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ORIGINAL ARTICLE

Clinicopathological characteristics of patients with multiple primary neoplasms - a retrospective analysis

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Summary

Purpose: *Multiple primary neoplasms (MPN) represent the occurrence of two or more primary neoplasms in the same individual during lifetime and today there is an increased interest in studying the implications of MPN in the outcome of oncological patients. In this study we aimed to evaluate the clinicopathological characteristics of patients with MPN.*

Methods: *In this nonrandomized, retrospective study patients with MPN treated in the Oncology Institute "Prof. Dr.Ion Chiricuta" Cluj-Napoca between 2008-2012 were included. Data were collected from the medical charts.*

Results: *278 patients with MPN were treated in our institute between 2008-2012: 120 patients with synchronous tumors and 158 with metachronous tumors. Of them, 260 patients presented with two MPN and 13 with three MPN. Fifty four percent (n=151) of the patients were females and 127 (46%) males, with a median age at diagnosis of 60 years. Most patients presented with early stage tumors, both for the initial primary tumor (54%) and for the second tumor (55%). The most frequent initial primary tumors were breast, head and neck, colorectal, ovarian, prostate and uterine body cancers and the most frequent second tumors were breast, colorectal, uterine body, head and neck, lung and thyroid cancers. Five-year survival was higher for patients with metachronous tumors (68%) compared with patients with synchronous tumors (54%; p=0.02).*

Conclusion: *MPN represent a real challenge in daily practice and their occurrence should not be overlooked. Lack of solid data from the literature makes it difficult to establish which patients are at risk for developing multiple neoplasms and should be closely followed up.*

Key words: *metachronous tumors, multiple cancers, multiple neoplasms, second primary, synchronous tumors*

Introduction

The increase in cancer patient's survival and the improvements made in the screening and diagnosis of cancer has led to a growing number of patients diagnosed with multiple cancers during life. Multiple primary neoplasms (MPN) are defined as two or more primary neoplasms diagnosed in the same patient simultaneously or at a certain time and that do not represent the progression, relapse or metastasis of the first neoplasm [1,2]. The incidence of MPN ranges between 0.7% and 11.7% [3-5] and continues to grow, in contrast with the first mentions of MPN in the literature, when they were described as sporadic cases.

The criteria on which a patient can be considered as having MPN are the ones first elaborated by Warren and Gates in 1932 and later refined by other authors [6-9]. Depending on the time of diagnosis of the first and second malignancies MPN can be classified as synchronous and metachronous [10,11].

Patients with MPN represent a real challenge for medical oncologists and radiotherapists and there are few data published in the literature evaluating all the aspects that MPN involve: risk factors, frequent associations, patient characteristics, treatment administered and survival.

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The aim of this study was to evaluate the possible risk factors implicated in the etiology of MPN and the clinicopathological characteristics of patients with MPN treated at the Oncology Institute "Prof.Dr.Ion Chiricuta", Cluj-Napoca, Romania.

Methods

In this nonrandomized, retrospective study were included patients with MPN diagnosed and treated in the Oncology Institute "Prof.Dr.Ion Chiricuta", Cluj-Napoca, between 2008-2012.

MPN were defined as two or more primary neoplasms diagnosed in the same patient simultaneously or at a certain time and that did not represent the progression, relapse or metastasis of the first neoplasm [1,2]. The criteria according to which patients were considered as having MPN were the following: 1) each cancer must have been malignant according to the histopathology report; 2) the cancers must have been geographically separate and histologically different; 3) the possibility of metastases among the cancers was excluded [6-9].

Patients with carcinoma *in situ* regardless of localization were excluded from the study.

