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# Neurological hospitalizations of patients with a history of past or present malignancy — an observational study from a tertiary neurology center

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## ABSTRACT

**Introduction.** Cancer and its treatment are causing a wide range of neurological complications. Current epidemiological studies on neurological hospitalizations in patients with history of malignancy and active cancer (AC) are lacking. The aim of the study was to assess the numbers and clinical profiles of patients with history of malignancy and AC among patients hospitalized in neurological departments of the University Hospital in Kraków, Poland.

**Material and methods.** Medical files of all patients who were treated in neurological departments of the University Hospital in Kraków, Poland, from January 2022 to March 2024 were reviewed. Included were patients with a confirmed history of past or present malignancy. The profile of malignancies and reasons for neurological hospitalizations were analyzed.

**Results.** Among all patients hospitalized in the neurological departments 10.5% had a history of past or present malignancy and 4.9% had AC. The profile of malignancies and reasons for neurological hospitalizations differed among patients with AC and non-active malignancies. In 30.7% of AC the diagnosis of cancer was made (or the diagnostic process started) during hospitalization in the neurological department.

**Conclusions.** Neurological complications of cancer and its treatment are very common in everyday practice of neurohospitalists and require multidisciplinary care, as well as good cooperation between oncologists and neurologists.

**Keywords:** cancer, malignancy, neurological complications of cancer, neurooncology

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## Introduction

The global burden of cancer is high. According to current statistics, cancer occurs in approximately 20% of all people during their lifetime and is one of the major causes of death worldwide [1]. At the same time, cancer mortality rates have been declining in the recent years [2], therefore more patients are expected to live to see the long-term complications of cancer treatments.

Neurological complications of cancer are well known, and they include direct nervous system infiltration by primary tumors [3] or metastases [4], indirect damage caused by paraneoplastic syndromes [5] or cerebrovascular events induced by the cancer-associated hypercoagulable state [6]. Cancer treatment may also cause adverse effects to the nervous system [7], examples being peripheral neuropathy caused by some types of chemotherapy, cognitive dysfunction as an

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effect of brain radiation [8], autoimmune neurological diseases (such as encephalitis or myasthenia gravis) in patients treated with immune checkpoint inhibitors [9] or possible neurotoxicity of new targeted chemotherapy agents [10] as well as some hormonal therapies [11]. Dealing with neurological complications of cancer and its treatment is a substantial part of everyday work by neurologists.

At the same time current epidemiological studies on rates and causes of neurological hospitalizations in patients with a history of cancer or active cancer are lacking. Therefore, the aim of the present study was an attempt to quantify the scale of the problem and gather basic epidemiological data on neurological hospitalizations of patients with past or active malignancies.

## Material and methods

In this retrospective, observational study medical files of all patients who were hospitalized in neurological departments of the University Hospital in Kraków, Poland (General Neurology and Stroke Unit, 48 beds in total) from January 2022 to March 2024 were analyzed. Inclusion criteria were:

1) confirmed diagnosis of a malignancy in patient's previous medical documentation;
2) diagnosis of a malignancy made during hospitalization;
3) malignancy suspected during hospitalization and confirmed later (i.e. during another hospitalization or in the outpatient clinics of the documented hospital).

Patients with incomplete previous medical documentation and those in whom further cancer evaluation was performed in another center and who were therefore lost to follow-up were excluded.

From the medical files of the included patients, information was collected about their age, biological sex, primary location of the malignancy, the presence of any metastases and their location, and their malignancy status. Patients with active cancer (AC) were defined as those currently undergoing any type of cancer treatment, being in the process of qualification for it, or having chosen to deny it, or presenting signs of cancer recurrence in auxiliary testing. The reasons for hospitalization in a neurological department were noted and it was assessed if the reason for hospitalization was most likely directly linked to cancer or its treatment.

