Small Cell Lung Cancer (SCLC) and Squamous Cell Carcinoma (SCC) of the External Auditory Canal as an Example of Synchronous Cancers – Case Report

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ABSTRACT

Small Cell Lung Cancer (SCLC) and Squamous Cell Carcinoma (SCC) of the External Auditory Canal as an Example of Synchronous Cancers – Case Report

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In recent years, the incidence of malignant tumors, including multiple tumors, has increased. The diagnosis of primary multiple tumors affects between 0.73% and 11.7% of oncology patients. Some patients are diagnosed with synchronous tumors, meaning independent tumor foci are identified within an interval of less than six months. The diagnosis requires histopathological confirmation of the different tumor morphologies and the exclusion of the lesions as metastatic foci. The most frequently diagnosed multiple cancers originate in the head and neck. The diagnosis of a second independent tumor in a patient significantly shortens the five-year survival rate and increases the risk of disease recurrence or the detection of additional primary tumors.

A 66-year-old (now 74-year-old) patient with hearing loss was diagnosed with cancer of the external auditory canal. In oncological diagnostics, it was decided to perform, among other tests, a PET-CT examination to exclude metastatic foci. A metabolically active lesion was visible in the hilum of the left lung and the right adrenal gland. Further diagnostics identified the lesion as an independent tumor in the lung, with the morphology of small cell carcinoma in stage IV, with metastases to the right adrenal gland. In the patient interview, nicotine addiction and chronic obstructive pulmonary disease requiring home oxygen therapy were noted. The patient was treated in accordance with the then NCCN, ESMO, and PTOK guidelines. The lesion in the external auditory canal was resected with an R1 margin.

STRESZCZENIE

Rak drobnokomórkowy płuca (SCLC) i rak kolczystokomórkowy (SCC) przewodu słuchowego zewnętrznego jako przykład nowotworów synchronicznych – opis przypadku

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W ostatnich latach odnotowano wzrost zachorowalności na nowotwory złośliwe, w tym nowotwory mnogie. Rozpoznanie pierwotnych nowotworów mnogich dotyczy od 0.73% aż do 11.7% pacjentów onkologicznych. U części chorych zostały zdiagnozowane jako nowotwory synchroniczne, co oznacza rozpoznanie niezależnych ognisk nowotworowych w odstępie mniejszym niż 6 miesięcy. Do rozpoznania jest wymagane potwierdzenie histopatologiczne odmiennej morfologii nowotworu oraz wykluczenie powiązania zmian jako ognisk przerzutowych. Najczęściej rozpoznawane nowotwory mnogie mają jedno źródło w obrębie głowy i szyi. Rozpoznanie drugiego niezależnego ogniska nowotworu u pacjenta znacznie skraca pięcioletnie przeżycie i powoduje wzrost ryzyka nawrotu choroby lub wykrycia kolejnych ognisk pierwotnych.

U 66-letniej (obecnie 74-letniej) pacjentki diagnozowanej z powodu pogorszenia słuchu rozpoznano nowotwór przewodu słuchowego zewnętrznego. W trakcie diagnostyki onkologicznej zdecydowano o wykonaniu m.in. badania PET-CT celem wykluczenia ognisk przerzutowych. Uwidoczniono aktywną metabolicznie zmianę we wnęce płuca lewego oraz nadnerczu prawym. W trakcie dalszej diagnostyki rozpoznano zmianę jako niezależne ognisko nowotworowe pierwotnie zlokalizowane w płucu o morfologii raka drobnokomórkowego w stadium IV z przerzutem do nadnercza prawego. W wywiadzie pacjentki warto zwrócić uwagę na nikotynizm oraz przewlekłą obturacyjną chorobę płuc wymagającą leczenia tlenoterapią w warunkach

Due to the diagnosis of small cell carcinoma, the patient underwent six cycles of EP chemotherapy (etoposide, cisplatin). The treatment was supplemented with radiotherapy of the lesion in the left lung and planned radiotherapy of the central nervous system (PCI – prophylactic cranial irradiation).
The aim of this study is to emphasize the importance of accurate diagnostics at the initial diagnosis of cancer and to consider the possibility of diagnosing metastatic lesions as second (and subsequent) primary lesions. This is crucial when assessing overall survival (OS) and relapse-free survival (RFS). It is also important to note the difficulties in planning the treatment of two independent cancer sites, which most often requires different therapeutic approaches. A complete response to treatment was achieved on the RECIST scale.