MPN were classified as synchronous and metachronous depending on the time of diagnosis of the first and second malignancies, respectively: synchronous when the second neoplasm was diagnosed within 6 months from the diagnosis of the first neoplasm and metachronous when the second neoplasm was diagnosed in more than 6 months after the diagnosis of the first neoplasm [10,11]. Furthermore, multiple neoplasms diagnosed during the initial workup of one cancer were classified

Table 1. Characteristics of patients with multiple primary neoplasms

Characteristics	*2008-2012*		
	Synchronous MPN *n (%)*	*Metachronous MPN* *n (%)*	*Total* *n (%)*
	120 (43)	158 (57)	278
Age (years) median	60	60	60
Sex			
Male	54 (43)	73 (57)	127 (46)
Female	66 (44)	85 (56)	151 (54)
PS			
Primary tumor			
0	45	86	131 (47)
1	73	72	145 (52)
2	2	0	2 (0.7)
3	0	0	0
Second tumor			
0	37	32	69 (25)
1	80	122	202 (73)
2	3	2	5 (1.8)
3	0	2	2 (0.7)
Histology			
Adenocarcinoma	111 (44)	140 (56)	251
Squamous cell carcinoma	70 (54)	60 (46)	130
Invasive ductal carcinoma	19 (32)	41 (68)	60
Urothelial carcinoma	14 (52)	13 (48)	27
Melanoma	6 (43)	8 (57)	14
Undifferentiated carcinoma	5 (39)	8 (61)	13
Stage			
Primary tumor			
0-II	58 (48)	90 (57)	148 (54)
III-IV	62 (52)	65 (41)	127 (46)
unclassifiable			3
Second tumor			
III-IV	43 (36)	78 (49)	121 (45)
unclassifiable			8

Table 2. Multiple primary neoplasms-distribution according to age groups

Age (age groups)	*Metachronous MPN, n(%)*	*Synchronous MPN, n(%)*	*Total, n(%)*
Young (0-14 years)	0	0	0
Adults (15-64 years)	112 (71)	85 (71)	197 (71)
Old (65+ years)	46 (29)	35 (29)	81 (29)
Total	158	120	278

Table 3. Multiple primary neoplasms-distribution according to stage

Stage	*n (%)*
Primary tumor	
0-II	148 (54)
III-IV	127 (46)
unclassifiable	3
Second tumor	
0-II	149 (55)
III-IV	121 (45)
unclassifiable	8
Total	278
Third tumor	
0-II	5 (38)
III-IV	8 (62)
Total	13

Table 4. Multiple primary neplasms-most common tumors

Most common tumors	*n (%)*
Primary tumor	
Breast	40 (14)
Head and neck	36 (13)
Colorectal	24 (9)
Ovarian	24 (9)
Prostate	23 (8)
Uterine body	20 (7)
Second tumor	
Breast	33 (12)
Colorectal	31 (11)
Uterine body	23 (8)
Head and neck	21 (8)
Lung	20 (7)
Thyroid	20 (7)
Third tumor	
Colorectal	3 (23)
Lung	2 (15)
Breast	2 (15)
Skin	2 (15)

as simultaneous. Metachronous neoplasms were further classified in metachronous <5 years and metachronous >5 years [1].

Possible risk factors implicated in the etiology of MPN, such as positive family history, significant personal history, environmental factors, were recorded and the cases were classified in one of the following categories according to major etiological factors: syndromic cases, iatrogenic neoplasms, neoplasms with common etiologic factors (genetic predisposition or environmental factors) and incidental cases.

The patient medical records were retrospectively reviewed and demographic, clinical, pathological and treatment related data were recorded and analyzed. All patients included in this study had an informed consent signed. The study design has been evaluated and approved by the Ethics Committee of the Oncology Institute "Prof.Dr.Ion Chiricuta", Cluj-Napoca, Romania.

Statistics

The above-mentioned data were used to create a database. For demographic and clinical characteristics of the patients descriptive analysis was performed. Kaplan-Meier method and log rank test were used to compare survival curves. Statistical significance was considered at a p value less than 0.05.

Results

Two hundred and seventy eight patients with MPN diagnosed and treated in the Oncology Institute "Prof.Dr.Ion Chiricuta" Cluj-Napoca, between 2008-2012 were included in this study. The incidence of MPN among the patients diagnosed and treated in the Oncology Institute "Prof.Dr.Ion Chiricuta" Cluj-Napoca between 2008-2012 was 0.8%.

Out of the 278 patients 120 (43%) presented with synchronous tumors and 158 (57%) with metachronous tumors. Simultaneous MPN were observed in 25% of the 278 patients. Ninety two percent of the patients with metachronous tumors developed a second neoplasm in the first 5 years after the diagnosis of the primary tumor. Most patients presented with two MPN (260 patients) and 13 patients presented with three MPN (Table 1).