The abovementioned data was gathered in a database and analyzed using SPSS Imago Pro 9.0 software. The whole group of patients who had a history of past or present malignancy was analyzed and separate analyses of the subgroups of patients with active (AC) and non-active cancer (non-AC) were made. Categorical data is presented as counts and percentages [n (%)] and continuous data as median and interquartile range [median (IQR)], as the data distribution was not normal which was tested using Kolmogorov-Smirnov test. Continuous data was compared using the U-Mann Whitney test and categorical data using the Chi-square test, with $p < 0.05$ considered statistically significant.

The study was performed in accordance with the Declaration of Helsinki and had a positive opinion of Jagiellonian University Medical College Ethics in Research Committee (decision number 118.0043.1.233.2024 dated 20.06.2024). Financial support is provided by Jagiellonian University Medical College grant (N41/DBS/001270).

## Results

During the analyzed period (January 2022 to March 2024; 27 months) there were 4027 patients hospitalized in neurological departments of the hospital, of whom 422 (10.5%) had a confirmed history of (past or present) malignancy. Active cancer (AC) was found in 199 patients (47.2% of all patients with a history of malignancy and 4.9% of all patients hospitalized in neurological departments). Each month approximately 15–16 people were hospitalized with a history of malignancy including 7–8 AC patients. Patients were almost equally divided between the Stroke Unit, 209 (49.5%), and General Neurology, 213 (50.5%). They were aged 23–93 with a median age of 69 years (IQR 63–77). There was a very slight predominance of female sex, 227 (53.8%). A direct link between cancer or its treatment and the reason for neurological hospitalization were identified in at least 110 (26.1%) of all patients including 97 patients with AC (48.7%).

In the group of all patients with a history of past or present malignancy the most common neoplasms were breast cancer, 56 (13.3%), prostate cancer 51 (12.1%), and colon cancer 49 (11.6%). Each of them separately was more common than primary central nervous system (CNS) tumors, 44 (10.4%). 260 patients (61.6%) had previously been treated with surgical procedures, 124 (29.4%) with chemotherapy, 117 (27.7%) with radiotherapy, 38 (9.0%) with hormonal therapy, and 17 (4.0%) with immunotherapy and/or hematopoietic stem cell transplant (HSCT). The most common reasons for neurological hospitalization were acute ischemic stroke or transient ischemic attack (TIA) 210 (49.8%), epileptic seizures 42 (10.0%), and presence of focal CNS lesions 34 (8.1%).

In 2 patients an assessment of whether the cancer was active or not was not possible. 199 AC patients compared to 221 patients not fulfilling AC definition (non-AC), were significantly younger, with a median age of 68 (IQR 62–76) *vs*. 70 years (IQR 64–79), $p = 0.047$. There were no differences in biological sex distribution.

Active cancer patients were most commonly diagnosed with primary CNS tumors 37 (18.6%), lung cancer 31 (15.6%), and hematological malignancies 26 (13.1%). Seventy-nine (39.7%) had been previously treated with surgery, 76 (38.2%) with chemotherapy, 47 (23.6%) with radiotherapy, 16 (8.0%) with hormonal therapy and 11 (5.5%) with immunotherapy, and/or HSCT. The most common reasons for neurological hospitalization were: acute ischemic stroke or TIA 73 (36.7%) and, ex aequo, epileptic seizures, and the presence of focal CNS lesions 33 (16.6%).

Non-AC patients most commonly had a history of breast cancer 36 (16.3%), colon cancer 31 (14.0%), and prostate cancer 30 (13.6%). They had mostly undergone surgical treatment 180 (81.4%), followed by radiotherapy 70 (31.7%), chemotherapy 47 (21.3%), hormonal therapy 17 (7.7%), and immunotherapy/HSCT 6 (2.7%). The most common reasons for neurological hospitalization in this group were stroke/TIA 135 (61.1%), followed by neuropathies 15 (6.8%) and epileptic seizures 9 (4.1%).

The group characteristics are summarized in Table 1.