Keywords: *small cell lung cancer, synchronous cancers, multiple primary cancers, squamous cell carcinoma*

domowych. Pacjentka była leczona zgodnie z ówczesnymi wytycznymi NCCN, ESMO, PTOK. Zmianę w przewodzie słuchowym zewnętrznych poddano resekcji z marginesem R1. Ze względu na rozpoznanie nowotworu drobnokomórkowego płuca lewego, pacjentka została poddana chemioterapii w schemacie EP (etopozyd, cisplatyna) w sześciu cyklach. Leczenie uzupełniono radioterapią zmiany w płucu lewym oraz elektywną radioterapią ośrodkowego układu nerwowego (PCI – ang. profilactic cranial irradiation). Uzyskano całkowitą odpowiedź na leczenie w skali RECIST.
Praca ma na celu podkreślenie istotności dokładnej diagnostyki pacjentów przy rozpoznaniu pierwszorazowym nowotworu oraz uwzględnieniu możliwości rozpoznania ognisk przerzutowych jako drugiego (i kolejnego) ogniska pierwotnego. Jest to bardzo ważne przy ocenie przeżycia całkowitego (OS – ang. overall survival) oraz przeżycia bez nawrotu nowotworu (RFS – ang. relapse-free survival). Warto zwrócić uwagę na trudności w planowaniu leczenia dwóch niezależnych ognisk nowotworowych, co najczęściej wymaga planowania odmiennych procesów terapeutycznych.

Słowa kluczowe: *rak drobnokomórkowy, rak kolczystokomórkowy, nowotwory synchroniczne, nowotwory mnogie*

Introduction

In recent years, the incidence of cancer, including primary multiple tumors, has increased. An epidemiological analysis was carried out in 2010. Between 0.73% and 11.7% of oncology patients were diagnosed with secondary neoplasms [1]. Multiple cancers can be diagnosed synchronously or metachronously, depending on the time between the diagnosis of both lesions. The original definition allows for a change detected over a period longer than six months to be considered synchronous. This definition has been clarified—the Surveillance, Epidemiology, and End Results (SEER) program limited this period to two months [2]. In contrast, the International Association of Cancer Registries and the International Agency for Research on Cancer (IACR/IARC) allow for the diagnosis of synchronous disease without time limits [3]. In the 2021 analysis, this definition was averaged to a four-month period [4]. Nevertheless, the primary definition that takes into account an interval of six months is most often used in the literature. A time exceeding this period indicates the diagnosis of metachronous cancer.

An increased tendency for the occurrence of multiple cancer foci has been observed when one of the foci is located in the head and neck. The first primary lesion recognized in such situations is referred to as the index lesion [5]. The main risk factors are mainly exposure to carcinogens, especially tobacco, betel nut, alcohol, and previous cancer treatment [6,7].

However, according to a retrospective study conducted in 2015, 68.0% of patients with multiple primary malignant tumors, where one of the lesions was located in the lungs, had no history of nicotine addiction [8].

This phenomenon raises questions about the influence of other carcinogenic factors. Recently, genetic diagnostics has played an important role in oncological diagnostics. Numerous mutations have been reported to increase the risk of various cancers. In this context, the literature points to the importance of genes such as MLH1, MSH2, MSH6, PMS2, EPCAM, BRCA1, BRCA2, PTEN, TP53, CDH1, and others. It is important to recognize genetic syndromes that increase the risk of cancer, such as Lynch syndrome, MEN1 (multiple endocrine neoplasia type 1), MEN2, Peutz-Jeghers, Li-Fraumeni, and others [9].

