23 August 2022
Available online 7 September 2022

clinical and pathological features leading to different outcomes when compared to older patients. Young adults often present with adenocarcinoma (Chen et al., 2019) and have molecular alteration, with the most common being anaplastic lymphoma kinase (ALK) rearrangements and epidermal growth factor receptor (EGFR) mutations (Garrana et al., 2021). Distinct lung cancer with separated genetic pathways that are caused by discrete mutations in tumor-promoting genes called driver mutations are also seen in people who never smoked. This is different from the genetic changes seen in lung cancers in smokers (Lee et al., 2011; Kim et al., 2012; Gazdar et al., 2004; Subramanian and Govindan, 2008; Han et al., 2013).

Lung cancers in never-smoking patients tend to have somatic mutations, acquired mutations, or tumor-promoting genes. Mutation in the EGFR is found in 40% of non-smokers' tumors (Chapman et al., 2016). EGFR is a receptor tyrosine kinase that has a role in cell differentiation, proliferation and maintenance in both normal and cancerous cells (Chapman et al., 2016). Mutations are often seen in the first four exons of EGFR that encode for tyrosine kinase domain in NSCLCs (Chapman et al., 2016).

Deletion mutation in exon 19 and point mutation at codon 858 in exon 21 are the most frequent mutations seen and are used as a predictor for sensitivity to treatment (Bircan et al., 2014; Takano et al., 2007; Li et al., 2014). Among NSCLC, 15–30% present with mutation in oncogenic Kirsten rat sarcoma viral oncogene homolog (KRAS) and 97% of NSCLCs have point mutation in codon 12 or exon 13 (Chapman et al., 2016). KRAS encodes GTPase activity in proteins that regulate cell growth, differentiation and apoptosis (Chapman et al., 2016).

Young patients who have never smoked present with mutations in KRAS and ALK at varying rates (Lee et al., 2011; Burns and Rudin, 2010; Couraud et al., 2012; Bircan et al., 2014; Li et al., 2013). Recent studies have pointed to a possibility of targeting these mutations with a multitude of chemotherapies to halt cancer progression and improve survival in patients with NSCLC (Carbonnaux et al., 2016; Kenfield et al., 2006; Barlesi et al., 2016).

Studies have shown that mutations in EGFR and ALK are more prevalent in female patients of Eastern-Asian ethnicity with adenocarcinomas. Chapman et al. showed that never-smoking patients of Asian and Caucasian descent with adenocarcinomas faced significantly increased odds of having EGFR mutation compared to other NSCLC. As the smoking status increased, there was a decrease in odds for exhibiting EGFR mutations (Chapman et al., 2016).

The diagnosis and treatment of lung cancer in young adults have unique health and psychosocial challenges. Since patients are at the peak of reproductive years, infertility resulting from chemotherapy is an important consideration (Benedict et al., 2016). Financial difficulties due to unemployment and being uninsured are of significant concern compared to other age groups (Garrana et al., 2021). Young adults with lung NSCLC may be faced with psychological and emotional issues, as the diagnosis rises at a time where rapid changes in cognitive and emotional development transpire (Zebrack, 2011). NSCLC in young patients most commonly occurs in never-smokers and is characterized by a higher proportion of adenocarcinoma histology and advanced disease at presentation. In addition, it more often harbors targetable genetic alterations.

In this paper, we will examine NSCLC in young patients, between 25 and 35 years of age. We will address depression and anxiety and their effect on QOL and will attempt to examine how improvement in quality of life in these young patients could affect their course of illness and prognosis. We will present a case of a patient and we will conduct a review of literature.

2. Case presentation

Patient is a 28-year-old with no known previous medical history initially presenting to an outside hospital with a 1-week history of feeling ill with fatigue and persistent dry cough. He was diagnosed with pneumonia, prescribed antibiotics, and was discharged home. He returned to the emergency department 2 weeks later complaining of no change in symptoms and a physical exam revealed cervical lymphadenopathy. The patient underwent a left subcortical lymph node excisional biopsy at an outpatient clinic that showed metastatic adenocarcinoma with mucinous and signet ring cell features.

