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Survival following orbital exenteration at a tertiary brazilian hospital

Sobrevida pós exenteração de órbita em hospital de referência

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A B S T R A C T

Objective: to analyze the epidemiology, clinical features and survival rate of patients undergoing orbital exenteration (OE) in a tertiary referral hospital. **Methods**: we conducted a retrospective study of all patients undergoing OE at the Hospital das Clínicas, FMUSP between January 2007 and December 2012. We collected data records related to gender, age, origin, length of stay, duration of the disease, other treatments related to the disease, number of procedures outside of the face related to the disease, follow-up and histological diagnosis. **Results**: we treated 37 patients in the study period. The average survival in one year was 70%, in two years, 66.1%, and 58.3% in three years. There was no significant difference in the one-year survival related to histological diagnosis (p=0.15), days of hospitalization (p=0.17), gender (p=0.43), origin (p=0.78), disease duration (p=0.27) or the number of operations for the tumor (p=0.31). Mortality was higher in elderly patients (p=0.02). The average years of life lost was 33.9 in patients under 60 years, 14.7 in patients in the 61-80 years range and 11.3 in patients over 80 years. **Conclusion**: the present series of cases is significant in terms of prevalence of orbital exenteration; on the other hand, it shows one of the lowest survival rates in the literature. This suggests an urgent need for improved health care conditions to prevent deforming, radical resections.

Key words: Orbital Evisceration. Survival Rate. Carcinoma, Squamous Cell. Carcinoma, Basal Cell.

INTRODUCTION

Orbit Exenteration (OE) is one of the most disfiguring procedures among ophthalmologic operations, and is characterized by the complete removal of the contents of the orbital cavity. According to the resection extent, it can be classified into: 1) total, if there is resection of the eyelids; 2) subtotal, when preserving the eyelids; or 3) extensive, when including removal of the bone surrounding walls[1,3].

OE is the therapy of choice when other less radical methods do not result in better prognosis. It is usually indicated in oncologic resections for local control of malignant tumors. However, aggressive diseases or benign tumors that cause uncontrollable pain and structural and/or extensive lesions also require it. Among the malignant lesions, Basal cell carcinoma (BCC) is the most common skin cancer (80-90%), followed by squamous cell carcinoma (SCC). Examples of non-malignant diseases include: neurofibromatosis, fibrous dysplasia, mucormycosis, sharply contracted anophthalmic cavity, recurrent meningioma and orbital myiasis[4,5].

The aesthetic consequences have a strong psychological impact on the patient and require a multidisciplinary approach. Many patients are referred to psychological services after the operation or even refuse to undergo the surgical procedure. Constant vigilance, good doctor-patient relationship, early diagnosis and prompt treatment would provide better prognosis, especially in emerging countries[6,7].

This retrospective study aims to analyze the epidemiology, clinical features and survival rate of patients undergoing orbital exenteration (OE) in a tertiary referral hospital.

METHODS

The research project was approved by the of the Hospital das Clínicas, University of São Paulo and we carried out a retrospective study of medical records and pathology reports of all patients who underwent orbital exenteration at the facility between January 2007 and December 2012.

We identified cases by the International Classification of Diseases (ICD-10). We requested the medical records and analyzed them manually. the following data were collected: gender, age, origin, days of hospitalization, time of disease, other operations/treatments performed related to the disease, number of procedures

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performed outside the area of the face related to the disease, follow-up, histologic diagnosis and recurrence of lesions. To analyze the survival rate, we contacted the patient's family members by telephone with the help of Social Service for identification and active search for the occurrence of death.

We analyzed the variables by the Kaplan-Meier method, and compared survival curves using the log-rank test, with the R software, version 3.1.1. We calculated the Years of Potential Life Lost (YPLL) by the method proposed by Romeder[8], adjusted to the life expectancy of Brazilians in 2013[9]. The age of reference used was 78.6 for patients under 60 years of age, 83.7 for patients between 61 and 81 years, and 96.7 for patients over 80.

RESULTS

We identified 39 patients, of whom two were excluded due to incorrect coding of the disease.

Demographic and clinical characteristics of patients

The study cohort included 17 men and 20 women, between 0 and 94 years of age (mean 62.2 years). São Paulo, capital, was the origin of 15 patients (40.5%), 13 (35.1%) were from towns in the interior of São Paulo and nine (24.4%) from other Brazilian regions. Thirty-three patients were white (89.2%), one was black (2.7%) and three brown (8.1%).

