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Two years of experience on eye tumors radical surgical treatments at a referential oncology hospital

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Abstract

Introduction: Maliganancies of eye and adnexa affect a variable percentage of all cancers. Several studies have described experiences in orbital exenteration and enucleation in Brazil and other countries around the world, but no such report is available describing the Amazonas State experience. Objectives: Review all cases of radical surgical eye treatment, including orbital exenteration and eye enucleation, at the Head and Neck Department of the Oncology Control Center Foundation (FCECON) – Brazil. Quantify the number of orbital exenterations and eye enucleations over 2 years. Identify the histopathological type of tumor, age, sex, racial group and patients' origin. Material and Methods: Observational case series of patients who underwent orbital radical surgery at the Head and Neck Department of FCECON between March 1, 2011 and March 31, 2013.Medical records were reviewed and analyzed using Epi-Info 7. Results: 40 patient charts were retrospectively analyzed. Ages ranged from 3 to 89 years (mean of 63.5 years). Of these, 21 were female and 19 were male, most of them European-Amerindian descents. All lesions that led to radical eye surgery were malignant neoplasms; however, none of them were metastatic. Most cases were classified as squamous cell carcinoma (20 cases). Eight eye enucleations and thirty-two orbit exenterations were performed. Conclusion: Late diagnosis of eye tumors seems to contribute to the orbital continuous invasion, conceiving poor prognosis to the patients and a great loss in quality of life.

Keywords: Orbit; Eye enucleation; Eye neoplasms.

Resumo

Introdução: As neoplasias do olho e anexos afetam uma percentagem variável de todos os cânceres. Vários estudos descreveram experiências de exenteração e enucleação

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orbital no Brasil e em outros países do mundo, mas não há nenhum relato disponível descrevendo a experiência do Estado do Amazonas. Objetivos: Revisar todos os casos de tratamento cirúrgico radical ocular, incluindo exenteração orbitária e enucleação ocular, no Departamento de Cabeça e Pescoço da Fundação Centro de Controle de Oncologia (FCECON) – Brasil. Quantificar o número de exenterações orbitais e enucleações oculares ao longo de 2 anos. Identificar o tipo histológico do tumor, idade, sexo, grupo racial e procedência do paciente. Material e Métodos: Série de casos observacionais de pacientes submetidos à cirurgia radical orbitária no Departamento de Cabeça e Pescoço da FCECON entre 01 de março de 2011 e 31 de março de 2013. Os prontuários foram revisados e os dados analisados no Epi-Info 7. Resultados: 40 prontuários foram analisados retrospectivamente. A idade variou de 3 a 89 anos (média de 63,5 anos). Destes, 21 eram do sexo feminino e 19 do sexo masculino, a maioria pardos. Todas as lesões que levaram à cirurgia ocular radical eram neoplasias malignas; no entanto, nenhuma delas era proveniente de metástase. A maioria dos casos foi classificada como carcinoma espinocelular (20 casos). Oito enucleações oculares e trinta e duas exenterações de órbita foram realizadas. Conclusão: O diagnóstico tardio de tumores oculares parece contribuir para a invasão orbital por continuidade, o que gera mau prognóstico aos pacientes e grande prejuízo na qualidade de vida pós-tratamento.

Palavras-chave: Órbita; Enucleação ocular; Neoplasias oculares.

1. Introduction

Maliganancies of the eye and adnexa affect a variable percentage of all cancers. Orbital exenteration is the removal of the orbit contents – eye, adnexa and part of bony orbit (ROCHE, 2012). Radical surgical procedures to remove orbital malignant neoplasias may involve partial or complete excision of the eyelids or resection of the orbit wall and neighboring sinuses (NASSAB, 2007). This type of surgery is most commonly performed for locally advanced cancer or recurrent periorbital malignances, in an attempt for cure (BEN SIMON, 2005). It is also performed in cases of painful or life-threatening orbital inflammations or infections. Malignancies of the ocular adnexa are the most prevalent cause of orbital exenteration and include squamous cell carcinoma (SCC), sebaceous cell carcinoma, and basal cell carcinoma (BCC) (BEN SIMON, 2005). Beteeen 40 to 50% of the published studies on exenterations are on tumors in the eyelid or periocular skin and show that the incidence of these tumors varies acording to patient's geographical area and racial group (TYERS, 2006). Eye enucleation is the removal of the eye globe leaving the remaining orbital contents intact, including eye muscles. This type of eye surgery is indicated for ocular tumors restricted to the eye globe, eyes that have suffered severe trauma, and eyes that are otherwise blind and painful (SHAH-DESAI, 2000).