The patient underwent CT scan of his neck, chest, abdomen and pelvis. The Chest CT showed mediastinal and bilateral hilar lymphadenopathy, extensive bilateral cervical lymphadenopathy and lack of contrast opacification of the right internal jugular vein consistent with venous thrombosis. The patient underwent excision of the left supraclavicular lymph node. The biopsy confirmed the presence of metastatic adenocarcinoma. Immunohistochemical staining was positive for AE1/AE3, CAM5.2, CK7, TTF-1, Napsin and E-cadherin. Flow cytometry was noncontributory. He was recommended to follow up with oncology.

The patient presented to our emergency department 2 weeks after he was diagnosed with lung adenocarcinoma, with cough, poor sleep, night sweats, lethargy and a 15-lb unintentional weight loss. Since the patient was not vaccinated for COVID-19, he underwent a Rapid SARS-CoV-2 (COVID)-19 test, which was positive. Polymerase chain reaction (PCR) testing confirmed this finding.

In the emergency department, the patient's vital signs showed a temperature of 98.2F, a heart rate of 68 beats/min, a respiratory rate of 22 breaths per minute, and a blood pressure of 114/72 mmHg. Oxygen saturation was 98% on room air. The patient's height was 180 cm and his weight was 77.278 kg with BMI of 23.85.

Physical exam showed a cachectic, ill-appearing male. He was tachypneic with mild subcostal retractions. Crackles and coarse breath sounds were heard at both lung bases. His heart rate was regular, without murmur, gallop or rub. No edema was noted in the lower extremities. His abdomen was soft and supple, not distended, and not tender. Bowel sounds were present and normal. The skin was pale, warm and dry. Cervical lymphadenopathy was present. The neurological exam did not demonstrate any abnormalities.(see Table 1)

Chest x-ray revealed bilateral interstitial infiltrates. Right upper quadrant ultrasound showed normal liver, gallbladder, bile ducts, pancreas, and kidneys; there was no abdominal ascites observed.

The patient received dexamethasone 4 mg every 6 h IV, benzonatate (Tessalon) and acetaminophen with Codeine, vancomycin and piperacillin-tazobactam (Zosyn). He was admitted to the intensive care unit and was placed on a nonrebreather. He began treatment with prednisone 40 mg daily.

The patient underwent a follow-up chest CT which showed multiple dense bilateral reticulonodular infiltrates and again demonstrated enlarged lymph nodes at the base of the neck. The patient underwent genomic testing and was found to have EML4-ALK fusion; he also was positive for BRCA1 mutation.

On admission day 14, Psychiatry was called to evaluate the patient for suspected depression and anxiety. The patient reported symptoms of adjustment disorder with depressed mood including sadness, hopelessness and helplessness. He denied suicidal ideations. He was noted to be wearing a "Do Not Resuscitate/Do Not Intubate" bracelet on his hand; when asked about this, he explained that he made a decision to not be resuscitated due to his physical distress. He endorsed an inability to fall asleep or maintain sleep due to anxiety and persistent cough. He stated that his appetite had been poor and he had lost interest in food. Upon further questioning, the patient endorsed significant loneliness resulting from isolation due to COVID-19 with no access to visitors. The patient stated that he misses his adoptive mother who is his closest supportive family member. The patient stated that he suffered from longstanding depression since he was removed from his home during his early childhood and was placed in numerous foster homes. He indicated that when he received his cancer diagnosis and prognosis, he felt despondent, and stated "Have I not suffered enough already?"

He denied symptoms consistent with mania or psychosis. The patient denied the use of tobacco, alcohol or other drugs. He denied

Table 1
Lab values are highlighted in table below.

Parameter	Value	Range
Electrolytes		
Sodium (mmol/L)	133	136–145
Potassium (mmol/L)	4.4	3.5–4.1
Chloride (mmol/L)	99	98–107
Bicarbonate (mmol/L)	23	23–29
Glucose (mg/dL)	102	65–99
Phosphorus (mg/dL)	4.1	2.5–5.0
Calcium (mg/dL)	8.0	8.6–10.0
Magnesium (mg/dl)	1.8	1.6–2.6
Kidney Function		
BUN (mg/dL)	11.7	6.0–20.0
Creatinine (mg/Dl)	0.82	0.70–1.20
Hepatic Function		
AST (IU/L)	26	15–41
ALT (IU/L)	45	7–40
Bilirubin (mg/dL)	0.9	0.3–1.2
Lactate Dehydrogenase (IU/L)	225	100–190
Serum Proteins		
Albumin (gm/dL)	1.9	3.5–5.0
Iron Studies		
Iron Level (mcg/dL)	15	50–175
Ferritin (ng/mL)	1162	24–336
TIBC (mcg/dL)	151	261–478
Haptoglobin (mg/dL)	332	36–195
CBC and Differential		
WBC (x10(9)/L)	15.7	3.5–10.0
RBC (x10(12)/L)	4.13	4.30–5.70
Hgb (g/dL)	11.5	13.5–17.0
HCT (%)	35.3	38.0–50.0
MCV (fL)	85.5	80.0–99.0
MCH (pg)	27.8	25.0–34.0
MCHC (g/dL)	32.6	31.0–36.0
Platelet (x10(9)/L)	174	150–400
MPV (fL)	10.2	9.3–13.0
Neutro Auto (%)	83.0	40.0–75.0
Lymph Auto (%)	8.8	20.0–45.0
Neutro Absolute (x10(9)/L)	32.80	2.00–7.50