The average time of diagnosis was 43.4 months (range three months to 12 years), except for congenital cases. The days of hospitalization ranged from 0 to 62, average 14. Twelve patients (35.3%) were not subjected to any other surgical procedure related to the current injury, another 12 (35.3%) underwent one operation and 10 (29.4%) underwent more than one. Seventeen patients had additional treatment such as radiotherapy (ten patients – 27%), chemotherapy (two patients – 5.4%) and cryosurgery (three patients – 8.1%). Most were not submitted to any other operation outside the face area (81.8%) and eight (21.6%) were previously treated at least once.

Histopathology

Histopathological findings included 16 cases of squamous cell carcinoma (43.2%) and ten of basal cell carcinoma (27.0%). Other diagnoses included adenoid cystic carcinoma, found in two patients, adenocarcinoma, sebaceous glands, cystic formation, inflammatory process, oncocytic schneiderian papilloma, esthesioneuroblastoma, capillary hemangioma, immature teratoma and malignant melanoma, each found in one patient (Table 1).

Survival Rate

We excluded congenital cases from the survival analysis. Two patients died during hospitalization.

At the time of the study, 15 patients had died, 15 were alive and six could not be contacted. The average survival rate at one year was 70% and this figure decreased to 66.1% and 58.3% in two and three years, respectively. Mean survival was 47.3 months.

The mortality rate was higher in older patients (p=0.02). There was no significant difference in one-year survival as for the histological diagnosis, if SCC (Figure 1), BCC or non-ECC/non-BCC (p=0.15), days of hospitalization (p=0.17), gender (p=0.43), origin (p=0.78), time of disease progression (p=0.27) or number of operations related to the tumor (p=0.31 – Table 2).

The average age of death in the age group under 60 was 44.7 years; between 61 and 80 years, 69, and in patients aged over 80 years, 85.4. Considering the life expectancy of Brazil in 2013, the average years of life lost were, respectively, 33.9 years, 14.7 years and 11.3 years. The total YPLL was 191 years (Figure 2).

DISCUSSION

Orbital exenteration is not a common procedure and is usually done in tertiary referral centers. Our case series presented one of the largest series per year (37 patients in six years). Rahman *et al.* reported 64 cases in a period of 13 years[10]; Mohr and Esser had 77 in 20 years[11]; Bartley *et al.* described 102 in 20 years[12]; and Maheshwari *et al.* published 15 in 10 years[13].

As the hospital where the study was conducted is a tertiary center, it is expected that 59.9% of patients originate from other cities as well as from São Paulo. The geographical distance from the origin to the hospital also explains the choice for OE, as the imprecise diagnosis of other health services and lagged time to admission to the

Figure 1 - *Example of squamous cell carcinoma with orbital invasion.*

Table 1 - Characteristics of patients undergoing orbital exenteration.

Patient	Gender	Age	Hospital stay (days)	Origim (State - City)	Time of disease till procedure (years)	Histopathology diagnosis	Other treatments	Number of procedures related to current lesion
1	M	74	49	SP – São Paulo	5	BCC	0	0
2	F	94	8	BA – Caculé	5	BCC	0	1
3	F	72	2	SP – São Paulo	5	CAC	RT	0
4	F	83	4	SP – Santos	7	CGS	0	2
5	M	81	22	CE – Cedro	7	SCC	0	1
6	F	65	1	MG	8	SCC	Cryosurgery	4
7	F	78	10	CE – Itapipoca	5	BCC	0	0
8	M	52	6	SP – Santos	1,7	SCC	QT	> 1
9	F	64	62	SP – São Lourenço da Serra	2	SCC	0	0
10	M	71	16	SP – São Paulo	0,4	SCC	RT + Cryosurgery	1
11	M	31	44	AM – Boca do Acre	0,3	SCC	0	0
12	F	49	16	SP – São Paulo	Unknown	SCC	Unknown	Unknown
13	F	63	2	SP – Mogi Guaçú	0,8	SCC	0	1
14	M	72	39	SP – Presidente Prudente	1	SCC	RT	1
15	F	66	2	SP – Uchôa	5	Cystic formation	0	7
16	M	49	9	SP – São Paulo	2	BCC	RT indicated	1
17	M	51	30	SP – São Paulo	2	SCC	RT	0
18	M	50	10	SP – São Paulo	5	Schneiderian papilloma	0	1
19	F	71	24	SP – Pompéia	0,5	Inflammatory process	0	2
20	M	58	9	SP – São Paulo	12	Esthesioneuroblastoma	RT	2
21	F	81	21	SP – São Paulo	2,3	SCC	Cryosurgery	2
22	M	82	4	SP – Santo Amaro	0,5	BCC	0	0
23	M	59	7	SP – Guarulhos	0,5	SCC	0	0
24	F	82	9	BA – Jequié	7	BCC	0	1
25	F	9	4	SP – Mogi Mirim	0	Capillary hemangioma	0	> 1
26	F	0	0	SP – São Paulo	0	Immature teratoma	QT	0
27	M	49	9	SP – Ibiúna	0,67	SCC	0	0
28	M	42	5	AM – Manaus	1	CAC	RT	0
29	M	69	7	SP – São Paulo	0,67	SCC	RT	0
30	F	82	7	BA – São Felix	5	BCC	0	1
31	F	42	8	SP – São Paulo	0,67	Adenocarci-noma	RT + QT	0
32	M	79	3	SP – Jandira	1	SCC	RT	1
33	M	51	7	AM – Manaus	2	SCC	0	4
34	F	82	27	SP – Mairipora	2	Malignant melanoma	0	1
35	M	60	21	SP – São Paulo	11	BCC	RT	6
36	M	51	11	SP – São Paulo	8	BCC	RT indicated	1
37	M	86	5	SP – São Paulo	6	BCC	0	3