Orbital exenterations result in facial deformity, representing a reconstructive challenge, especially in elderly patients with significant comorbidities (ROCHE, 2012; QASSEMYAR, 2014). Several studies have described experiences in orbital exenteration in Brazil and other countries but no such report is available describing the Amazonas State experience, a region in which most individuals are of European-Amerindian descendants (77.2% of the population). The present study analyzed the clinical, histopathological and epidemiological data over a two-year period of patients who underwent radical eye surgical treatment as orbital exenteration and eye enucleation.

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2. Method

Medical records from March 2011 to March 2013 were retrieved from the Department of Head and Neck of the Oncology Control Center Foundation (FCECON). FCECON is located in Manaus, State of Amazonas and is the reference for cancer treatment in the state and in Northern Brazil. The Amazonas State population is over three million people. Information concerning demographic profile, ethnical group, mortality, pathology, as well as, patient's primary lesion site was obtained from medical records. This retrospective study complied with the policies determined by the local institute review board, was granted official approval and exemption of the Informed Consent Form from the Research Ethics Committee (REC), (Protocol CAAE 19258313.0.0000.0004).

All cases of orbital exenteration treated at FCECON were analyzed by using Epi-Info 7, a freely distributed software developed by Center of Disease Control - CDC (www.cdc.gov/epiinfo). The inclusion criteria to be included in the study was histopathological diagnosis of orbital or periorbital malignancy.

The database was presented in tables, in which simple, absolute and relative frequencies were determined for categorical data. For quantitative analysis, we calculated the median because the Shapiro-Wilk test indicated no normal distribution at 5% significance. The chi-square test with Yates correction and the Fisher exact test were applied for categorical data; when the Yates test was not possible, we used 2x2 tables. The nonparametric Mann-Whitney test was applied to compare the median age and categorical data.

3. Results

Forty patients underwent radical orbital procedures during the studied period. The criteria applied to indicate the need for these radical eye surgeries were locally advanced cancer or recurrent periorbital malignances. Eight eye enucleations (20%) and 32 orbit exenterations (80%) were performed. The intent in doing these surgeries was to treat tumors at early stages (36 cases) but salvage surgery was also done (4 cases). Three patients had been previously submitted to chemotherapy. There were two cases of retinoblastoma and one multiple myeloma. Ages ranged from 1 to 89 years (mean of 63.5 years). A total of 21 patients were female (52.5%) and 19 were male (47.5%); most of them were European-Amerindians descents (87.5%).

The histopathology analysis revealed that 20 out of 40 tumors were squamous cell carcinoma (50%). Other diagnoses found, and their frequencies, are in Table1. During the 3-year period of follow up, 14 patients (35%) died before one year past surgery while 26 (65%) remained alive. Eight patients were treated with eye enucleation due to retinoblastoma (4 cases), squamous cell carcinoma (2 cases), malignant melanoma (1 case) and meningioma (1 case). According to the Mann-Whitney's Test, the average age of squamous cell carcinoma was 73.5 years, with little variation in the ages of patients with this type of tumor. And among the other tumors observed, the average age was 44 years with great variation.

