Prevalence of neurological symptoms in palliative care cancer patients: A retrospective study

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Abstract

Background: This study aims to investigate the prevalence of neurological symptoms in cancer patients followed up in a palliative care centre and the relation of these symptoms to the diagnosis, length of stay, discharge status and presence of metastasis. *Methods:* The records of inpatients with cancer diagnosed in a palliative care centre in Ankara, Turkey were retrospectively reviewed. The neurological symptoms observed in patients were classified as pain, insomnia, seizures, paresis, delirium and depression. Age, gender, length of stay, presence of metastasis, discharge status and diagnosis of patients who were included in the study were compared to the symptoms. *Results:* The mean age of 192 patients was 68.41 ± 14.15 years and length of stay in the Centre was 18.12 ± 17.64 days. The most common neurological symptoms were pain, insomnia, delirium, seizures, depression and paresis (27.1%, 17.2%, 15.1%, 13.5%, 11.5%) respectively. Pain was most commonly observed in genitourinary and gynecologic cancers (72.4%), and gastrointestinal cancers (69.3%). Pain was significantly higher in patients with metastasis ($p < 0.005$) and patients who have passed away ($p < 0.032$). Paresis and seizures were significantly higher in patients with head and neck cancers ($p < 0.001$ and 0.001, respectively). The number of days under palliative care was significantly higher in patients who were diagnosed with head and neck cancers ($p < 0.007$) and patients who experienced seizures ($p < 0.004$).
Conclusion: Except for pain, the other neurological symptoms were not as prevalent as the non-neurological symptoms such as breathlessness, nausea and vomiting, fatigue, anorexia and constipation as reported in the literature.

Keywords: Cancer, neurological symptoms, palliative care

INTRODUCTION

With the extension of the human lifespan, increases are observed in the prevalence of cancers as in all chronic diseases. Studies suggested that the number of cancer patients increases by 25% every decade, reaching 16 million deaths due to cancer by year 2050.[1,2] Cancer patients experience many difficult-to-control symptoms in the course of the disease, after treatment and during terminal phase.[3] At present, integration with palliative care is recommended in the treatment of cancer patients starting from the early stage.[4]

The central and peripheral nervous systems are highly sensitive to cancer and its treatment. Cancer and cancer treatment may result in serious neurological morbidity and mortality as it affects the nervous system.[5] The control of the manifested symptoms is an important part of palliative care, and studies showed that the quality of life decreases with the increases in the number and severity of symptoms in cancer patients.[6,7]

Neurological symptoms observed in cancer patients change the treatment compliance, course of disease and mortality rates[8,9] and there is a limited number of studies about the neurological symptoms of cancer patients followed up under palliative care.[10,11] We think that the determination of the relation between cancer and neurological symptoms will provide benefits in estimating, taking measures against and controlling problems by focusing on commonly manifested symptoms. The purpose of this study is to investigate the prevalence of neurological symptoms in cancer patients followed up under palliative care and the relation of these symptoms to the diagnosis, hospitalisation period, discharge status and presence of metastasis.

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METHODS

This study was approved by the Ankara Numune Training and Research Hospital Ethics Committee (dated 04.10.2018 and approval no. E-18-2238). All procedures were applied in accordance with the principles of the Declaration of Helsinki. The records of 239 patients who were hospitalised in the Ulus State Hospital palliative care centre (PCC), Ankara, Turkey between January 1, 2016 and November 31, 2018 were reviewed retrospectively. All patients in our study consisted of inpatient palliative care in PCC. Patients who were deficient in the patient file records, who had a hospitalisation period of less than 2 days, and who did not have a sufficient number of cancer diagnoses were excluded from the study.

Patients were diagnosed with head and neck cancers, lung cancer, breast cancer, gastrointestinal system (GIS) cancers, genitourinary system (GUS) + gynecologic cancers and other cancers (leukaemia, lymphoma, skin cancer, etc). As there were four patients in the diagnosis group under other cancers, this group was not included in the statistical assessment. The neurological symptoms observed in patients were classified as pain, insomnia, seizures, paresis, delirium and depression. Patients whose symptoms were determined in the results of neurological and psychiatric consultation evaluations and who have started treatment for these symptoms were included in the study. Age, gender, length of stay in PCC, presence of metastasis, discharge status and diagnosis of patients who were included in the study were compared to the symptoms.