Source: Medical records of the Hospital das Clínicas, Universidade de São Paulo (2007-2012).
BCC: basal cell carcinoma; CAC: cystic adenoid carcinoma; SGC: Sebaceous Glands Carcinoma; SCC: squamous cell carcinoma; RT: radiotherapy; QT: chemotherapy.

tertiary hospital may have made OE the only possible procedure for the control of local disease.

Among the patients cohort, three constituted non-malignant cases. SCC and BCC together accounted for 70.2% of the histological diagnosis, which is consistent with other studies. BCC is the most common skin cancer in the periorbital area, but SCC spreads more easily and requires a quick management to prevent disease progression[2,10,12,14,15]. Our findings are similar to current literature, insofar as BCC represented 27% of the OE cases, while SCC accounted for 43.2%.

Although SCC is more aggressive than BCC, the difference in survival at one year was not statistically significant between histopathologic diagnoses (p=0.15). The difference was evident only among the first 30 months or so. Some studies, however, had higher mortality after SCC

Table 2 - Comparison of age, gender, days of hospitalization, origin, time of disease, number of operations and histological diagnosis with survival rate.

Variable	Number of Cases	Number of Deaths	Mean Survivala (months)	One-year Survival
Age range				
< 60	11	4	47.1	72.7
61-80	10	3	48.4	70
> 80	9	8	23.2	66.7
Gender				
F	13	8	41.8	61.6
M	17	7	52.4	76.6
Hospital stay (days)				
< 15	18	7	54.7	83.3
15-30	8	6	28.7	60
> 30	4	2	43.8	50
Origin				
Other States	8	5	37.9	76
Capital	13	5	46.7	69.2
Towns from State interior	9	5	39	66.7
Time to diagnosis				
< 1 year	7	5	27.1	42.9
1-5 years	14	6	47	78.6
> 5 years	8	3	44.9	87.5
Number of procedures				
0	11	6	38.6	63.6
1	10	6	35.3	70
> 1	8	2	56.3	87.5
Histological diagnosis				
BCC	9	4	46.3	88.9
SCC	13	9	33.7	46.2
Non-BCC / non-SCC	8	2	62.8	87.5

Source: Medical records of the Hospital das Clínicas, Universidade de São Paulo (2007-2012).
* LogRank Test
BCC: basal cell carcinoma; SCC: squamous cell carcinoma.

than BCC[16-18]. Additional treatments, such as Mohs micrographic surgery, may have been beneficial in the management of some SCC cases[19,20].

The average mortality rate after OE also differs from the literature, since our series showed lower survival. Rahman et al. reported a survival rate of 93% in one year[10]; Mohr and Esser had 89%[11] and Chih-Hung Kuo, 97%[15]. Karabekmez *et al.*, whose study also come from an emerging country, showed a low survival rate of 50.5%[7]. Bartley *et al.* reported a survival rate of 88.6%[12].

Younger patients had on average 33.9 years of life lost as a result of diseases that lead to OE, and older

Table 3 - Years of life lost according to age group.

Age Group	N	Interval	Mean age at death time	Average years of life lost	YPLL
< 60	4	31-51	44.7	78.6	33.9
60-80	3	64-71	69	83.7	14.7
> 80	8	81-94	85.4	96.7	11.3

Source: Medical records of the Hospital das Clínicas, Universidade de São Paulo (2007-2012).
YPLL: Years of Potential Life Lost.
** According IBGE (Instituto Brasileiro de Geografia e Estatística), 2013*