occupational exposure to environmental pollutants and/or toxins such as asbestos, heavy metals, pesticides, and ionizing radiation.

Mental status examination showed: A tall, cachectic male with missing upper front teeth who appeared his stated age and was dressed in hospital attire. He was cooperative, had downcast eyes with distant gaze at times, and did not exhibit any motor abnormalities. His speech was fluent and he described his mood as "hopeless," with a congruent, dysphoric affect that was constricted in range. He was able to express his thoughts in a linear fashion and he denied suicidal/homicidal ideations or hallucinations but was fixated on his physical symptoms. He was alert and oriented x3, with grossly intact cognition, memory, attention and concentration. Judgment was ostensibly fair, but the patient appeared to be minimizing his depressive symptoms and was dismissive of questions regarding his emotional response to his cancer prognosis.

As his hospital course progressed, the patient was ultimately diagnosed with major depressive disorder according to the Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (DSM-5) due to depressed mood, impaired sleep, anhedonia, feelings of fatigue, diminished appetite, hopelessness and a sense of worthlessness for over two weeks. Hamilton Depression Rating Scale yielded a score of 26, indicative of significant depression.

In accordance with Psychiatry's recommendation, the patient began treatment with escitalopram 10 mg daily and gabapentin 300 mg nightly; escitalopram was titrated to 15 mg daily and gabapentin was titrated to 600 mg twice daily. Due to psychomotor agitation accompanied by respiratory distress and restlessness, olanzapine 2.5 mg nightly was initiated. Olanzapine was increased to a final dose of 5 mg for greater therapeutic effect until the patient apparently developed a dystonic reaction resulting in an inability to move his tongue. Olanzapine was subsequently discontinued and replaced by quetiapine, which provided improvement in anxiety and insomnia as it was titrated from 50 to 100 mg at bedtime.

During the patient's hospital course, the patient expressed wishes to begin treatment with chemotherapy but as time progressed, he began reporting increasing depression and hopelessness about the future despite treatment. His anxiety remained elevated, and he often verbalized the feeling of being a burden on his family. He denied anger or irritability.

The patient was discharged home 2 weeks after his first contact with Psychiatry. Given the relatively short duration of the patient's hospitalization, the benefits of escitalopram were difficult to ascertain. He ultimately expired 2 weeks later.

3. Review of the literature

3.1. NSCLC associated genetic markers

To further the investigation of young patients with lung adenocarcinoma and their quality of life, we explored the genetic components and treatment options available to this age group affected by this disease. Studies have shown that lung cancer in young people appears to be a distinct disease, when focusing on clinical presentation and the cancer's genetic makeup, with several genomic changes associated (Sacher et al., 2016).

Nino et al. (Galvez-Nino et al., 2020) studied 3823 patients with lung cancer from 2009 to 2017. NSCLC histology was defined using International Classification of Diseases for Oncology (WHO, 2015) and included adenocarcinoma, squamous cell carcinoma, adenosquamous cell carcinoma, large cell carcinoma and carcinoma not otherwise specified. Data such as age, sex, smoking history, family history, symptoms and stage at presentation were identified. In this study, 166 patients were 40 years old or younger, with a median age of 36. Within this group, 158 patients had confirmed histology and 137 of them had a confirmed diagnosis of NSCLC. The most common histological type present was adenocarcinoma (63%). All of the patients were symptomatic at the time of diagnosis and mean time from onset of symptoms to diagnosis was 4 months. Of these patients, 90.5% had unresectable disease at diagnosis (58% were at stage III while 84.7% were at stage IV at diagnosis). Smoking history was present in 14% of patients. Family history was reported in 19% of cases. Young females represented 59.1% of occurrences (Galvez-Nino et al., 2020).