Cancer was metastatic in 97 of all patients (23.0%) including 84 AC patients (42.2%). Brain metastases were found in 26 patients (6.2% of the whole group) — 7 patients with lung cancer (26.9%), 5 with breast cancer (19.2%), 3 with melanoma and kidney cancer (11.5% each), 2 with endometrial cancer and hematological malignancies (7.7% each), and 1 with stomach cancer, esophageal cancer and ovarian cancer (3.8% each). Leptomeningeal metastases were found in 8 patients (1.9% of the whole group) — half of them had breast cancer and the others had lung cancer, endometrial cancer, melanoma, and stomach cancer.

In 61 cases (14.5% of all patients and 30.7% of AC patients), the malignancy was either diagnosed during hospitalization in a neurological department or a neurologists referred the patient for a further oncological evaluation that turned out positive. Those patients were mostly admitted to neurology due to acute ischemic stroke or TIA 16 (26.2%), differential diagnosis of focal CNS lesions 13 (21.3%), and epileptic seizures 7 (11.5%). The most commonly found malignancies were primary CNS tumors 22 (36.1%), lung cancer 14 (23.0%), and hematological malignancies 8 (13.1%). Detailed information on this subgroup is shown in Table 2.

## Discussion

The results of the present study show that neurological complications of cancer and its treatment represent a very common problem among patients hospitalized in neurological wards. Almost 1 in every 20 patients hospitalized in the neurological departments had active cancer. In almost one third of AC patients the diagnosis of malignancy was made (or the diagnostic process was started) during hospitalization in the neurological department.

The types of malignancies most commonly found in the whole study group as well as the non-AC subgroup (breast, prostate, and colorectal cancer), are also among the malignancies most commonly diagnosed in the Polish population in general (which are prostate, lung and colorectal cancer in males and breast, lung and colorectal cancer in females) [12]. The profile of malignancies among AC patients was different. Primary CNS tumors (18.6%) were causing mainly neurological symptoms. Lung cancer most commonly causes brain metastases as a neurological complication [13] but it is also the type of cancer most commonly causing neurological paraneoplastic syndromes [14]. Neurological complications are reported to occur in almost 20% of hematological malignancies and most commonly are a result of direct infiltration of the CNS or peripheral nerves [15].

The reasons for neurological hospitalizations also differed between the subgroups of AC and non-AC patients. Although in all groups the most common cause for hospitalization was acute ischemic stroke (AIS)/ /TIA, its incidence was much higher in non-AC subgroup (61.1%) than AC subgroup (36.7%). Acute ischemic stroke may be caused by a cancer-associated hypercoagulable state but may also result from adverse effects of the therapies, such as post-radiation vasculopathy [6], or the use of some chemotherapeutics including 5-fluorouracil, gemcitabine, bleomycin and cisplatin [16]. Studies on stroke in patients with active cancer show that it is associated with higher recurrence rate and mortality [17]. Epileptic seizures were also a common cause for hospitalization (16.6% of the AC subgroup and 4.1% of the non-AC subgroup). The occurrence of epilepsy in cancer patients depends on the type and location of the tumor and/or metastases, but apart from direct infiltration of CNS by the malignancy, seizures may also be caused by concomitant stroke, infections, metabolic disturbances or treatment with chemo- and radiotherapy [18]. Seizures caused by drug toxicity usually occur early after chemotherapeutic administration and most often when high doses are used or in patients with concomitant renal or hepatic failure [19]. In the AC group a common cause for hospitalization (16.6%) was the need for differential diagnosis of focal CNS lesions — for obvious reasons. In the non-AC group neuropathies were common (6.8%) — peripheral neuropathy is a well-known adverse effect of many chemotherapeutics, occurring in about 30–40% patients treated with neurotoxic chemotherapy, such as platinum or taxanes [20]. It is worth noting that toxicity to the nervous system