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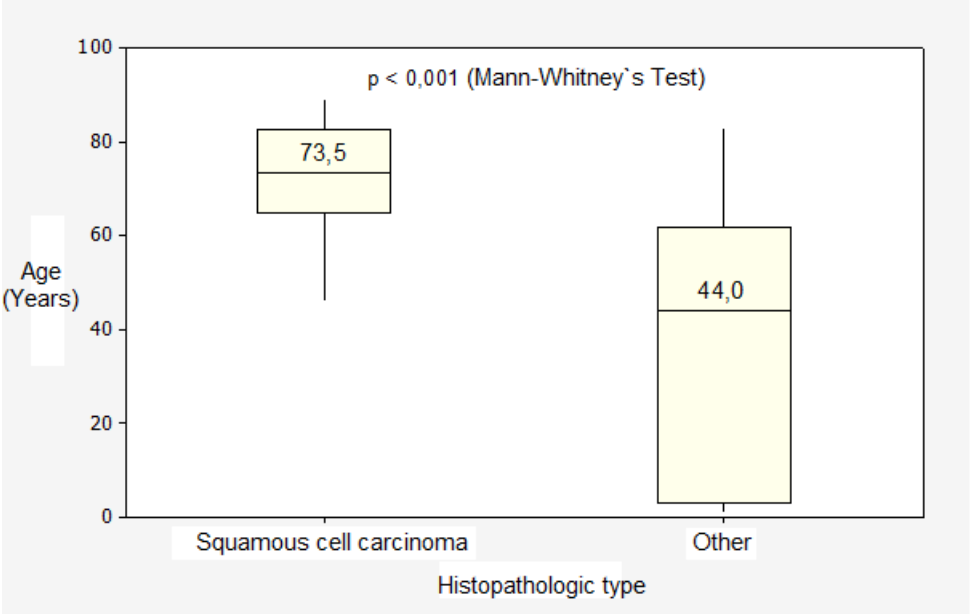

Figure 1. Patients' ages treated with radical eye surgery at FCECON, Amazonas state, Brazil according to the histopathological type of tumor (Mann-Whitney's Test).

It is known that some tumors cannot be properly staged, not being possible to compare the TNM stage. An overview of the 40 cases presented in this study is in Table 1.

Table 1. Overview of 40 tumor cases treated with radical eye surgery in a two-year study done in the Amazonas state, Brazil.

Gender	Age (years)	Patients´s race	Histopathological diagnosis	TNM stage	First treatment	Type of surgery performed	Death in 3 years follow-up
Male	3	European-Amerindian	Retinoblastoma	T4N0M0	Surgery	Orbit exenteration (Rescue surgery)	YES
Female	37	European-Amerindian	Multiple Myeloma	T4N0M0	Chemotherapy	Orbit exenteration (Rescue surgery)	YES
Female	61	European-Amerindian	Chondroblastic osteosarcoma	T3N0M0	Surgery	Orbit exenteration + maxillectomy (Inicial treatment)	YES
Female	63	European-Amerindian	Fusocellular sarcoma	T4N0M0	Surgery	Orbit exenteration + maxillectomy (Inicial treatment)	NO
Female	64	European-	Squamous cell	T2N0M0	Surgery	Orbit	YES

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		Amerindian	carcinoma			exenteration (Inicial treatment)	
Female	75	European-Amerindian	Squamous cell carcinoma	T4N0M0	Surgery	Orbit exenteration + maxillectomy Inicial treatment	NO
Female	65	Caucasian	Squamous cell carcinoma	T4N1M0	Surgery	Orbit exenteration Inicial treatment	NO
Male	48	Afro-descendant	Multiple myeloma	T1N0M0	Surgery	Orbit exenteration Inicial treatment	NO
Female	73	European-Amerindian	Squamous cell carcinoma	T4N0M0	Surgery	Orbit exenteration Inicial treatment	NO
Male	69	European-Amerindian	Squamous cell carcinoma	T4N0M0	Surgery	Orbit exenteration + maxillectomy Inicial treatment	YES
Female	64	European-Amerindian	Maxillary sinus adnexal microcystic carcinoma	T4N0M0	Surgery	Orbit exenteration + maxillectomy Inicial treatment	YES
Female	57	European-Amerindian	Basal cell carcinoma	T2N0M0	Surgery	Orbit exenteration Inicial treatment	NO
Male	52	European-Amerindian	Squamous cell carcinoma	T4N0M0	Surgery	Orbit exenteration Inicial treatment	NO
Male	78	European-Amerindian	Squamous cell carcinoma	T4N0M0	Surgery	Orbit exenteration + maxillectomy Inicial treatment	NO
Male	66	European-Amerindian	Squamous cell carcinoma	T3N0M0	Surgery	Orbit exenteration Inicial treatment	NO
Male	51	European-Amerindian	Fusocellular sarcoma	T4N1M0	Surgery	Orbit exenteration Inicial treatment	YES
Female	39	European-Amerindian	Meningeoma	T4N0M0	Surgery	Eye enucleation Inicial treatment	NO