To diagnose a synchronous tumor, it is necessary to confirm a different histopathological structure of the subsequent lesion and, if possible, to exclude a link with the primary lesion as a metastatic lesion [3].

Case report

A 66-year-old (currently 74-year-old) female patient with diagnosed hearing loss was referred to the Oncology Department with a diagnosis of squamous cell carcinoma of the external auditory canal on October 14, 2016. The patient is under long-term treatment for chronic obstructive pulmonary disease and requires oxygen therapy at home. During the interview, the patient confirmed her nicotine addiction. She was assessed as ECOG stage 2.

A computed tomography (CT) scan of the head revealed obstruction of the left external auditory canal in the bony section due to pathological thickening of soft tissues on October 19, 2016. Magnetic resonance imaging (MRI) showed contrast enhancement in the walls of the left external auditory canal. There were no signs of infiltration through the temporal bone or penetration of the skull cavities on December 15, 2016.

A biopsy of the lesion was performed on November 10, 2016. Histopathological examination revealed moderately differentiated squamous cell carcinoma (stage G2). The change covered the entire cross-section of the reported, fully examined section. The patient was referred to a specialized center for resection of the lesion. The treatment applied was in line with the then recommendations of NCCN (National Comprehensive Cancer Network), ESMO (European Society of Medical Oncology), and PTOK (Polish Society of Clinical Oncology).

A decision was made to perform a positron emission tomography (PET-CT) examination to exclude metastatic foci on December 17, 2016. The image showed a nodular lesion in the hilum of the left lung (dimensions 16x13 mm; SUV_{max} 6.3), a tumor in the right adrenal gland (dimensions 11x8 mm, SUV_{max} 6.4), and a metabolically inactive nodule in the right lobe of the thyroid gland (12 mm). The presence of a primary lesion located in the lung with metastases to the right adrenal gland was suspected. The patient was referred for further diagnostics.

Diagnostic bronchofiberoscopy with conventional transbronchial aspiration (TBNA) was performed, with a negative biopsy result on December 29, 2016. The examination using endobronchial transbronchial aspiration under ultrasound guidance (EBUS-TBNA) was repeated due to the high risk of obtaining a false negative result in the previous examination on January 23, 2017. As a result of histopathological analysis of the material collected from the station 11L lymph nodes (left interlobar nodes), the presence of metastatic cancer cells resembling small cell carcinoma (Latin: carcinoma microcellulare) was detected. The diagnosis was confirmed by immunohistochemical methods. The preparations were stained positively for the CD 56 antigen and cytokeratin (CK) on the cell surface, partially positively for synaptophysin, and negatively for the CD 45 antigen (LCA – leukocyte common antigen). The diagnosis was made: small cell carcinoma of the left lung, stage IV, due to metastases to the right adrenal gland.

During the diagnostics of the lesion located in the lung, a sleeve resection (with an R1 margin) of the lesion located in the external auditory canal was performed on January 10, 2017. The stage of progression was pT1N0M0 with a grade of G2. Treatment of the lesion in the external auditory canal was completed. It was decided to subject the patient to close observation and start treatment for small cell carcinoma.

Due to the diagnosis of small cell carcinoma, systemic treatment was administered. The patient, in average health condition (assessed on the ECOG scale as grade 2), with a body weight of 51 kg, height of 158 cm, and body surface area (BSA) of 1.5 m², was qualified for six cycles of chemotherapy in the EP regimen (etoposide, cisplatin) at the following doses: cisplatin – 25 mg/m² i.v. on days 1–3 of the cycle and etoposide – 100 mg/m² on days 1–3. The cycle was administered from January 25–27, 2017. Due to the presence of a metastatic lesion, a right adrenalectomy was proposed, but the patient was disqualified from the procedure due to systemic diseases. After the second treatment cycle (February 15–17, 2017), the patient was referred for radiotherapy of the lung tumor area, the affected lymph nodes of the pulmonary hilum of group 11L, and elective areas in the mediastinum. Treatment according to the Turissi regimen was carried out at a dose of 45 Gy in 30 fractions, administered twice a day from February 27 to March 17, 2017. Good, immediate tolerance was achieved. The treatment was complicated by hospitalization due to unspecified pneumonia and concomitant anemia and thrombocytopenia from March 28–31, 2017.

