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HISTOLOGICAL TYPES OF OVARIAN CANCER IN THE "DR. SALVATOR VUIA" CLINICAL OBSTETRICS AND GYNECOLOGY HOSPITAL ARAD DURING THE 2000-2009 PERIOD

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ABSTRACT. The purpose of this study is to examine the histological types of ovarian cancer in our hospital during the 2000-2009 interval. The data was collected from the Histopathology Exams (HPE) registers. Ovarian cancer was discovered in 82 cases, representing 6.59% of all genital cancers (1244 cases). There were 78 cases of primary cancer (95.12%) and five cases of ovarian metastatic cancer (6.10%), one patient having a combination of the two. Different types of carcinoma were detected in 72 cases of primary cancers (92.31%) and non-carcinoma types in eight cases (10.39%). Two cases (2.60%) had an association of two cancer types. All five metastases were represented by carcinomas. The mean age of the patients, 51,46±14,28 years, was statistically different from uterine and vulvar ones (p≤0,000001), but not from cervical cancer (p=0.33). The results of our study are similar to those in previous researches regarding the frequency of different histological types and the median age. Ovarian cancer still remains a serious public health issue, thus demanding a well organized screening programme.

KEYWORDS: ovarian cancer, ovarian carcinoma, yolk sac tumor, granulosa tumor, disgerminoma, immature teratoma, Sertoli-Leydig tumor, embrional carcinoma, ovarian metastasis, histology, mean age

INTRODUCTION

World Health Organization Classification of Malignant Ovarian Tumors (Young, 2005)
COMMON EPITHELIAL TUMORS
Malignant serous tumor
Adenocarcinoma, papillary adenocarcinoma, papillary cystadenocarcinoma
Surface papillary carcinoma
Malignant adenofibroma, cystadenofibroma
Malignant mucinous tumor
Adenocarcinoma, cystadenocarcinoma
Malignant adenofibroma, cystadenofibroma
Malignant endometrioid tumor
Carcinoma
Adenocarcinoma
Adenoacanthoma
Malignant adenofibroma, cystadenofibroma
Endometrioid stromal sarcoma
Mesodermal (mullerian) mixed tumor: homologous and heterologous
Clear cell (mesonephroid) tumor, malignant
Carcinoma and adenocarcinoma
Brenner tumor, malignant
Mixed epithelial tumor, malignant
Undifferentiated carcinoma
Unclassified
SEX CORD AND STROMAL TUMORS
Granulosa and stromal cell tumor
Granulosa cell tumor
Tumor in the thecoma-fibroma group
Fibroma
Unclassified
Androblastoma: Sertoli-Leydig cell tumor

Well differentiated
Tubular androblastoma, Sertoli cell tumor (tubular adenoma of Pick)
Tubular androblastoma with lipid storage, Sertoli cell tumor with lipid storage
Sertoli-Leydig cell tumor (tubular adenoma with Leydig cells)
Leydig cell tumor, hilus cell tumor
Of intermediate differentiation
Poorly differentiated (sarcomatoid)
With heterologous elements
Gynandroblastoma
Lipid (lipoid) cell tumors
Unclassified
Germ cell tumor
Dysgerminoma
Endodermal sinus tumor
Embryonal carcinoma
Polyembryoma
Choriocarcinoma
Immature teratoma
Mature dermoid cyst with malignant transformation
Monodermal and highly specialized
Struma ovarii
Carcinoid
Struma ovarii and carcinoid
Others
Mixed forms
GONADOBLASTOMA
Pure
Mixed with dysgerminoma or other form of germ cell tumor

1. Common epithelial tumors

The current classification of ovarian cancers is the one published by the WHO (Young, 2005).

Approximately 90% of ovarian cancers are derived from cells of the coelomic epithelium or modified mesothelium (Jemal et al, 2009) and approximately 75% to 80% of epithelial cancers are of the serous histologic type. Less common types are mucinous (10%), endometrioid (10%), clear cell, Brenner, and undifferentiated carcinomas, each of the latter three representing less than 1% of epithelial lesions (Scully et al, 1998).

Each tumor type has a histologic pattern that reproduces the epithelial features of a section of the lower genital tract (Kindelberger et al, 2007; Callahan et al, 2007; Carlson et al, 2008; Levanon et al, 2008).

Nonepithelial malignancies of the ovary account for approximately 10% of all ovarian cancers (Scully et al, 1998; Chen et al, 2000).