In this study as well as others, the frequency of adenocarcinoma histology has been found to be higher in young patients who present with advanced disease at diagnosis. In addition, no clear risk factor was ascertained; NSCLC is described frequently in non-smokers. Based on extensive cohort analysis from an American institution database, EGFR and ALK gene mutations were significantly associated with young patients. ERBB2 and ROS1 were present but not as frequent (Sacher et al., 2016). Young patients with NSCLC represent a genetically unique subgroup that may require a new method of treatment.

Yoneyama et al. (2019) evaluated the availability of therapeutic modalities including induction, neoadjuvant chemotherapy, and surgical resection for young patients with lung cancer. Of young patients presenting with stage IV lung cancer, 68% had only a single organ affected at the time of diagnosis, suggesting that aggressive local and systemic treatments could lead to a better prognosis. They also reported that overall survival in young patients with NSCLC ranged between 62.3 and 83.1% at 1 year, 53.3%–64.6% at 3 years, and 53.3–57.0% at 5 years, despite the higher rate of advanced stage of lung cancer. This finding may be attributable to the benefits of treatment.

Liu et al. (2019) conducted a retrospective review study of patients with lung cancer from 2010 to 2017. They included young patients between 18 and 35 years old with the mean age of 31.39 years at diagnosis and found that only 2 patients were 18 years old at diagnosis. The family history was unremarkable in 98.68% of the cases, while 71.60% of the patients in the study never smoked and 91.36% had no

history of alcoholism. They observed that 49.21% had adenocarcinoma and late stage disease at diagnosis. The pleura was the most common metastatic site (35.71%) and present with malignant pleural effusion, followed by the bone (35.48%), lung (25.81%), and liver (12.90%). The majority of the patients (68%) had a single organ metastasis (oligometastases), which indicated that aggressive local and systemic treatment could lead to better prognosis in these patients. Other pathologies observed were small cell lung cancer (26%), squamous carcinoma (11%) and neuroendocrine lung tumors (6%), which include adenosquamous carcinoma, adenoid cystic carcinoma and large cell carcinoma.

A total of 53 patients underwent genetic testing for driver gene mutations: 18.87% (10 patients) had ECFR TKI sensitive mutation, 7.55% (5 patients) had ALK rearrangement. The patients underwent surgery (47.89%), radiotherapy which consisted of thoracic radiotherapy and or cranial irradiation (25.42%), chemotherapy (68.33%) and targeted therapy with EGFR and ALK TKIs (26.92%). More than one treatment modality was utilized in 41.79% of the patients.

The survival rate at 1 year was 62.31%, and the 3- and 5- year survival rates were 53.31%. The study showed that patients who were positive for driver gene mutations such as TKI-sensitive, EGFR mutations or ALK rearrangements had superior overall survival when compared with patients with negative or unknown status of the driver gene mutations. Patients with negative mutations had a 15-month survival rate. Staging of the cancer has also significant prognostic factors on survival, with a shorter survival rate for patients with stage IV vs. stage 0-III.

The study has shown that negative detection of driver gene mutation and stage IV disease predicts poorer outcomes and lower overall survival. This study, however, did not find significant difference in overall survival in male sex or pathological tumor type, which pointed to considerable heterogeneity among young adults with lung cancer. Therefore, it is important to fully explore the features of the cancer to determine the optimal interventions to improve prognosis for early-age onset lung cancer.

The etiology of lung cancer in young patients is currently a “hotspot” in research and studies have shown that NSCLC in patients younger than 40 years of age frequently show genomic alterations. Of those patients with adenocarcinoma, 40% have EGFR mutation and 34% have ALK rearrangement. Also, patients less than 45 years old have high frequency of human epidermal growth factor receptor 2 (HER2) and ALK genetic alteration with concurrence of EGFR/TP53 mutations. Meanwhile, they have lower frequency of EGFR exon 20 mutations, KRAS and serine/threonine kinase 11 (STK11) mutations compared to patients aged greater than 45 years old.