For metachronous tumors the median interval between the diagnosis of the primary and subse-

quent tumor was 30.98 months, ranging between 6.07 and 85.47 months. The median follow-up for the patients included in the study was 6.1 years.

Fifty four percent of the patients were females (151 patients), 66 with synchronous tumors and 85 with metachronous tumor, and 46% of the patients were males (127 patients), 54 with synchronous tumors and 73 with metachronous tumors (Table 1).

Median age at diagnosis was 60 years (range 26-87). When age was analyzed according to synchronous and metachronous tumors, median age at diagnosis was also 60 years in both groups. When age was analyzed according to age groups (young 0-14 years, adults 15-64 years and old 65+ years), most patients with MPN were in the age group 15-64 years (197;71%), with only 81 (29%) patients being in the age group 65+ (Tables 1 and 2).

Most patients had a performance status (PS) 0 or 1 at the diagnosis of the primary tumor (276 patients, 47% PS 0 and 52% PS 1), with only two patients with synchronous MPN with PS 2. At the time of diagnosis of the second malignancy 25% (69) of the patients had PS 0, 73% (202) had PS 1, 1.8% (5) had PS 2 and 0.7% (2) of patients had PS 3, the latter belonging to the group of patients with metachronous tumors (Table 1).

One hundred and forty eight (54%) patients presented with stage 0-II primary tumor and 127 (46%) with stage III-IV primary tumor. For the second tumor most patients also presented with stage 0-II tumor (149 patients-55%) with 121 (45%) patients presenting with stage III-IV tumor. Out of the 13 patients with three MPN 38% (n=5) presented with stage 0-II tumors and 62% (n=8) with stage III-IV tumors. Staging was not possible for 3 primary tumors and 8 second tumors, information for staging not being available for these cases or these patients being diagnosed with leukemia or central nervous system tumors. For the other patients staging was performed according to the American Joint Committee on Cancer (AJCC) staging system (Tables 1 and 3).

The first 6 most frequent initial primary tumors identified were breast (40 patients, 14%), head and neck (36 patients, 13%), colorectal (24 patients, 9%), ovarian (24 patients, 9%), prostate (23 patients, 8%) and uterine body tumors (20 patients, 7%), while the most frequent second tumors were breast (33 patients, 12%), colorectal (31 patients, 11%), uterine body (23 patients, 8%), head and neck (21 patients, 8%), lung (20 patients, 7%) and thyroid tumors (20 patients, 7%), and the most frequent third tumors were colorectal (3 patients, 23%), lung (2 patients, 15%), breast (2 patients, 15%) and skin tumors (2 patients, 15%) (Table 4). For synchronous tumors, ovarian, head and neck, cervix, breast, bladder and skin tumors were the most frequent initial primary tumors observed, and uterine body, breast, colorectal, head and neck and skin tumors were the most frequent second tumors. For metachronous tumors breast, head and neck, prostate, colorectal, lung and uterine body tumors were the most frequent initial primary tumors, while breast, colorectal, thyroid, lung, head and neck and prostate tumors were the most frequent second tumors.

In women the most frequently diagnosed 6 tumors were breast (74 patients, 24%), uterine body (41 patients, 13%), ovarian (36 patients, 12%), cervix (31 patients, 10%), colorectal (29 patients, 9%) and thyroid tumors (23 patients, 7%; Figure 1). In men the most frequently diagnosed 6 tumors were head and neck (51 patients, 20%), prostate (42 patients, 16%), lung (32 patients, 12%), colorectal (29 patients, 11%), bladder (20 patients, 8%) and skin tumors (19 patients, 7%; Figure 2). Regarding the first tumor diagnosed in women, the most frequent tumors were breast, uterine body, ovarian, cervix, colorectal and skin tumors and in men head and neck, prostate, colorectal, lung, bladder, skin and renal tumors. The most frequent second tumors diagnosed in women were breast, thyroid, colorectal, uterine body, cervix and lymphoma and in men lung, colorectal, prostate, head and neck, renal and bladder tumors.