Patients who were estimated to have depression were diagnosed by psychiatrists using the criteria obtained from the classification of psychiatric disorders according to the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition*.[12] Delirium was determined using the 'Confusion Assessment Method' survey.[13] Meanwhile, insomnia was determined with the help of the Athens Insomnia Scale[14], which consisted of eight items, and each item was evaluated in a 0 to 3 scale (0 = no problem and 3 = very serious problem). A total of these eight items varied between 0 and 24 points, and 6 or more points were evaluated as sleeping disorder.

Data obtained from this study were analysed using the IBM SPSS Statistics version 22 packaged software. While investigating the normal distribution of variables, Shapiro Wilk's was used depending on the unit number. While interpreting the results, 0.05 was used as the threshold level for significance; $p < 0.05$ indicated that variables did not have normal distribution, whereas $p > 0.05$ values indicated that variables had normal distribution. While reviewing the differences among the groups, Mann-Whitney U and Kruskal-Wallis H tests were used for non-normal distribution. After determining the significant difference in Kruskal-Wallis H test, post hoc multiple comparison test was used to determine the groups that had difference between them. Chi-square analysis was applied while investigating the relation between the nominal variable groups. Pearson chi-square analysis was applied in RxC tables with the help of Monte Carlo simulation. While interpreting the results, 0.05 was used as the threshold level for significance; $p < 0.05$ indicated a significant relation, whereas $p > 0.05$ indicated no significant relation.

RESULTS

Fifteen patients who were missing from the file records and 28 patients with hospital stay of 2 days or less were excluded from the study. A total of four patients with leukaemia, lymphoma and skin cancer were excluded because they did not constitute a sufficient number of cancer diagnosis groups.

A total of 192 patients, 84 (43.8%) of whom were female and 108 (56.3%) were male, were been included in the study. The mean age was 68.41 ± 14.15 years and length of stay in PCC was 18.12 ± 17.64 days. The most common neurological symptoms were pain (60.9%), insomnia (27.1%), delirium (17.2%), seizures (15.1%), depression (13.5%) and paresis (11.5%). Primary tumours were determined to be due to GIS cancers in 75 patients (39.1%), lung cancer in 46 patients (24%), GUS + gynecologic cancers in 29 patients (15.1%), head and neck cancers in 27 patients (14.1%) and breast cancer in 15 patients (7.8%) (Table 1).

There was a statistically significant relation between pain, paresis and seizures and diagnosis of patients ($p < 0.05$). Pain was determined in 25.9% of patients with head and neck cancers, 63% of patients with lung cancer, 53.3% of patients with breast cancer, 69.3% of patients with GUS cancers, and 72.4% of patients with GUS + gynecologic cancers (Table 2). Paresis was determined in 37% of patients with head and neck cancers, 8.7% of patients with lung cancer, 13.3% of patients with breast cancer, 4% of patients with GUS cancers, and 4% of patients with GUS + gynecologic cancers

Table 1: Demographic characteristics of patients

Variable		Value
Age (Years)*		68.41±14.15
Gender**	Female	84 (43.8)
	Male	108 (56.3)
Hospitalization days (days)*		18.12± 17.64
Cancer type**		
	Head/neck	27 (14.1)
	Lung	46 (24.0)
	Breast	15 (7.8)
	GI	75 (39.1)
	GU+ Gyn	29 (15.1)
Neurological symptoms **		
	Pain	117 (60.9)
	Delirium	33(17.2)
	Depression	26 (13.5)
	Paresis	22 (11.5)
	Seizures	29 (15.1)
	Insomnia	52 (27.1)

*Values are presented as mean±standard deviation.
**Values are presented as n (%).
GI: gastrointestinal, GU: genitourinary, Gyn: gynecologic

(Table 2). Seizures were determined in 51.9% of patients with head and neck cancers, 13% of patients with lung cancer, 20% of patients with breast cancer, 5.3% of patients with GUS cancers, and 6.9% of patients with GUS + gynecologic cancers (Table 2).

There was a statistically significant relation between pain and seizures and metastasis ($p < 0.05$). Whereas pain was observed in 66.7% of patients with metastasis, seizures was observed in 11.8% of patients with metastasis and 25% of patients who did not have metastasis (Table 3).