2. Sex cord and stromal tumors

Granulosa and stromal cell tumor

Sex-cord-stromal tumors of the ovary account for approximately 5% to 8% of all ovarian malignancies (Scully et al, 1998; Gershenson et al, 1994; Young et al 1988; Miller et al, 1997; Malmström et al, 1994; Segal et al, 1995; Cronje et al, 1999). This group of ovarian neoplasms is derived from the sex cords and the ovarian stroma or mesenchyme. Granulosa-stromal-cell tumors include granulosa cell tumors, thecomas, and fibromas; granulosa cell tumor is a low-grade malignancy (Segal et al, 1995; Cronje et al, 1999; Aboud et al, 1997; Young et al, 1989).

Germ cell tumors

Germ cell tumors are derived from the primordial germ cells of the ovary (Scully et al, 1998; Chen et al, 2000). Although 20% to 25% of all benign and malignant ovarian neoplasms are of germ cell origin, only some 3% of these tumors are malignant (Scully et al, 1998). Teratoma, the most common benign germ cell tumor, accounts for more than 90% of the tumors in this group. Primary malignant germ cell tumors are also uncommon and include dysgerminoma, embryonal carcinoma, yolk sac tumor, and choriocarcinoma. Except for dysgerminoma, all other primary germ cell tumors are high-grade malignancies and are not graded.

The dysgerminoma is the most common malignant germ cell tumor, accounting for approximately 30% to 40% of all ovarian cancers of germ cell origin (Kurman et al, 1979; Chen et al, 2000). The tumors represent only 1% to 3% of all ovarian cancers (Scully et al, 1998; Gershenson et al, 1994; Obata et al, 1995). The pure immature teratoma accounts for fewer than 1% of all ovarian cancers, but it is the second most common germ cell malignancy (Scully et al, 1998).

Endodermal sinus tumors (ESTs) have also been referred to as yolk sac carcinomas because they are derived from the primitive yolk sac (Scully et al, 1998).

Embryonal carcinoma of the ovary is an extremely rare tumor (Ueda et al 1990).

Pure nongestational choriocarcinoma of the ovary is an extremely rare tumor (Simosek et al, 1998).

Polyembryoma of the ovary is another extremely rare tumor, which is composed of “embryoid bodies”

(Scully et al, 1998, Kurman et al, 1979).

Mixed germ cell malignancies of the ovary contain two or more elements of the lesions described above. In one series (Tay et al, 2000), the most common component of a mixed malignancy was dysgerminoma. The most frequent combination was a dysgerminoma and an EST.

Sertoli-Leydig tumors

Sertoli-Leydig tumors account for less than 0.2-1% of ovarian cancers (Scully et al, 1998).

Lipoid cell tumors are thought to arise in adrenal cortical rests that reside in the vicinity of the ovary. More than 100 cases have been reported, and bilaterality has been noted in only a few (Scully et al, 1998).

Malignant mixed mesodermal sarcomas of the ovary are extremely rare (Le et al, 1997; Piura et al, 1998; Topuz et al, 2001 van Rijswijk et al, 1994; Berek et al, 1987; Barakat et al, 1992; Fowler et al 1996). Most lesions are heterologous.

Metastases

Approximately 5% to 6% of ovarian tumors are metastatic from other organs, most frequently from the female genital tract, the breast, or the gastrointestinal tract (Petru et al, 1992; Demopoulos et al, 1987; Young et, al 1991; Moore et al, 2004; Ayhan et al, 1995; Curtin et al, 1994; Yada-Hashimoto et al, 2003; Kim et al, 2001; Yakushiji et al,1987; Misdraji et al, 2003; Chou et al, 2003; Seidman et al, 2003; Lee et al, 2003; McBroom et al, 2000; Schofield et al, 2001). The metastases may occur from direct extension of another pelvic neoplasm, by hematogenous spread, by lymphatic spread, or from transcoelomic dissemination, with surface implantation of tumors that spread in the peritoneal cavity.

The Krukenberg tumor, which can account for 30% to 40% of metastatic cancers to the ovaries, arises in the ovarian stroma and has characteristic mucin-filled, signet-ring cells (Kim et al, 2001; Yakushiji et al 1987).

Rare cases of malignant melanoma metastatic to the ovaries have been reported (Young et al, 1991).