**Table 1. Localization of primary malignancies and reasons for neurological hospitalizations in patients with any history of malignancy, active cancer (AC) and non-active cancer (non-AC)**

| | Patients with any history of malignancy | | AC patients | | Non-AC patients | |
|---|---|---|---|---|---|---|
| | n = 422 | | n = 199 | | n = 221 | |
| Location of primary malignancy | Breast | 56 (13.3%) | CNS | 37 (18.6%) | Breast | 37 (16.7%) |
| | Prostate | 51 (12.1%) | Lung | 31 (15.6%) | Colon | 31 (14.0%) |
| | Colon | 49 (11.6%) | Hematological malignancies | 26 (13.1%) | Prostate | 30 (13.6%) |
| | CNS | 44 (10.4%) | Prostate | 22 (11.1%) | Bladder | 14 (6,3%) |
| | Hematological malignancies | 40 (9.5%) | Breast | 19 (9.5%) | Endometrium | 13 (5.9%) |
| | Lung | 38 (9.0%) | Colon | 18 (9.0%) | Skin malignancies | 13 (5.9%) |
| | Bladder | 23 (5.5%) | Kidney | 9 (4.5%) | Hematological malignancies | 13 (5.9%) |
| | Endometrium | 20 (4.7%) | Pancreas | 9 (4.5%) | Kidney | 11 (5.0%) |
| | Kidney | 20 (4.7%) | Bladder | 8 (4.0%) | Cervix | 10 (4.5%) |
| | Skin malignancies | 18 (4.3%) | Endometrium | 7 (3.5%) | Thyroid | 10 (4.5%) |
| | Stomach/esophagus | 14 (3.3%) | Stomach/ /esophagus | 7 (3.5%) | Lung | 7 (3.2%) |
| | Cervix | 13 (3.1%) | Ovary | 5 (2.5%) | CNS | 7 (3.2%) |
| | Pancreas | 12 (2.8%) | Skin malignancies | 5 (2.5%) | Stomach/esophagus | 7 (3.2%) |
| | Thyroid | 10 (2.4%) | Cervix | 3 (1.5%) | Head and neck | 6 (2.7%) |
| | Ovary | 9 (2.1%) | Biliary ducts | 2 (1.0%) | Larynx | 5 (2.3%) |
| | Larynx | 6 (1.4%) | Unknown | 2 (1.0%) | Ovary | 4 (1.8%) |
| | Head and neck | 6 (1.4%) | Larynx | 1 (0.5%) | Pancreas | 3 (1.3%) |
| | Biliary ducts | 3 (0.7%) | Liver | 1 (0.5%) | Small intestine | 2 (0.9%) |
| | Liver | 2 (0.5% | Thymus | 1 (0.5%) | Testes | 1 (0.5%) |
| | Thymus | 2 (0.5%) | Paraganglioma | 1 (0.5%) | Liver | 1 (0.5%) |
| | Small intestine | 2 (0.5%) | Sarcoma | 1 (0.5%) | Biliary ducts | 1 (0.5%) |
| | Unknown | 2 (0.5%) | | | Thymus | 1 (0.5%) |
| | Sarcoma | 2 (0.5%) | | | Adrenal glands | 1 (0.5%) |
| | Testes | 1 (0.2%) | | | Sarcoma | 1 (0.5%) |
| | Adrenal glands | 1 (0.2%) | | | | |
| | Paraganglioma | 1 (0.2%) | | | | |
| Reasons for neurological hospitalization | AIS/TIA | 210 (49.7%) | AIS/TIA | 73 (36.7%) | AIS/TIA | 135 (61.1%) |
| | Epileptic seizures | 42 (10.0%) | Epileptic seizures | 33 (16.6%) | Neuropathies | 15 (6.8%) |
| | Focal CNS lesions | 34 (8.1%) | Focal CNS lesions | 33 (16.6%) | Epileptic seizures | 9 (4.1%) |
| | Neuropathies | 25 (5.9%) | Neuropathies | 10 (5.0%) | Intracerebral hemorrhage | 8 (3.6%) |
| | ICH | 12 (2.8%) | Acute spinal cord syndrome | 7 (3.5%) | Headache | 7 (3.2%) |
| | Headache | 11 (2.6%) | Cognitive decline | 5 (2.5%) | TGA | 6 (2.7%) |
| | Demyelinating dis | 8 (1.9%) | Intracerebral hemorrhage | 4 (2.0%) | Demyelinating diseases | 5 (2.3%) |
| | Vertigo | 8 (1.9%) | Vertigo | 4 (2.0%) | Myopathy | 5 (2.3%) |
| | Neuromuscular junction dis. | 8 (1.9%) | Headache | 4 (2.0%) | Neuromuscular junction diseases | 5 (2.3%) |