All patients with NSCLC should be tested for NSCLC cancer markers in order to enhance targeted immunotherapy, chemotherapy, and radiotherapy, both in isolation and combination. Various psychotherapies can be used, such as antidepressants, which increase the immune response, as well as other various coping strategies. Patient education regarding appropriate coping skills is necessary to deal with the burden of NSCLC treatment, as well as other cancer treatments. The burden of cancer in young people, especially in the prime of their lives, is another aspect of oncology that should be addressed. Psychiatric treatment is not specific for NSCLC, but can be utilized globally to enhance survival in patients undergoing treatment for NSCLC. The role of psychiatry in oncology is to address the coping associated with cancer. The ability to cope with cancer is both beneficial for the patient with NSCLC, and beneficial for patients undergoing treatment for various other cancers.

3.2. Psychological manifestations of lung cancer

Patients with lung cancer continue to experience the burden of symptoms despite significant advances in treatment, specifically in immunotherapy and targeted therapies, which impacts patient QOL. The most frequent symptoms seen include fatigue, pain, shortness of breath, cough, and psychological manifestations such as depression and anxiety. Studies have shown that QOL and survival rate can improve when symptoms are addressed effectively (Molassiotis et al., 2021).

Major depression is common in cancer patients and the prevalence rate is 4 times higher than the general population (Shoval et al., 2019). Depression and anxiety significantly increased in patients with poorer prognosis, including terminal illness. In patients with cancer, depression is associated with increased physical distress, reduced quality of life, prolonged hospital stays and diminished compliance with cytotoxic medications, which leads to reduced survival (Lee et al., 2011; Prieto et al., 2002; Shoval et al., 2019). Depression in cancer patients may present as a normal reaction to cancer diagnosis, as a psychiatric disorder, and or as a somatic consequence of the cancer treatment itself (Levenson, 2011). Patients with cancer complicated by depression present an independent risk for suicide. Recent studies have shown a 2–4 fold increased risk of suicide in patients with certain cancers that is the highest in the first 6 months following diagnosis (Shoval et al., 2019).

Anxiety often increases during treatment and before surgery. Studies have shown that 60–80% of patients experience anxiety preoperatively. The anxiety that patients develop prior to surgery stem from fear of death, fear of pain, fear of losing control of one’s body, fear regarding anesthesia, fear about the social outcome such as losing one’s ability to work, and disruption in the home routines. Anxiety leads to an increase in sympathetic stimulation which in turn increases heart rate, cardiac output and oxygen consumption (Genc and Saritas, 2020).

3.3. Coping mechanisms

Various methods are available to assist patients with reducing anxiety prior to surgery or any other intervention. These include progressive relaxation exercises, deep breathing exercises, distraction using visual and auditory techniques, imagery, music therapy, hypnosis, biofeedback and aromatherapy. Using humor is also an effective method of distraction, which stimulates sensory and affective systems, improves ability to tolerate pain and decreases anxiety and distress. Laughter, spontaneous or as part of therapy, was observed to improve respiratory and circulatory system functioning via stimulation of the hypothalamus. It also decreases muscle tension via endorphin production (Genc and Saritas, 2020).

Aleksandra I Czerw et al. (2016) evaluated coping skills strategies, pain management, disease acceptance and adjustment in patients with lung cancer. Two hundred and forty patients, diagnosed with lung cancer and undergoing chemotherapy and molecularly targeted therapies were recruited at the oncology center. The patients were given the following rating scales to evaluate their adjustment to cancer, including: Beliefs About Pain Questionnaire (Sacher et al., 2016), Pain Coping Strategies Questionnaire (Piccirillo et al., 2004), Acceptance of Illness Scale (Jorgensen et al., 2012), and Mental Adjustment to Cancer (Garrana et al., 2021). It was apparent that pain has a significant influence on adjustment to illness, especially in end-stage disease. Pain affects 90% of patients with lung cancer, making selection of pain management important. In this study, it became evident that patients with lung cancer attributed most power over pain management to physicians, and internal factors such as social, marital status, and employment were deemed less important. Pain was associated with anxiety and hopelessness. The coping skills that patients used to overcome the difficulty related to disease depended on the patient’s psychological factors, including distracting, diverting attention, praying/hoping, and “fighting spirit.” Education significantly impacts coping skills and adjustment. The study has shown that acceptance of cancer decreases negative emotions and enhances daily function.