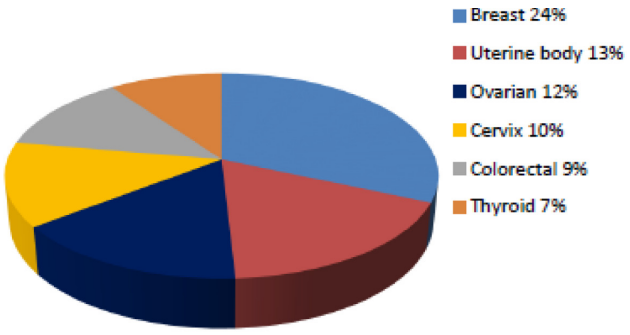

Figure 1. Most common tumors in women.

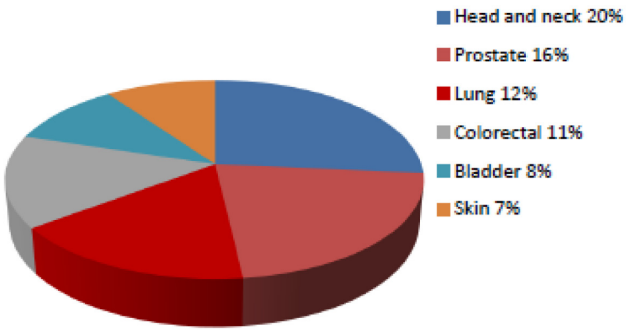

Figure 2. Most common tumors in men.

When sex-related tumors were excluded from the analysis we observed that in our MPN group 6 cancers were more frequent in men than in women: head and neck (51 patients vs 6 patients), lung (32 patients vs 7 patients), bladder (20 patients vs 6 patients), stomach (9 patients vs 3 patients), renal (15 patients vs 7 patients) and skin (19 patients vs 17 patients) cancers and 6 cancers were diagnosed only in men: esophagus (10 patients), thymus (2 patients), renal pelvis (1 patient), ureter (1 patient), small bowel (1 patient) and cholangiocarcinoma (1 patient). Thyroid cancer was the only cancer significantly more frequent in women than in men (23 patients vs 7 patients).

The most frequent histology observed in our MPN population was adenocarcinoma (251 cases, 111 synchronous and 140 metachronous), followed by squamous cell carcinoma (130 cases, 70 synchronous and 60 metachronous), invasive ductal carcinoma (60 cases, 19 synchronous and 41 metachronous), urothelial carcinoma (27 cases, 14 synchronous and 13 metachronous), melanoma (14 cases, 6 synchronous and 8 metachronous) and undifferentiated carcinoma (13 cases, 5 synchronous and 8 metachronous) (Table 1).

When tumor grading was analyzed in the cases in which it was available (187 initial primary tumors and 176 second tumors), grade 2 tumors were more frequent, both for initial primary tumors (81 cases) and second tumors (79 cases). Grade 3 tumors were observed in 58 cases for the initial primary tumor and 49 cases for the second tumor, and grade 1 tumors in 43 initial primary tumor cases and 42 second tumor cases. Grade 4 tumors were observed in 5 cases of initial primary tumor and in 6 cases of second tumor.

Regarding the classification according to the major etiological factors possibly implicated in the etiology of MPN, 73 (26%) cases were classified as syndromic cases, 15 (5%) cases were iatrogenic neoplasms, 95 (34%) were neoplasms with common etiologic factors (23 (8%) cases with genetic predisposition and 72 (26%) cases with environmental factors) and 95 (34%) cases were incidental cases. The most frequent environmental factors observed were smoking in 22% of the cases and alcohol consumption in 11% of the cases, other toxic substances being identified in 3% of the cases. Three percent of the patients had a positive family history of cancer on the paternal line, 4% on the maternal line and 5% of the patients had other relatives of first degree diagnosed with cancer in their families (Table 5).

Forty-five percent of the patients (n=125) with MPTs had diabetes.