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**Table 1 cont. Localization of primary malignancies and reasons for neurological hospitalizations in patients with any history of malignancy, active cancer (AC) and non-active cancer (non-AC)**

| | Patients with any history of malignancy | | AC patients | | Non-AC patients | |
|---|---|---|---|---|---|---|
| | n = 422 | | n = 199 | | n = 221 | |
| Reasons for neurological hospitalization | Cognitive decline | 7 (1.7%) | General medicine problems | 4 (2.0%) | Movement disorders | 5 (2.3%) |
| | TGA | 7 (1.7%) | Autoimmune encephalitis | 3 (1.5%) | Vertigo | 4 (1.8%) |
| | Acute spinal cord syndrome | 7 (1.7%) | Demyelinating diseases | 3 (1.5%) | Functional disorders | 4 (1.8%) |
| | Myopathy | 6 (1.4%) | Radiculopathy | 3 (1.5%) | CNS trauma | 3 (1.3%) |
| | Movement disorders | 5 (1.2%) | Neuromuscular junction diseases | 3 (1.5%) | Cognitive decline | 2 (0.9%) |
| | Radiculopathy | 4 (0.9%) | Disturbance of consciousness | 3 (1.5%) | ALS | 2 (0.9%) |
| | Disturbance of consciousness | 4 (0.9%) | Cerebral venous thrombosis | 2 (1.0%) | Cerebellar syndrome | 2 (0.9%) |
| | Cerebellar syndrome | 4 (0.9%) | Cerebellar syndrome | 2 (1.0%) | Cerebral venous thrombosis | 1 (0.5%) |
| | General medicine problems | 4 (0.9%) | Myopathy | 1 (0.5%) | Radiculopathy | 1 (0.5%) |
| | Functional disorders | 4 (0.9%) | TGA | 1 (0.5%) | Focal CNS lesions | 1 (0.5%) |
| | Cerebral venous thrombosis | 3 (0.7%) | ALS | 1 (0.5%) | Vasculitis | 1 (0.5%) |
| | Autoimmune encephalitis | 3 (0.7%) | Vasculitis | 1 (0.5%) | Disturbance of consciousness | 1 (0.5%) |
| | CNS trauma | 3 (0.7%) | Neuroinfection | 1 (0.5%) | | |
| | ALS | 3 (0.7%) | | | | |
| | Vasculitis | 2 (0.5%) | | | | |
| | Neuroinfection | 1 (0.2%) | | | | |

AIS — acute ischemic stroke; ALS — amyotrophic lateral sclerosis; CNS — central nervous system; ICH — intracerebral haemorrhage; TGA — transient global amnesia; TIA — transient ischemic attack

(peripheral and/or central) is the second most common dose-limiting complication of systemic chemotherapy [7].

Neurological complications of cancer and its treatment may negatively impact the patients' quality of life, cause severe disability or may even be fatal. Oncologists should routinely check for the presence of neurological symptoms in their patients and, if needed, promptly refer them to neurology. The cooperation between the two specialties is also important because neurological and oncological treatments can influence one another, an example being possible interactions between antiepileptic medications and chemotherapy [21]. It is also worth noting that in some cases the sole presence of an atypical manifestation of a neurological disorder may lead to a diagnosis of a previously unknown cancer. For example, in a patient with multi-territorial acute ischemic stroke, having no conventional stroke risk factors and presenting features of hypercoagulation (such as elevated D-dimer level), cancer screening should be considered, as these are typical features of cancer-related stroke (CRS) caused by malignancy-associated hypercoagulability [22].