The acceptance of lung cancer is about 23%, which is lower than the acceptance rate for diabetes, multiple sclerosis, and breast and uterine cancers in women (Levenson, 2011). There is significant correlation between disease acceptance and socioeconomic variables. Unfortunately, low disease acceptance often worsens cancer progression and overall outcome due to low motivation and participation in care (Vandervoort et al., 1997; Stuifbergen et al., 2000).

3.4. Quality of life

Mick van de Wiel et al. (van de Wiel et al., 2021) assessed the influence of psychological symptoms such as anxiety and depression on QOL and prognosis in patients with advanced lung cancer. They also looked at whether coping strategies have a role in affecting QOL. The study was conducted for 2 months and 125 patients participated. It became apparent that acceptance and emotional support were the most important in improving QOL in patients with advanced lung cancer, while denial and self-blame lead to negative effects. Anxiety was shown to significantly correlate with poor emotional well-being, increased pain, dyspnea, insomnia and constipation. Anxiety also led to poorer adherence and increased length of hospital stay. Depression was correlated with worse general QOL, poor physical and emotional wellbeing, decreased survival and an increase in pain, dyspnea, insomnia and constipation due to loss of appetite. Adequate coping strategies showed positive correlation to better QOL, emotional and physical wellbeing with less fatigue, loss of appetite and nausea.

Hopwood et al.[44] studied 987 patients from three palliative treatments. Of these, 526 (53%) were diagnosed with SCLC with poor prognosis and 461 (47%) patients were diagnosed with NSCLC with good prognosis. It was apparent that depression is common in patients with lung cancer, with a tendency to persist beyond the initial reaction to a new diagnosis.

Depression in patients with lung cancer adds burden during treatment, resulting in low motivation and compliance with treatment, which can lead to increased difficulty managing symptoms, increased length of stay and reduced survival. Depression is an important predictor of QOL. Depression was found in highest frequency in patients with advanced disease, severe illness, and poor physical state with poor prognosis.

Polanski et al. (2020) studied the association between satisfaction with life, which is defined as the global perception of one's quality of life based on one's individual criteria, and QOL in-patients with lung cancer. This study enrolled 250 patients with a mean age of 63 years with lung cancer confirmed by histology between January 2019 and June 2019. A European Organization for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire-Core-30 with QLQ-LC13 lung cancer–specific module was administered to allow a comprehensive analysis of a patient's perceived health and functioning in the physical, emotional and social dimension. The 30 item core questionnaire included 5 functional scales, 3 symptom scales (fatigue, nausea/vomiting and pain and 6 clinical items including shortness of breath, insomnia, loss of appetite, constipation, diarrhea and financial difficulties). The EORTC QLQ-OC13 consisted of 13 items specific to lung cancer. Researchers used the Satisfaction with Life Scale to assess satisfaction with life, along with a visual analogue scale to assess pain.

Other scales including the Acceptance of Illness Scale and the Mental Adjustment to Cancer Scale were used to assess the patient's ability to cope with cancer. In the study, 27.2% of patients with lung cancer had a low level of satisfaction with life, 43.9% of patients had a moderate level of satisfaction with life and 28.8% had a high level of satisfaction. A positive outlook on a person's situation may be associated with a greater satisfaction with life and some patients with cancer may find a positive aspect to their illness. Satisfaction with life may have different sources in healthy patients vs. ill patients. In healthy people, satisfaction with their life may be related to their daily activities, contact with others and "extraversion and negative emotionality." While in ill people, satisfaction in life stems from "inhibition and consciousness" that may predict satisfaction in one's life.

Polanski et al. (2020) observed in their study that satisfaction with life was negatively affected by being a non-smoker, having chest pain, longer duration of illness, side effects during treatment and high degree of physical disability. Patients with a negative family history of cancer showed greater satisfaction with life. It was apparent that satisfaction with life was related to using positive coping skills, illness acceptance, ability to adjust and an ability to "spiritually fight the cancer." As a result, more satisfaction in life was associated with lower severity of symptoms and improvement in QOL. In addition, Samuel et al.[43] reported that QOL and satisfaction with life depend on symptoms, especially on the presence of pain and the patient's ability to participate in the treatment plan. An improvement in life satisfaction can be achieved cognitively by positive thinking, improvement in goals and finding new meanings to life.