Seventy eight patients (28%) underwent surgery alone for the primary tumor, 94 patients (34%) were subjected to surgery and adjuvant chemotherapy or radiotherapy, 21 patients (8%) to surgery with adjuvant chemotherapy and radiotherapy, with the remaining patients having chemotherapy or radiotherapy or hormone therapy alone or different combinations of the various treatment options. Regarding the treatment of the second tu-

Table 5. Classification according to the major etiological factors possibly implicated in the etiology of MPN

	Metachronous MPN *n (%)*	*Synchronous MPN* *n (%)*	*Total* *n (%)*
Syndromic cases			
Yes	35 (22)	38 (32)	73 (26)
No	123 (78)	82 (68)	205 (74)
Iatrogenic neoplasms			
Yes	15 (10)	0	15 (5)
No	143 (90)	120 (100)	263 (95)
Genetic predisposition			
Yes	15 (10)	8 (7)	23 (8)
No	143 (90)	112 (93)	255 (92)
Enviromental factors			
Yes	37 (23)	35 (29)	72 (26)
No	121 (77)	85 (71)	206 (74)
Incidental cases			
Yes	56 (35)	39 (33)	95 (34)
No	102 (65)	81 (67)	183 (66)
Total	158	120	278

mor, 32% of the patients underwent surgery alone, 13% underwent surgery and adjuvant chemotherapy, 12% surgery and adjuvant radiotherapy, with the remaining patients having chemotherapy or radiotherapy or hormone therapy alone or different combinations of the various treatment options. For 2 primary tumors and 7 second tumors treatment was unspecified (Table 6).

Treatment toxicity of the primary tumor was mild or moderate, most common toxicities were grade 1-2 to all evaluated toxicities (hematological 69%, renal 6%, gastrointestinal 12%, cardiac, pulmonary and liver toxicity 8%). Grade 3-4 toxicities were observed in 3.4% of the cases (2% anemia, 1% neutropenia and 0.4% diarrhea). Grade 1-2 toxicity to the treatment of the second tumor was also the most common toxicity observed: 78% hematological toxicity, 5% renal toxicity, 10% gastrointestinal toxicity, 0.4% cardiac toxicity, 0.4% pulmonary toxicity and 9% liver toxicity. There was more grade 3-4 hematological toxicity to the treatment of the second tumor: 5% anemia (p=0.27), 3% leucopenia (p=0.04), 3% neutropenia (p=0.22) and 2% thrombocytopenia (p=0.30) (Table 7).

Statistically significant difference was noted between the 5-year overall survival of patients with

Table 6. Treatment for the primary and second tumor (RTE- radiotherapy, CH-surgery, CT-chemotherapy, HT-hormone therapy)

	Treatment 1 *n (%)*	*Treatment 2* *n (%)*
RTE HT	9 (3)	3 (1)
RTE CT	17 (6)	23 (8)
RTE	11 (4)	12 (4)
HT	9 (3)	7 (2.5)
CT	13 (5)	34 (12)
CH RTE HT	8 (2.8)	4 (1.4)
CH RTE CT	21 (8)	14 (5)
CH RTE CT HT	0	8 (3)
CH RTE	45 (16)	33 (12)
CH HT	8 (2.8)	5 (2)
CH CT HT	8 (2.8)	4 (1.4)
CH CT	49 (18)	36 (13)
CH	78 (28)	88 (32)
Unspecified	2 (1)	7 (2.5)
Total	278	278

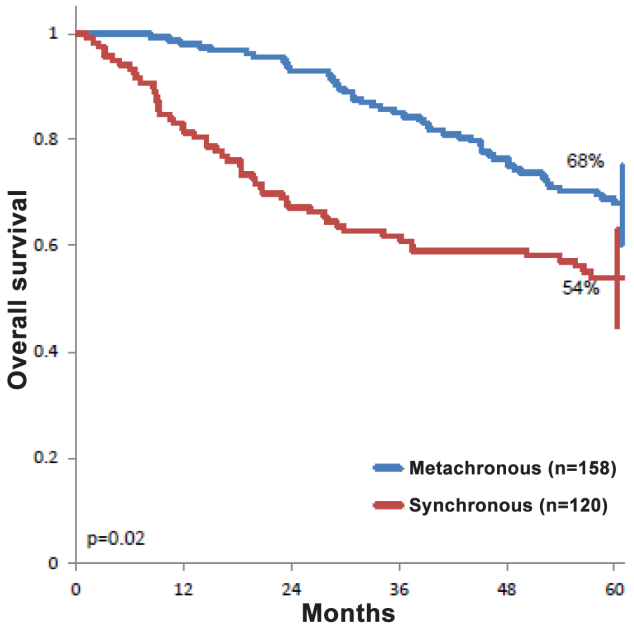

Figure 3. Survival of patients with multiple primary neoplasms-synchronous vs metachronous tumors.