A statistically significant relation was determined between pain and discharge status upon comparing discharge status to symptoms ($p < 0.05$). Pain was observed in 69.2% of patients who have passed away, 51.6% of patients in intensive care and 50% of patients who were discharged to go home (Table 4).

According to the number of hospitalisation days, a statistically significant difference was determined between pain and seizures ($p < 0.05$). The number of hospitalisation days was significantly lower in patients with pain symptom compared to those who do not have pain ($p < 0.003$). The number of hospitalisation days was significantly lower in patients who did not have seizures than those who experienced seizures ($p < 0.004$) (Table 5).

A statistically significant difference was determined upon comparing the number of hospitalisation days and discharge status ($p < 0.05$). The number of hospitalisation days in patients with lung cancer and GUS + gynecologic cancer patients was significantly lower compared to patients with head and neck cancer and breast cancer (Table 6).

DISCUSSION

The most common cancer group in our palliative care was GIS cancers (39.1%), lung cancer (24%) and GUS + gynecologic cancers (15.1%). Studies have shown that the prevalence of breast and lung cancers is high.[15] Due to the limited number of PCCs in our country, insufficient palliative care awareness of patients and doctors, and the fact that very few of cancer patients can benefit from palliative care services, we think that the higher prevalence of GIS cancers may be arbitrary higher in our study. The most common symptoms in these patients were pain (60.9%) and insomnia

Table 2: Relationship between neurological symptoms and cancer type

		Head/neck		Lung		Breast		GI		GU+ Gyn		Total		p
		n	%	n	%	n	%	n	%	n	%	n	%	
Pain	present	7	25.9	29	63.0	8	53.3	52	69.3	21	72.4	117	60.9	**0.001**
	absent	20	74.1	17	37.0	7	46.7	23	30.7	8	27.6	75	39.1	
	Total	27	100	46	100	15	100	75	100	29	100	192	100	
Delirium	present	6	22.2	10	21.7	2	13.3	11	14.7	4	13.8	33	17.2	0.776
	absent	21	77.8	36	78.3	13	86.7	64	85.3	25	86.2	159	82.8	
	Total	27	100	46	100	15	100	75	100	29	100	192	100	
Depression	present	3	11.1	5	10.9	3	20	12	16.0	3	10.3	26	13.5	0.819
	absent	24	88.9	41	89.1	12	80	63	84.0	26	89.7	166	86.5	
	Total	27	100	46	100	15	100	75	100	29	100	192	100	
Paresis	present	10	37.0	4	8.7	2	13.3	3	4	3	10.3	22	11.5	**0.001**
	absent	17	63.0	42	91.3	13	86.7	72	96	26	89.7	170	88.5	
	Total	27	100	46	100	15	100	75	100	29	100	192	100	
Seizures	present	14	51.9	6	13.0	3	20	4	5.3	2	6.9	29	15.1	**0.001**
	absent	13	48.1	40	87.0	12	80	71	94.7	27	93.1	163	84.9	
	Total	27	100	46	100	15	100	75	100	29	100	192	100	
Insomnia	present	5	18.5	15	32.6	6	40	20	26.7	6	20.7	52	27.1	0.465
	absent	22	81.5	31	67.4	9	60	55	73.3	23	79.3	140	72.9	
	Total	27	100	46	100	15	100	75	100	29	100	192	100	

p<0.05 ,Statistically significant,GI: gastrointestinal, GU: genitourinary, Gyn: gynecologic

Table 3: Relationship between neurological symptoms and metastasis

		Metastasis negative		Metastasis positive		Total			
		n	%	n	%	n	%	Value	p
Pain	present	21	43.8	96	66.7	117	60.9		
	absent	27	56.3	48	33.3	75	39.1	7,943	**0.005**
	Total	48	100	144	100	192	100		
Delirium	present	10	20.8	23	16.0	33	17.2		
	absent	38	79.2	121	84.0	159	82.8	0,305	0.581
	Total	48	100	144	100	192	100		
Depression	present	6	12.5	20	13.9	26	13.5		
	absent	42	87.5	124	86.1	166	86.5	0	1
	Total	48	100	144	100	192	100		
Paresis	present	9	18.8	13	9	22	11.5		
	absent	39	81.3	131	91	170	88.5	2,464	0.116
	Total	48	100	144	100	192	100		
Seizures	present	12	25	17	11.8	29	15.1		
	absent	36	75	127	88.2	163	84.9	3,913	**0.048**
	Total	48	100	144	100	192	100		
Insomnia	present	11	22.9	41	28.5	52	27.1		
	absent	37	77.1	103	71.5	140	72.9	0,316	0.574
	Total	48	100	144	100	192	100		

p<0.05; Statistically significant, Value: Mean± standard deviation.