After the third cycle of chemotherapy, elective CNS radiotherapy (PCI) was planned. Treatment was administered with a fractional dose of 2.5 Gy to a total dose of 25 Gy in 10 fractions using X 6 MV photons in 3D from April 3–14, 2017. The patient received treatment in planned doses without interruptions or complications, with good immediate tolerance. The treatment applied was in accordance with the then NCCN, ESMO, and PTOK recommendations.

After the start of the fourth cycle of chemotherapy (April 18–20, 2017), the patient developed symptoms of deep vein thrombosis in the left lower limb. Doppler ultrasound examination of the lower limbs revealed occluded, clot-filled posterior tibial veins in the middle and lower part of the lower leg, with preserved patency in the upper third of the left lower limb on May 4, 2017. Treatment with enoxaparin at a dose of 80 mg subcutaneously was recommended once a day. A follow-up ultrasound examination on May 8, 2017, revealed central recanalization of the posterior tibial veins and an obstruction of one of the lateral veins branching from the posterior tibial vein in the lower third of the lower leg, approximately 20 mm in length. A follow-up ultrasound examination on June 12, 2017, showed patent venous vessels in the lower limbs, without the presence of thrombi.

Chemotherapy ended on June 1, 2017, after the sixth treatment cycle. The patient did not require postponement of subsequent courses; however, after each cycle, complications occurred in the form of drug-induced neutropenia. Filgrastim was prescribed as treatment at a dose of 48 million units once daily by subcutaneous injection for ten consecutive days.

A follow-up PET-CT examination revealed complete regression of the disease on July 17, 2017. This result was confirmed by a computed tomography scan performed six months later on February 14, 2018.

An additional examination of circulating tumor cells was performed on September 25, 2017. Automated microfluorometric imaging analysis of EpCAM (epithelial cell adhesion antigen) showed a slightly increased number of viable, potentially malignant cancer cells circulating in the blood (350 potential cancer cells in 1 ml of EDTA blood).

A year later, a follow-up PET-CT scan was performed using the 18-F-FDG (18F-Fluorodeoxyglucose) tracer on June 8, 2018. A focus of trace activity (SUV_{max} = 1.9; previously 3.1) with a diameter of approximately 10 mm was visible at the border of the bony and cartilaginous parts of the left external auditory canal. A metabolically inactive lesion with a diameter of 9 mm was detected in the right lobe of the thyroid gland. No areas of pathological tracer activity were found in the chest and abdominal cavity, indicating regression of the disease. A complete response to treatment was achieved on the RECIST scale.

The patient was closely monitored, with a recommendation to perform computed tomography of the chest and abdominal cavity every four months and regular ENT examinations every six months.

Three years after achieving disease remission, the patient reported fatigue and significant weight loss lasting for several weeks on March 21, 2020. The patient was referred for echocardiography, which did not reveal any abnormalities on June 8, 2020. Laboratory test results showed anemia and thrombocytopenia, leading to suspicion of bone marrow metastases. However, subsequent, regularly performed laboratory tests did not reveal any abnormalities in blood count.

Since the end of treatment, the patient has undergone additional biochemical and hematological tests, demonstrating a predisposition to episodes of hyponatremia and hypochloremia. It was decided to regularly assess the concentration of adrenocorticotropic hormone, which remained within laboratory limits. Periodically, increased concentrations of NT-proBNP (N-terminal prohormone of brain natriuretic peptide) to values not exceeding 350 pg/ml (normal <250 pg/ml) and D-dimer to 1300 ng/ml were observed. Additionally, decreased concentrations of albumins, including IgG gamma-globulins, were observed several times, with plasma values within the range of 550–650 mg/dl (normal 700–1600 mg/dl), while other classes of antibodies remained normal.