Table 7. Toxicity to the treatment of the primary and second tumor

	Toxicity to treatment 1			*Toxicity to treatment 2*			*p value*
	Grade 1-2 *n (%)*	*Grade 3-4* *n (%)*	*Unspecified* *n (%)*	*Grade 1-2* *n (%)*	*Grade 3-4* *n (%)*	*Unspecified* *n (%)*	
Hematological toxicity							
Hb	79 (28)	6 (2)	66 (24)	79 (28)	13 (5)	63 (23)	0.27
WBC	39 (14)	0	66 (24)	52 (19)	7 (3)	63 (23)	0.04
N	37 (13)	4 (1)	66 (24)	45 (16)	9 (3)	63 (23)	0.22
Pl	38 (14)	0	66 (24)	42 (15)	5 (2)	63 (23)	0.30
Renal toxicity	17 (6)	0	66 (24)	15 (5)	0	63 (23)	0.60
Gastrointestinal toxicity							
Nausea/Vomiting	22 (8)	0	66 (24)	18 (6)	0	63 (23)	0.53
Diarrhea	10 (4)	1 (0.4)	66 (24)	12 (4)	0	63 (23)	0.91
Cardiac toxicity	0	0	66 (24)	1 (0.4)	0	63 (23)	0.56
Pulmonary toxicity	0	0	66 (24)	1 (0.4)	0	63 (23)	0.56
Liver toxicity	23 (8)	0	66 (24)	25 (9)	0	63 (23)	0.61

synchronous tumors (54%) when compared with patients with metachronous tumors (68%;p=0.02) (Figure 3).

Discussion

The analysis of patients with MPN treated in the Oncology Institute "Prof.Dr.Ion Chiricuta" Cluj-Napoca, between 2008-2012 revealed a 0.8% incidence of MPN, with most patients presenting with metachronous tumors (57%) and a median interval between the diagnosis of the primary and subsequent tumor of 30.98 months, data that are consistent with the data published in the literature [1,9,12-16].

The median age at diagnosis was 60 years both in the group of patients with synchronous tumors and in the group of patients with metachronous tumors. Most patients diagnosed with MPN were adult (71%), included in the age group 15-64 years. Age groups were balanced between synchronous and metachronous MPN, 57% of the patients being diagnosed with metachronous tumors both in the age group 15-64 years and in the >65+ years and 43% of the patients being diagnosed with synchronous tumors in both groups.

Most patients presented with PS 0 or 1 at the diagnosis of the primary tumor (276 patients, 47% PS 0 and 52% PS 1). PS was not influenced by the previous malignancy or by the treatment administered for the primary tumor, with 98% of patients presenting with PS 0 or 1 at the diagnosis of the second tumor.

In contrast with the studies published in the literature, the patients included in our study presented with early-stage tumors, both for the initial primary tumor and for the second tumor (54% stage 0-II vs 46% stage III-IV primary tumor; 55% stage 0-II vs 45% stage III-IV second tumor). Only for the third tumor 8 out of 13 patients presented with stage III-IV tumor. Also, when analyzed according to synchronous or metachronous tumors, most patients presented with early-stage tumors. In a study on 322 patients with MPN Amer et al. showed that patients present with a more advanced second primary tumor: 5.9% stage 0, 30.4% stage I, 22.4% stage II, 14.9% stage III and 36.4% stage IV tumor in contrast with 3.7% stage 0, 43.5% stage I, 31.7% stage II, 11.2% stage III and 9.9% stage IV tumor for the initial primary tumor. Also, this study showed that in contrast with patients with metachronous tumors, patients with synchronous tumors present with advanced-stage tumors (2.1% synchronous vs 4.0% metachronous stage 0, 23.4% vs 46.9% stage I, 17% vs 34.2% stage II, 23.4% vs 9.1% stage III and 34% vs 5.8% stage IV) [1].