(27.1%) followed by delirium (17%), seizures (15.1%), depression (13.5%) and paresis (11.5%). In a review study performed to determine the prevalence of symptoms in 25,075 cancer patients, Teunissen *et al*.[10] determined that the most common diagnosis was GIS cancers (17%) and lung cancer (13%). Although the symptoms with the highest rate were pain (71%) and exhaustion (74%) in their study, neurological symptoms such as insomnia (36%), depression (39%) and hemiplegia and paresis (15%) were also observed to be high.

Pain is one of the most common symptoms observed in cancer patients.[7] Although pain may dependon the primary location of the tumour in these patients, it may also be due to metastasis or applied treatments. In a review including the meta-analysis of 52 studies, Van den Beuken-Van Everdingen *et al*. determined that pain was most common in head and neck cancers (70%) and GIS cancers (59%) and observed that there was a high rate of pain (64%) in patients with metastasis or in patients in the terminal phase.[16] In consistent with the previous reports, our study showed that pain was most common in GUS + gynecologic cancers (72.4%) and GIS cancers (69.3%). Pain was observed to be significantly higher in patients with metastasis (66.7%) and patients who have passed away (69.2%; $p < 0.005$ and 0.032, respectively). The number of days spent in palliative care was also significantly lower in patients with pain ($p < 0.003$). This was because the patients with pain mostly had metastasis and their discharge status was exitus.

Seizures has been reported in 38% of patients with primary brain tumours and 20% of patients with brain metastasis.[17] It was found that focal neurological deficits such as hemiparesis, aphasia and sensory changes may appear in 40% of patients with brain metastasis.[18] We found that paresis (37%) and seizures (51%) were significantly higher in patients with head and neck cancers ($p < 0.001$ and 0.001, respectively). We also determined that the number of days under palliative care was significantly higher in patients who were diagnosed with head and neck cancers and who experienced seizures ($p < 0.007$ and 0.004, respectively). This result suggested

Table 4: Relationship between neurological symptoms and discharge status

		Exitus		ICU		Home		Total		Value	p
		n	%	n	%	n	%	n	%		
Pain	present	74	69.2	16	51.6	27	50	117	60.9		
	absent	33	30.8	15	48.4	27	50	75	39.1	6,884	**0.032**
	Total	107	100	31	100	54	100	192	100		
Delirium	present	15	14.0	9	29.0	9	16.7	33	17.2		
	absent	92	86.0	22	71.0	45	83.3	159	82.8	3,821	0.148
	Total	107	100	31	100	54	100	192	100		
Depression	present	15	14.0	2	6.5	9	16.7	26	13.5		
	absent	92	86.0	29	93.5	45	83.3	166	86.5	1,802	0.406
	Total	107	100	31	100	54	100	192	100		
Paresis	present	11	10.3	1	3.2	10	18.5	22	11.5		
	absent	96	89.7	30	96.8	44	81.5	170	88.5	4,87	0.088
	Total	107	100	31	100	54	100	192	100		
Seizures	present	13	12.1	4	12.9	12	22.2	29	15.1		
	absent	94	87.9	27	87.1	42	77.8	163	84.9	2,979	0.225
	Total	107	100	31	100	54	100	192	100		
Insomnia	present	30	28	9	29.0	13	24.1	52	27.1		
	absent	77	72	22	71.0	41	75.9	140	72.9	0,357	0.837
	Total	107	100	31	100	54	100	192	100		

p<0.05; Statistically significant, Value: Mean± standard deviation, ICU: Intensive care unit

that hospitalisation period may be extended in patients diagnosed with head and neck cancers depending on complications due to seizure control and paresis.

Delirium prevalence has been reported to be between 11% and 35% in cancer patients, and it might be as high as 85% in cancer patients in the terminal stage.[19] It is known that delirium accompanies primary or metastatic intracranial masses, leptomeningeal disease and paraneoplastic syndromes more and that it is associated with high mortality incidence.[20,21] Şenel *et al*. reported the incidence of delirium to be 49.8% in their study with palliative care in cancer patients.[22] We found the delirium incidence to be 17.2% in our study and there was no relation between cancer diagnosis and presence of metastasis. A previous study by Frang *et al*.[19] also did not find any relationship between cancer patients with brain metastasis and delirium symptom.