Metastatic carcinoid tumors are rare, representing fewer than 2% of metastatic lesions to the ovaries (Motoyama et al, 1991).

Lymphomas and leukemia can involve the ovary.

The SEER databse (http://seer.cancer.gov/csr/1975_2008/browse_csr.php?section=21&page=sect_21_table.16.html) shoes the following distribution of the histological types:

Histology	All Races	
	Count	Percent
Carcinoma	22,533	92.1%
Epidermoid carcinoma	177	0.7%
Adenocarcinoma	20,671	84.5%
Adenocarcinoma	3,223	13.2%
Papillary adenocarcinoma	531	2.2%
Clear cell adenocarcinoma	1,263	5.2%
Endometrioid carcinoma	2,479	10.1%
Cystadenocarcinoma	143	0.6%
Serous cystadenocarcinoma	3,490	14.3%
Papillary serous cystadenocarcinoma	6,840	28.0%
Mucinous cystadenocarcinoma	519	2.1%
Mucinous adenocarcinoma	880	3.6%
Mucin-producing adenocarcinoma	75	0.3%
Other adenocarcinoma	1,228	5.0%
Other specific carcinomas	544	2.2%
Stromal cell tumor	327	1.3%
Other	217	0.9%
Unspecified, Carcinoma	1,141	4.7%
Sarcoma and other soft tissue tumors	87	0.4%
Other specific types	1,629	6.7%
Mullerian mixed tumor	697	2.9%
Teratoma, malignant	358	1.5%
Other	574	2.3%
Unspecified	206	0.8%
Total	24,455	100.0%

MATERIALS AND METHODS

Our study concerning the histological types of ovarian cancer covers the 2000-2009 time-span, the data being collected from the Histopathology Exams (HPE) registers. During this period, 83.006 Ob-Gyn patients and newborns were admitted in our hospital

and 16.063 HPEs were performed (19.35% of all patients).

RESULTS

During the ten year period, a number of 1244 gynecological cancers were diagnosed in our hospital by the anatomopathology department: 731 cervical cancers (58.76%), 392 uterine cancers (31.51%), 82 ovarian cancers (6.59%), 31 vulvar cancers (2.49%), and 8 vaginal cancers (0.65%). There were 78 cases of primary ovarian cancers and five metastases with different origins, with one patient having a combination of primary cancer and metastasis.

The mean ages were 52,94±12,96 years for cervical cancer (age range 22-87 years), 61,71±9,06 years for uterine cancer (age range 38-85 years), 51,46±14,28 years for ovarian cancer (age range 18-77 years), 66,25 years for vaginal cancer (age range 51-81 years), and 65,90±9,65 years for vulvar cancer (age range 39-81 years).

Figure 1 shows the age distribution of the cases; the mean age was 51.46±14.28 years (age range 18-77 years).