The single-center character of this study is an important limitation of the observations and more data from other centers is needed to confirm the scale of the problem. That being said, many patients were not included in the present study as their past medical documentation was incomplete or follow-up not available, therefore results that consider the numbers of cancer patients hospitalized in the neurology wards are most likely underestimated. Another limitation is that the association between cancer or its treatment and the cause for neurological hospitalization was not

**Table 2. Patients diagnosed with malignancy during their hospitalization in the neurological department or referred for further cancer evaluation by neurologists**

| Causes of hospitalization | | Types of malignancies found | |
|---|---|---|---|
| AIS/TIA | 16 (26.2%) | CNS primary tumors | 22 (36.1%) |
| Focal CNS lesions | 13 (21.3%) | Lung cancer | 14 (23.0%) |
| Epileptic seizures | 7 (11.5%) | Hematological malignancies | 8 (13.1%) |
| Acute spinal cord injury | 5 (8.2%) | Prostate cancer | 5 (8.2%) |
| Cognitive decline | 4 (6.6%) | Colon cancer | 4 (6.6%) |
| Autoimmune encephalitis | 3 (4.9%) | Bladder cancer | 2 (3.3%) |
| Headache | 3 (4.9%) | Pancreatic cancer | 2 (3.3%) |
| Neuropathies | 2 (3.3%) | Breast cancer | 1 (1.6%) |
| Demyelinating diseases | 2 (3.3%) | Ovarian cancer | 1 (1.6%) |
| Vertigo | 2 (3.3%) | Skin malignancies | 1 (1.6%) |
| ICH | 2 (3.3%) | Thymoma | 1 (1.6%) |
| Radiculopathy | 1 (1.6%) | | |
| Neuromuscular junction dis. | 1 (1.6%) | | |
| General medicine | 1 (1.6%) | | |
| Vasculitis | 1 (1.6%) | | |

AIS — acute ischemic stroke; CNS — central nervous system; ICH — intracerebral haemorrhage; TIA — transient ischemic attack

always possible to assess retrospectively, so the number of hospitalizations directly linked to cancer (26.1% in the present group, including 48.7% of AC patients) is also most likely underrated.

## Conclusions

In Poland neurooncology is not an independent medical specialty. Patients with nervous system tumors or metastases as well as neurological complications of cancer treatment should be taken care of by interdisciplinary teams consisting of neurologists, oncologists, neurosurgeons and/or radiotherapists. Neurologists should be educated in many aspects of oncology, because, as the current study confirms, neurological complications of cancer and its treatment are a common problem in everyday practice of neurohospitalists. It is worth noting that in almost one in three AC patients, the cancer diagnosis started in neurological department, so oncological vigilance among neurologists is needed. Oncologists should pay attention to neurological symptoms present in their patients, as they may suggest serious and sometimes even possibly life-threatening complications of cancer. A prompt referral to neurology is crucial. Moreover, there are possible interactions between neurological and oncological treatments. A careful cooperation between the two specialties is needed.

## Article Information and Declarations

### Data availability statement

Data confirming the results of the study is available from the corresponding author upon reasonable request.

### Ethics statement

The study was performed in accordance with the Declaration of Helsinki and had a positive opinion of Jagiellonian University Medical College Ethics in Research Committee (decision number 118.0043.1.233.2024 dated 20.06.2024).

### Author contributions

K.S.: conceptualisation, data aquisition, draft writing and editing; M.D., T.H., M.S.B.: conceptualisation, data acquisition; A.B., J.Jóźwik, K.Z.: data acquisition; J.Jagiełła: data acquisition, draft editing; A.S.: conceptualisation, draft editing, supervision.

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## Conflict of interest

The authors declare no conflict of interest.

## Supplementary material

None.

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