Montfort et al. (van Montfort et al., 2020) examined the psychological profiles of patients with lung cancer in order to assess impact on the quality of life following such a diagnosis. Notably, the severity of psychological distress is highest in lung cancer compared to any other type of cancer. It was hypothesized that such psychological profiles in lung cancer patients are not only identifiable, but also correlated with specific sociodemographic and medical characteristics, and distinct in their effects on quality of life. Voluntary participants were selected from a group of patients who were diagnosed with lung cancer within a 5-month interval, 18 years or older, and did not exhibit pre-existing psychiatric or cognitive issues. This sample consisted of 130 patients (mean age $\pm$ SD $=$ 68.3 $\pm$ 8.6 years; 49% men) of which 113 were diagnosed with NSCLC of variable staging. After combining mean scores of psychological characteristics and analyzing information criteria, a model of labeling 4 latent psychological profiles was constructed. These 4 psychological profiles were as follows: anxious with extensive coping (33%), depressive with avoidant coping (23%), low emotional symptoms with active/social coping (16%), and low emotional symptoms with limited coping (29%).

Medical characteristics (such as comorbidities and lung cancer type) and sociodemographic characteristics (including age, sex, employment status, and educational level) were not found to be significantly different between the profiles.

Statistically significant differences in quality of life were demonstrated between the profiles when comparing the anxious and depressive profiles (1 and 2) to either of the lower emotional symptom profiles (3 and 4). Differences between profiles 1 and 2 or between profiles 3 and 4 were statistically insignificant.

It was theorized that anxiety symptoms may serve a motivational purpose, necessitating the use of extensive coping strategies perhaps as a means of regaining control over one's life. Depressive symptoms were accompanied by avoidance and low perceived social support, as these individuals may withdraw from others. The juxtaposition of similar coping strategies with different emotional symptoms such as seen in profiles 1 and 3 shows how the presence of social support influences the effectiveness of a particular approach.

Quality of life was lower in the anxious and depressive profiles compared to the 2 profiles with lower emotional symptoms, supporting previous findings. The impact on quality of life was significantly more contingent upon specific psychological factors rather than medical or sociodemographic characteristics. Awareness of a given patient's psychological profile may improve shared decision-making and allow for individualization of psychological interventions; for instance, a patient with a limited coping repertoire may benefit from specialized cognitive behavioral therapy. Certain behaviors may also be understood by a corresponding psychological profile, as avoidant coping styles may result in non-adherence to treatment.

One limitation of this study is the use of self-reported instruments. A second limitation includes the underrepresentation of patients with stage IV non-small cell lung cancer. Further elaboration upon the extent of emotional symptoms and coping styles within each profile may be beneficial in understanding and predicting quality of life.

4. Conclusion

Patients with lung cancer who develop a malignancy at young age are likely to harbor a targetable genotype, which is an important and underused biomarker for NSCLC. It is important to fully explore the

nature of the cancer, including mutation types. Our case demonstrates that the detection of the driver gene mutation EGFR and ALK rearrangement could affect treatment and prognosis in this patient population. This has significant value, because young patients with NSCLC have poorer survival rates compared to older patients with NSCLC. Young patients with NSCLC who harbor mutations tend to respond favorably to treatment with increased survival. There are many studies available that highlight targeted therapies for these mutations as well as chemotherapy and radiation. Receiving a diagnosis of lung cancer is difficult at any age but it is exceptionally devastating to young patients. Adjustment disorder, anxiety and depression are commonly seen. The medical staff, including physicians and nurses, have an important role in recognizing emotional difficulties and addressing them.

Depression and anxiety are important predictors of QOL in patients with NSCLC, which has a significant impact on survival. Depression tends to persist beyond the reaction to a new cancer diagnosis. Studies have shown that doctors and nurses often fail to detect emotional distress in patients, who often do not disclose symptoms of depression to their medical team unless asked directly.[44] Our patient presented to our consultation team as Do Not Resuscitate/Do Not Intubate in the context of depression and beyond his new cancer diagnosis. He harbored many symptoms that led to a lower quality of life including pain, lack of motivation due to physical and mental obstacles, and limited social support. As shown in our review, young people with similar diagnoses can survive up to 5 years if offered appropriate treatment. However, our patient passed away before a more targeted therapy could be offered.

Declaration of competing interest

We, the authors of this submitted article, disclose no financial conflict of interests. With respect to the submitted article, there has been no relevant (indirect or direct) financial relationship between the authors (and/or spouse/partner) and any for-profit company in the past 24 months which could be considered a conflict of interest.

Data availability

The authors do not have permission to share data.

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