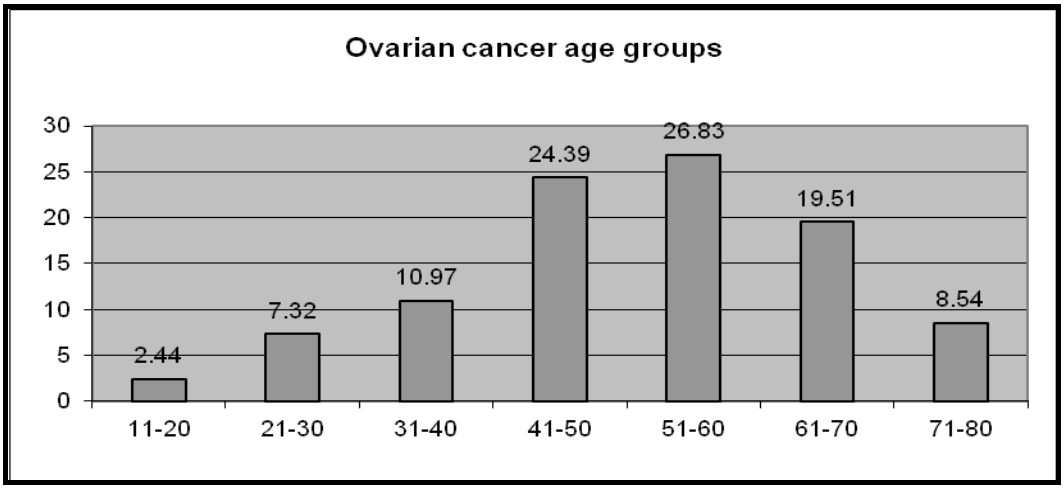

Figure 1 Ovarian cancer age groups

Cancer type	No.	% of all individual cancers types (86)	% of primary cancers (81)	% of all cancer patients (82)	% of primary cancer patients (78)
Common epithelial tumors					
Papilliferous serous cystadenocarcinoma	20	23.26	24.69	24.39	25.64
Papilliferous mucinous cystadenocarcinoma	15	17.44	18.52	18.29	19.23
Clear cell carcinoma	5	5.81	6.17	6.10	6.41
Anaplastic carcinoma	4	4.65	4.94	4.88	5.13
Clear cell adenocarcinoma	4	4.65	4.94	4.88	5.13
Endometrioid adenocarcinoma	3	3.49	3.70	3.66	3.85
Papilliferous secretory cystadenocarcinoma	3	3.49	3.70	3.66	3.85
Anaplastic small cell carcinoma	2	2.33	2.47	2.44	2.56
Serous carcinoma	2	2.33	2.47	2.44	2.56
Serous cystadenocarcinoma	2	2.33	2.47	2.44	2.56
Endometrioid cystadenocarcinoma	1	1.16	1.23	1.22	1.28
Mucinous cystadenocarcinoma	1	1.16	1.23	1.22	1.28
Neuroepithelial carcinoma	1	1.16	1.23	1.22	1.28
Nondifferentiated carcinoma	1	1.16	1.23	1.22	1.28
Papilliferous cystadenocarcinoma	1	1.16	1.23	1.22	1.28
Papilliferous endometrioid adenocarcinoma	1	1.16	1.23	1.22	1.28
Papilliferous endometrioid cystadenocarcinoma	1	1.16	1.23	1.22	1.28
Papilliferous serous adenocarcinoma	1	1.16	1.23	1.22	1.28
Secretory cystadenocarcinoma	1	1.16	1.23	1.22	1.28
Serous adenocarcinoma	1	1.16	1.23	1.22	1.28
Squamous epidermoid carcinoma	1	1.16	1.23	1.22	1.28
Sex cord and stromal tumors		1.15			0.00
Yolk sac tumor	3		3.70	3.66	3.85

Granulosa cell tumor	2	3.49	2.47	2.44	2.56
Immature teratoma	2	2.33	2.47	2.44	2.56
Disgerminoma	1	2.33	1.23	1.22	1.28
Embrional carcinoma	1	1.16	1.23	1.22	1.28
Sertoli-Leydig tumor	1	1.16	1.23	1.22	1.28
Metastases					
Immature teratoma with mucinous adenocarcinoma of intestinal metastatic origin	1	1.16		1.22	
Metastatic carcinoma, unknown origin	1	1.16		1.22	
Papillary mucinous adenocarcinoma of sigmoidian metastatic origin	1	1.16		1.22	
Metastatic carcinoma, unknown origin (gastric, breast, colonum)	1	1.16		1.22	
Metastatic diffuse type carcinoma(gastric or breast) +lobular carcinoma	1	1.16		1.22	

Table 1 Histological types of ovarian cancer

Table 1 shows the histological types of all the 82 patients with 86 types of ovarian cancer. Different types of carcinoma were detected in 71 cases of primary cancers (92.31% of the 78 patients, 87.65% of the 81 different types of primary cancers). Four cases (2.56%) had an association of two cancer types (yolk sac tumor+embrional carcinoma, immature teratoma with neuroepithelial carcinoma, papiliferous serous adenocarcinoma in one ovary and clear cell carcinoma in the other, anaplastic carcinoma with endometrioid adenocarcinoma); one patient had a mature teratoma with squamous epidermoid carcinoma.

Table 2 shows the histological types of the 71 cases of ovarian carcinoma, with adenocarcinoma being present in 55 cases (77.46%); different papillary adenocarcinoma types represented 42 cases of all adenocarcinomas (76.36%).