As of the date of publication of this study, no disease recurrence or metastases have been observed. The patient remains under the care of the center in her place of residence. She feels well and functions independently in her daily life.

Table 1. The course of the diagnostic and therapeutic process

Date	Procedure	Annotations
14.10.2016	Consultation at the Oncology Clinic	
19.10.2016	CT of the head	Obstruction of the external auditory canal in the bony section was revealed due to the pathological thickening of soft tissues.
10.11.2016	Histopathological examination of the lesion in the external auditory canal	An image of moderately differentiated squamous cell carcinoma (stage G2) was obtained. The change covered the entire cross-section of the reported, fully examined section.
15.12.2016	Head MRI	An image with increased contrast of the walls of the external auditory canal was obtained. There were no signs of infiltration through the temporal bone or penetration of the skull cavities.
17.12.2016	PET-CT	A nodular lesion was detected in the hilum of the left lung (dimensions 16x13 mm; SUV_{max} 6.3), a tumor in the right adrenal gland (dimensions 11x8 mm, SUV_{max} 6.4) and a nodule in the right lobe of the thyroid gland (12 mm).
29.12.2016	TBNA	The biopsy result was negative – no cancer cells were found.
10.01.2017	Resection of a lesion in the external auditory canal	The procedure was performed with an R1 margin.
23.01.017	EBUS-TBNA	The presence of cancer cells with the morphology of small cell carcinoma (metastases) was demonstrated.
25.01–27.01.2017	I cycle of EP chemotherapy	Good immediate tolerance was achieved, without the need to delay the dose. The cycle was complicated by neutropenia, so filgrastim was prescribed with positive results.
15.–17.02.2017	II cycle of EP chemotherapy	Good immediate tolerance was achieved, without the need to delay the dose. The cycle was complicated by neutropenia, so filgrastim was prescribed with positive results.

Date	Procedure	Annotations
27.02–17.03.2017	Radiotherapy for a left lung tumor	Treatment according to the Turissi regimen was administered at a dose of 45 Gy in 30 fractions twice a day. Good immediate tolerance was achieved.
21.–23.03.2017	III cycle of EP chemotherapy	Good immediate tolerance was achieved, without the need to delay the dose. The cycle was complicated by neutropenia, so filgrastim was prescribed with positive results.
28.03–31.03.2017	Hospitalization at the Department of Lung Diseases	Unspecified pneumonia with concomitant anemia and thrombocytopenia.
3.04–14.04.2017	PCI	Treatment with a fractional dose ranging from 2.5 Gy to a total dose of 25 Gy in 10 fractions using X 6 MV photons in the 3D technique was used. Treatment with the assumed doses was carried out without interruptions and complications, with good immediate tolerance.
18.–20.04.2017	IV cycle of EP chemotherapy	Good immediate tolerance was achieved, without the need to delay the dose. The cycle was complicated by neutropenia, so filgrastim was prescribed with positive results.
4.05.2017	Doppler ultrasound of the lower limbs	Obstruction, clot-filled posterior tibial veins were found in the middle and lower parts of the shin, with preserved patency in the upper third of the shin of the left lower limb.
8.05.2017	Doppler ultrasound of the lower limbs	An image of the central recanalization of the posterior tibial veins and an obstruction of one of the laterals branching from the posterior tibial vein in the lower third of the shin was obtained for a length of approximately 20 mm.
9.–11.05.2017	V cycle of EP chemotherapy	Good immediate tolerance was achieved, without the need to delay the dose. The cycle was complicated by neutropenia, so filgrastim was prescribed with positive results.
30.05–1.06.2017	VI cycle of EP chemotherapy	Good immediate tolerance was achieved, without delays, with a dose reduction of 25% due to concomitant thrombosis of the veins of the left lower leg. The cycle was complicated by neutropenia, and the use of filgrastim was prescribed with positive results.
12.06.2017	Doppler ultrasound of the lower limbs	Patent veins of the lower limbs are visible, without the presence of thrombi.
17.07.2017	PET-CT	A focus of trace metabolic activity was visualized on the border of the cartilaginous and bony parts of the left external auditory canal, with no pathological activity of the tracer in the chest and abdominal cavity.
25.09.2017	Examination of circulating tumor cells	Automated microfluorometric imaging analysis of EpCAM (epithelial cell adhesion antigen) showed a slightly increased number of viable, potentially malignant tumor cells circulating in the blood. The presence of 350 potential cancer cells in 1 ml of EDTA blood was demonstrated.
21.11.2017	Chest CT	There were no signs of disease recurrence.
14.02.2018	Chest CT	There were no signs of disease recurrence.
8.06.2018	PET-CT	No pathological metabolic activity in the area of the left external auditory canal. No metabolic trace of recurrence or metastases.
18.06.2019	Chest CT	No signs of disease recurrence.
21.03.2020	Consultation at the Oncology Clinic	Weight loss and weakness for several weeks. Laboratory tests revealed anemia and thrombocytopenia.
8.06.2020	Echocardiographic examination	No significant deviations were detected.
29.09.2021	Laboratory tests	No significant abnormalities. No bone marrow metastases were detected.
05.05.2022	Laboratory tests	No significant abnormalities. No bone marrow metastases were detected.
20.04.2023	Chest, Abdominal and Pelvic CT	No signs of disease recurrence.
21.02.2024	Chest, Abdominal and Pelvic CT	No signs of disease recurrence.
17.02.2024	Head MRI	No signs of disease recurrence.