Depression and insomnia are associated symptoms, and they are reported to be higher in chronic diseases such as cancer that significantly affects the quality of life.[21,23] Whereas the prevalence of sleeping disorders may vary from 24% to as high as 95%, depression was reported to vary between 7% and 49%.[24-26] In some studies, the rate of depression was reported to be higher in oropharyngeal, pancreas, breast and lung cancers and the rate of insomnia was higher in breast, lung, and head and neck cancers.[27,28] We found an incidence of depression in 13.3% and insomnia in 27.1% of patients in our PCC. We observed no relation with any type of cancer and determined no significant relation with discharge status and number of hospitalisation days.

The limitations of this study were that it was retrospective with a limited number of patients, and we did not evaluate other neurological symptoms such as sensory symptoms and cranial nerve symptoms (visual symptoms, hearing, diplopia, dysphagia and dysarthria), dizziness/ vertigo, muscle cramps bladder and bowel problems.

In our study, we have determined that pain and insomnia were most common in cancer patients who we have followed up under palliative care. We observed that pain was more common in patients with GUS + gynecologic and GIS cancers and paresis and seizures were higher in patients

Table 5: The relationship between hospitalization days and neurological symptoms

		n	Hospitalization Days					OR	Mann Whitney U Test	
			Mean	Median	Minimum	Maximum	SD		z	p
Gender	Male	108	19	12	3	70	16	91.57		
	Female	84	23	17	2	95	20	102.84	-1.396	0.163
	Total	192	20	15	2	95	18			
Metastasis	Negative	48	26	19	4	95	23	107.45		
	Positive	144	19	14	2	83	16	92.85	-1.578	0.115
	Total	192	20	15	2	95	18			
Pain	present	117	17	12	2	69	14	86.97		
	absent	75	26	18	4	95	22	111.37	-2.971	**0.003**
	Total	192	20	15	2	95	18			
Delirium	present	33	23	18	3	83	19	106.79		
	absent	159	20	14	2	95	18	94.36	-1.17	0.242
	Total	192	20	15	2	95	18			
Depression	present	26	24	20	4	83	18	113.88		
	absent	166	20	13	2	95	18	93.78	-1.718	0.086
	Total	192	20	15	2	95	18			
Paresis	present	22	25	16	4	65	20	113.14		
	absent	170	20	14	2	95	18	94.35	-1.494	0.135
	Total	192	20	15	2	95	18			
Seizures	present	29	32	26	4	95	25	124.14		
	absent	163	18	13	2	83	16	91.58	-2.91	**0.004**
	Total	192	20	15	2	95	18			
Insomnia	present	52	24	19	4	95	19	108.69		
	absent	140	19	14	2	83	17	91.97	-1.855	0.064
	Total	192	20	15	2	95	18			

p<0.05 Statistically significant, SD: Standard deviation, OR:Odds ratio

Table 6: The relationship between diagnosis and hospitalization days

		Hospitalization Days						Kruskal Wallis H Testi	
		n	Mean	Median	Minimum	Maximum	SD	OR	H	p
Diagnosis	Head/neck	27	30	22	5	69	21	126.69		
	Lung	46	16	13	4	54	12	85.2		
	Breast	15	33	35	4	95	29	120	13.97	**0.007**
	GI	75	19	11	3	83	17	91.23		
	GU + Gyn	29	16	12	2	51	12	87.81		
	Total	192	20	15	2	95	18			

p<0.05; Statistically significant, SD: Standard deviation, OR:Odds ratio, GI: gastrointestinal, GU:genitoürinary, Gyn:gynecologic

with head and neck cancers. We conclude that except for pain, the other neurological symptoms were not as prevalent as the non-neurological symptoms such as breathlessness, nausea and vomiting, fatigue, anorexia and constipation as reported in the literature. We suggest that the recognition, prevention and treatment of neurological symptoms experienced by cancer patients may result in better quality of life of patients and their families. There is a need for further studies with larger patient groups and more detailed information of the neurological symptoms.

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DISCLOSURE

Conflict of interest: None

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