Primary ovarian carcinoma type	No.	% of patients
Papilliferous serous cystadenocarcinoma	20	28.17
Papilliferous mucinous cystadenocarcinoma	15	21.13
Clear cell carcinoma	5	7.04
Anaplastic carcinoma	4	5.63
Clear cell adenocarcinoma	4	5.63
Endometrioid adenocarcinoma	3	4.23
Papilliferous secretory cystadenocarcinoma	3	4.23
Anaplastic small cell carcinoma	2	2.82
Serous carcinoma	2	2.82
Serous cystadenocarcinoma	2	2.82
Endometrioid cystadenocarcinoma	1	1.41
Mucinous cystadenocarcinoma	1	1.41
Neuroepithelial carcinoma	1	1.41
Nondifferentiated carcinoma	1	1.41
Papilliferous cystadenocarcinoma	1	1.41
Papilliferous endometrioid adenocarcinoma	1	1.41
Papilliferous endometrioid cystadenocarcinoma	1	1.41
Papilliferous serous adenocarcinoma	1	1.41
Secretory cystadenocarcinoma	1	1.41
Serous adenocarcinoma	1	1.41
Squamous epidermoid carcinoma	1	1.41

Table 2 Histological types of primary ovarian carcinoma

Primary ovarian adenocarcinoma type	No.	%of adenocarcinomas
Papilliferous serous cystadenocarcinoma	20	36.36
Papilliferous mucinous cystadenocarcinoma	15	27.27
Clear cell adenocarcinoma	4	7.27
Endometrioid adenocarcinoma	3	5.45
Papilliferous secretory cystadenocarcinoma	3	5.45
Serous cystadenocarcinoma	2	3.64

Endometrioid cystadenocarcinoma	1	1.82
Mucinous cystadenocarcinoma	1	1.82
Papilliferous cystadenocarcinoma	1	1.82
Papilliferous endometrioid adenocarcinoma	1	1.82
Papilliferous endometrioid cystadenocarcinoma	1	1.82
Papilliferous serous adenocarcinoma	1	1.82
Secretory cystadenocarcinoma	1	1.82
Serous adenocarcinoma	1	1.82

Table 3 Histological types of ovarian adenocarcinoma

We have also compared the mean age of the 82 patients in the group with the mean ages of other gynecological cancers diagnosed in our hospital during the same ten-year period (Table 4) by using Student's t-test:

Type	p value
Cervical vs. ovarian	0,33
Uterine vs. ovarian	**<0,000001**
Ovarian vs. vulvar	**0,000001**

Table 4 Mean age comparisons

DISCUSSIONS, CONCLUSIONS

Several ovarian cancer histological types in our study are similar or close to those in literature, the differences being partially explained by the relatively small number of cases in our study. The following table shows the data from our study compared to several references:

	All Races		**Present study**	**Other**
Histology [seer.gov]	**Count**	**Percent**		
Carcinoma	22,533	92.10%	92.31%	90%
Epidermoid carcinoma	177	0.70%	1.23%	
Adenocarcinoma	20,671	84.50%	87.65%	
Adenocarcinoma	3,223	13.20%		
Papillary adenocarcinoma	531	2.20%		
Clear cell adenocarcinoma	1,263	5.20%	4.94%	
Endometrioid carcinoma	2,479	10.10%	7.39% (all types)	
Cystadenocarcinoma	143	0.60%		
Serous cystadenocarcinoma	3,490	14.30%	2.47%	
Papillary serous cystadenocarcinoma	6,840	28.00%	24.69%	
Mucinous cystadenocarcinoma	519	2.10%	1.23%	
Mucinous adenocarcinoma	880	3.60%		
Mucin-producing adenocarcinoma	75	0.30%		
Other adenocarcinoma	1,228	5.00%	1.23%	
Anaplasic carcinoma			4.94%	5%
Other specific carcinomas	544	2.20%	2.47%	
Stromal cell tumor	327	1.30%	2.47%	
Other	217	0.90%		
Sertoli-Leydig tumor			1.23%	0.2-1%
Dysgerminoma			1.23%	1-3%
Unspecified, Carcinoma	1,141	4.70%		
Sarcoma and other soft tissue	87	0.40%		

tumors				
Other specific types	1,629	6.70%		
Mullerian mixed tumor	697	2.90%		
Teratoma, malignant	358	1.50%	2.47%	
Other	574	2.30%		
Unspecified	206	0.80%		
Total	24,455	100.00%		

Ovarian cancer, although less frequent than other gynecological cancers, is usually diagnosed in advanced stages due to the non-specific signs and symptoms, which lead to many errors in interpreting them and to undesired delays in diagnosis and treatment, and to the lack of an organized and well conducted screening program.

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