Similar to the data published in the literature, the most frequent initial primary tumors observed in our study were breast, head and neck, colorectal, ovarian, prostate and uterine body cancers and the most frequent second tumors were breast, colorectal ,uterine body, head and neck, lung and thyroid cancers. The different studies published in the literature reported head and neck, breast, prostate, colorectal and gynecological cancers as the most frequent initial primary cancers and head and neck ,breast, lung, colorectal and gynecological cancers as the most frequent second cancers [1,9,12,13-15].

In our study the most frequently diagnosed 6 tumors in women were breast, uterine body, ovarian, cervix, colorectal and thyroid tumors. When comparing this data with the incidence of these cancers for Romania in the same interval we observed that for uterine body, ovarian and thyroid cancer, the incidence in our MPN population was more than double (13% vs 4.3%, 12% vs 5.2% and 7.4% vs 1.9%) [17]. The most frequently diagnosed 6 tumors in men were head and neck, prostate, lung, colorectal, bladder and skin tumors. The incidence for head and neck and prostate cancers observed in our MPN population was higher than the incidence reported for our country (20% vs 11% and 16% vs 10.5%) and for lung cancer it was lower (12% vs 21.6%) [17].

Twenty six percent of the cases included in our study were classified as being syndromic cases, considered to have a cancer syndrome as the major etiological factor for the development of MPN. Hereditary nonpolyposis colorectal syndromes (Lynch I and II syndromes), BRCA related breast and ovarian cancers, Li Fraumeni syndrome, neurofibromatosis, familial adenomatous polyposis and multiple endocrine neoplasm syndromes represent hereditary cancer syndromes associated with DNA microsatellite instability in which the occurrence of MPN is described [9,18,19].

Smoking and alcohol consumption represent the most important environmental factors implicated in the development of MPN, implication that can be explained by the field cancerization theory [9,12]. Multiple neoplasms are described in approximately 35% of cancer survivors who continue to smoke [20]. Environmental factors were incriminated in 26% of our MPN cases, smoking and alcohol consumption being the most frequent ones observed (smoking in 22% of the cases, alcohol consumption in 11% of the cases).

Treatment for the primary tumor can induce second neoplasms especially after 5-15 years from the treatment. Chemotherapeutic agents such as alkylating agents, topoisomerase II inhibitors, anthracyclines and ionizing radiation could be re-

sponsible for MPN in up to 30% of the cases [12,20-26]. Only 15 patients included in our study were considered as having iatrogenic tumors. In a study published by Babacan et al. the authors showed that second malignancies developed in the radiotherapy field in 4.6% of the patients who received radiation therapy for their primary tumor [12].

Most patients in our study were subjected to surgery with or without adjuvant chemotherapy, hormone therapy or radiation therapy for their primary and second tumor, data that are consistent with the data published in the literature [1,9,12,13], with more patients receiving chemotherapy alone or radiotherapy alone or hormone therapy alone for their second tumor when compared to the treatment of the primary tumor.

Treatment of the primary tumor might influence the ability to administer the treatment of the second tumor, with more grade 3-4 toxicities. Both grade 1-2 and 3-4 toxicities evaluated in our study were more frequent in the treatment of the second tumor, especially hematological toxicity. Grade 3-4 leucopenia was statistically significant more frequent in the treatment of the second tumor.

Survival of patients with metachronous tumors was better than in patients with synchronous tumors (68 vs 54%, p=0.02), with median survival not reached at the time of the analysis both for the patients with synchronous and metachronous tumors. In a study on 72 Chinese patients with MPN Jiao et al. also showed that patients with metachronous tumors have a better survival (median survival 17.3years) than patients with synchronous tumors (median survival 3.8 years) [16].

Conclusions

The posibility of MPN occurence should be taken into consideration by phisicians both during the initial work-up of their oncological patients, but also during their follow-up, as MPN are a reality in our daily practice, with more and more such cases being diagnosed. There is a need for more studies evaluating the complex implications of MPN in order to understand which patients are at risk of developing MPN and should be closely monitored.

Conflict of interests

The authors declare no conflict of interests.

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