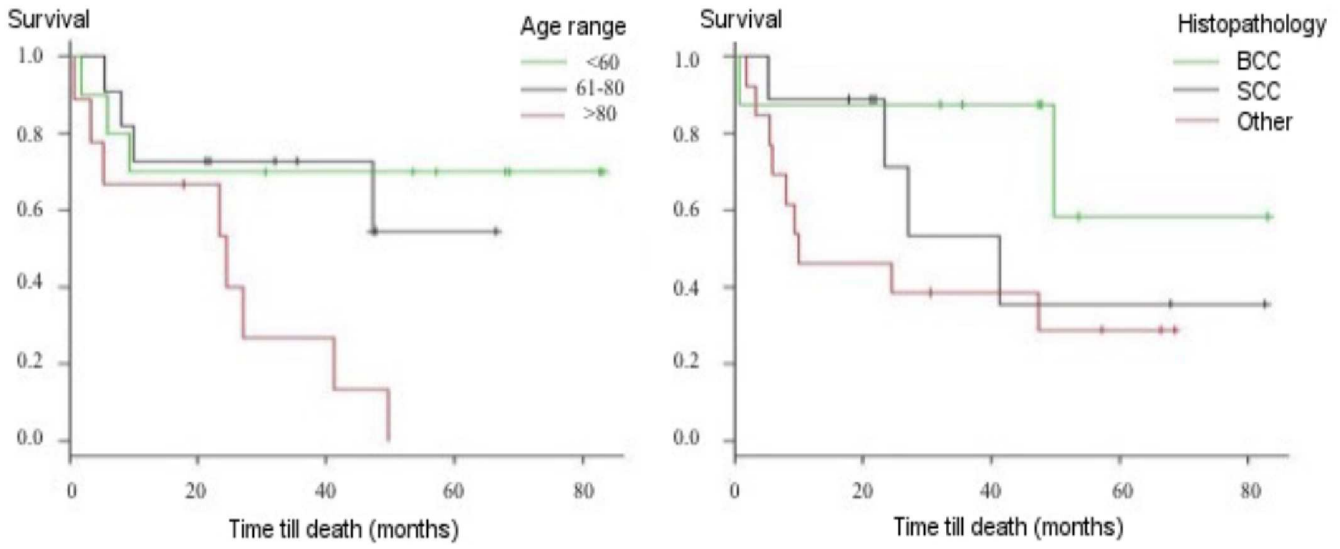

Figure 2 - *Comparison of age and histological diagnosis with survival rate.*

patients lost more than ten years. Not only the aggressiveness of the disease, but also the lack of information, difficulty in access to health care and delay in correct diagnosis justify the current low survival rate[6,21]. Studies suggest differences in post-SCC mortality between developed and developing countries[22].

Advanced age may act as a confounding variable because, generally, it is related to comorbidities and other causes of death unrelated to the tumor. However, the predominance of advanced malignant disease is already an indicator of difficulty in access to adequate medical services for immediate treatment, which could improve survival even in the older age group.

In conclusion, this case series is significant in terms of prevalence of Orbit Exenteration; On the other hand, it displayed one of the lowest survival rates in the literature. This suggests an urgent need for improved health care conditions to prevent deforming, radical resections.

R E S U M O

Objetivo: *analisar o perfil epidemiológico, as características clínicas e a taxa de sobrevida dos pacientes submetidos à exenteração orbitária (EO) em um hospital de referência terciário.* ***Métodos:*** *estudo retrospectivo de todos os pacientes submetidos à EO no Hospital das Clínicas da FMUSP entre janeiro de 2007 e dezembro de 2012. Foram coletados em prontuários dados referentes ao sexo, idade, procedência, dias de internação, tempo de evolução da doença, outros tratamentos relacionados à doença, número de procedimentos fora da face relacionados à doença, tempo de seguimento e diagnóstico histológico.* ***Resultados:*** *trinta e sete pacientes foram identificados no período de estudo. A sobrevida média em um ano foi 70%, em dois anos, 66,1% e em três anos 58,3%. Não houve diferença significativa na taxa de sobrevida de um ano em relação ao diagnóstico histológico (p=0,15), dias de hospitalização (p=0,17), sexo (p=0,43), procedência (p=0,78), tempo de evolução da doença (p=0,27) ou número de operações referentes ao tumor (p=0,31). A mortalidade foi maior em pacientes idosos (p=0,02). A média de anos de vida perdidos foi 33,9 em pacientes com menos de 60 anos, 14,7 em pacientes de 61-81 anos e 11,3 em pacientes com mais de 80 anos.* ***Conclusão:*** *a presente série de casos é significativa em termos de prevalência de exenteração orbitária; por outro lado, apresenta uma das menores sobrevidas da literatura. Isso sugere uma necessidade urgente de melhora das condições de assistência médica para a prevenção de ressecções radicais deformadoras.*

Descritores: *Exenteração Orbitária. Taxa de Sobrevida. Carcinoma de Células Escamosas. Carcinoma Basocelular.*

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