Discussion

Malignant tumors of the external auditory canal are rare, with an incidence of approximately 1–6 persons per 1,000,000 people. Middle ear lesions are mainly squamous cell carcinomas [10].

Treatment of the limited form (stage T1) includes sleeve resection of the lesion and close monitoring. Lesions infiltrating adjacent structures (in stages T2-T4) and those with R1 or R2 resection margins require postoperative radiotherapy (RTH). Chemoradiotherapy is the recommended treatment method for patients with unresectable lesions (stage III and IV) [11,12] It is routinely recommended to use cisplatin at a dose of 100 mg/m² on the 1st, 22nd, and 43rd day of irradiation or at a dose of 35–40 mg/m² administered once a week [13,14].

This type of cancer has a relatively good prognosis and a high five-year survival rate. In patients with stage I or II, this percentage ranges from 85% to 100%. Stage III tumors have a lower survival rate – 50% to 68.8%, and stage IV tumors – only 19.6% to 30%. The best treatment results are achieved in patients after radical surgical resection with adjuvant postoperative radiotherapy [10].

In this case, one of the two primary lesions was cancer of the external auditory canal. Finally, the second lesion was diagnosed, located in the hilum of the left lung. According to the report of the National Cancer Registry for 2020, in Poland, 31 men and 10 women were diagnosed with D02 (middle ear cancer in situ and respiratory system). At the same time, no deaths were recorded in this group [15].

It is worth noting that among many cancer diagnoses, one of the foci is most often located in the head and neck area [14]. In the case described above, the patient was also diagnosed with small cell lung cancer, which accounts for approximately 15% of lung cancer cases. It is characterized by rapid growth and unfavorable prognosis. Median survival in this group of patients is 7 to 11 months. This shows how unprecedented it is to achieve complete remission in a patient with stage IV disease. However, the patient is in good condition eight years after diagnosis. It is estimated that only 1% of patients survive five years after diagnosis [16,17].

Treatment for small cell carcinoma mainly involves chemotherapy (CTH) combined with radiotherapy. The regimen of choice is the combination of cisplatin with etoposide in the EP regimen in various modifications (e.g., cisplatin at a dose of 80 mg/m² on day 1 or 30 mg/m² on days 1, 2, and 3 and etoposide at a dose of 100 mg/m² on days 1, 2, and 3) in cycles every 21 days. Additionally, in stage IV disease, immunotherapy with atezolizumab is recommended. In patients with limited disease progression (stages I-III in the TNM classification), the treatment that offers the greatest chance of cure or long-term remission is chemoradiotherapy (CRTH). It is recommended to start radiotherapy together with the initiation of systemic treatment or, if this is not possible, by the second chemotherapy cycle. Treatment with conventional fractionated RTH (60–66 Gy in 30–33 fractions) or hyperfractionated RTH (45 Gy in 2 fractions of 1.5 Gy daily for 3 weeks with a minimum interval between fractions of 6 hours) is recommended. Additionally, all patients are recommended scheduled prophylactic cranial irradiation to minimize the risk of brain metastases. Surgical treatment is used in <5% of cases [17,18,19]. Additionally, the NCCN recommendations recommend the use of durvalumab in combination with etoposide and carboplatin or cisplatin as the preferred first-line systemic treatment option, followed by maintenance treatment with durvalumab in patients with advanced disease [20]. The preferred regimens for extensive-stage SCLC may also include atezolizumab, which may improve overall survival and progression-free survival compared to chemotherapy alone [20,21,22]. Currently, numerous clinical trials are being conducted using monoclonal antibodies and new molecules in the treatment of small cell lung cancer. Research is underway to assess the effectiveness of, among others, trilaciclib, cosibelimab, taladegib, pembrolizumab, as well as TAK-243 molecules or BMS 986012 immunoglobulin in combination with nivolumab [22,23,24,25,26,27,28,29,30]. Talazoparib and temozolomide in combination with olaparib have shown promising efficacy in early phase studies [21,29]. Some of the studies were successful. The CASPIAN study demonstrated the effectiveness of durvalumab in the treatment of small cell lung cancer, showing, among other things, a three-fold increase in overall survival (OS) [31]. Based on these conclusions, durvalumab was included in the primary treatment of extensive-stage SCLC [20].

Cases of synchronous and metachronous cancers have been described in the literature. The authors of these texts draw attention to the need for thorough clinical assessment and extensive diagnostics using modern technologies. They emphasize the importance of follow-up examinations and close observation after radical treatment of patients [14,32]. It is also important to remember genetic diagnosis because some synchronous cancers have their origins in syndromes predisposing to cancer [9].

The diagnosis of a second independent tumor in a patient significantly shortens five-year survival and increases the risk of disease recurrence or detection of additional primary tumors. The median survival of patients with synchronous cancer (diagnosis of another neoplasm within 60 days) is 13.5 months (95% CI 7.1–

19.9 months). The median survival of patients with metachronous cancer (time from diagnosis of the second neoplasm exceeds 60 days) is 3.2 months (95% CI 0.0–9.8 months) [33]. Survival time from diagnosis also depends on the type of cancer diagnosed [34].

The above case report describes a patient who has been in remission for eight years after being diagnosed with multiple primary cancers. The survival time from diagnosis differs significantly from the average in this group of patients.

In the described situation, the challenge is to plan simultaneous treatment for a patient diagnosed with two cancers requiring completely different therapeutic procedures. Patients in remission and those undergoing treatment also require further close monitoring, including regular imaging tests, because in this group of patients the risk of developing cancer again increases significantly. It is estimated that approximately 16% of patients who have completed oncological treatment will develop a second, independent, primary cancer. However, the diagnosis of the third and subsequent primary tumor site is much less common in clinical practice [35,36].

Conclusions

despite the increase in incidence in recent years, synchronous and metachronous cancers are still rare in clinical practice. The aim of the study is to emphasize the importance of precise, thorough diagnostics of patients at the first diagnosis of cancer and to consider the possibility of diagnosing metastatic foci as a second (and subsequent) primary lesion. This is crucial when assessing overall survival (OS) and recurrence-free survival (RFS). It is important to pay attention to the difficulties in planning the treatment of two independent cancer sites, which most often requires different therapeutic approaches. Regardless of the diagnosis, an individual approach to the patient should be maintained, considering the possibility of an atypical course of the disease. The work also highlights the importance of using personalized medicine and a holistic approach to the patient.

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