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Female	79	European-Amerindian	Multiple Myeloma	T1N0M0	Surgery	Orbit exenteration Inicial treatment	NO
Male	67	European-Amerindian	Squamous cell carcinoma	T4N0M0	Surgery	Orbit exenteration Inicial treatment	NO
Female	40	European-Amerindian	Meningeoma	T4N0M0	Surgery	Orbit exenteration Inicial treatment	NO
Male	82	Caucasian	Squamous cell carcinoma	T4N0M0	Surgery	Orbit exenteration + maxillectomy Inicial treatment	NO
Female	46	European-Amerindian	Squamous cell carcinoma	T4N0M0	Surgery	Orbit exenteration Inicial treatment	NO
Male	3	European-Amerindian	Rhabdomyosarcoma	T4N0M0	Surgery	Orbit exenteration Inicial treatment	NO
Female	86	Amerindian	Squamous cell carcinoma	T2N0M0	Surgery	Eye enucleation Inicial treatment	NO
Male	62	European-Amerindian	Basal cell carcinoma	T2N0M0	Surgery	Orbit exenteration Inicial treatment	NO
Male	65	European-Amerindian	Squamous cell carcinoma	T4N0M0	Surgery	Orbit exenteration Inicial treatment	NO
Female	83	European-Amerindian	Fusocellular sarcoma	T3N0M0	Surgery	Orbit exenteration Inicial treatment	YES
Female	47	Caucasian	Squamous cell carcinoma	T2N0M0	Surgery	Orbit exenteration Inicial treatment	NO
Female	89	European-Amerindian	Squamous cell carcinoma	T4N0M0	Surgery	Orbit exenteration Inicial treatment	YES
Male	76	European-Amerindian	Squamous cell carcinoma	T4N0M0	Surgery	Orbit exenteration Inicial treatment	NO
Male	83	European-Amerindian	Squamous cell carcinoma	T4N0M0	Surgery	Orbit exenteration Inicial treatment	NO
Male	48	European-	Malignant melanoma	T4N0M0	Surgery	Orbit	NO

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		Amerindian				exenteration Inicial treatment	
Male	74	European-Amerindian	Squamous cell carcinoma	T4N0M0	Surgery	Eye enucleation Inicial treatment	NO
Female	1	European-Amerindian	Retinoblastoma	T4N0M0	Surgery	Eye enucleation Inicial treatment	NO
Male	2	European-Amerindian	Retinoblastoma	T4N0M0	Chemotherapy	Eye enucleation Rescue surgery	YES
Female	83	European-Amerindian	Squamous cell carcinoma	T2N0M0	Surgery	Orbit exenteration Inicial treatment	NO
Female	87	European-Amerindian	Squamous cell carcinoma	T4N0M0	Surgery	Orbit exenteration Inicial treatment	YES
Female	3	European-Amerindian	Retinoblastoma	T4N0M0	Surgery	Eye enucleation Inicial treatment	YES
Male	1	European-Amerindian	Retinoblastoma	T4N3M1	Chemotherapy	Eye enucleation Rescue surgery	YES
Male	33	European-Amerindian	Malignant melanoma	T4N3M1	Surgery	Eye enucleation Inicial treatment	YES

The average survival rate in the presente study in three years was 65%, 40% in five years and 20% in ten years (Figure 2). A study conducted in the southeastern region of Brazil reported 14 cases of orbital exenteration from 1993 to 2016, with an average five-year survival rate of 71.4% (Ferreira, 2016) whereas another study conducted at a referral oncology center in São Paulo reported 37 cases of orbital exenteration from 2007 to 2012, with an average three-year survival rate of 58.3% (Kato, 2016).

4. Discussion

Orbital exenteration and eye enucleation are invasive surgical procedures reserved for the treatment of malignant lesions, locally invasive or recurrent tumors, recalcitrant ocular inflammatory disorders with intractable pain, or fungal infections of the orbit (Maheshwari, 2010). While these procedures are radical treatments aimed at curing the disease, they may result in surgical sequelae and disfigurement for the patient. Managing these patients requires a multidisciplinary approach involving head and neck surgeons, ophthalmologists, wound care specialist nurses, and clinical psychologists (Rahman, 2005). (RAHMAN, 2005).

During the study period (2 years), 40 patients underwent radical eye surgery, 32 orbital exenterations and 8 eye enucleations, performed in order to treat malignant diseases, according to topatients' diagnosesdescribed above. Considering only orbital

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exenterations, our study performed 16 surgeries per year. Comparison with publications available from 2010 to 2014 shows that, in Australia, approximately 2.53 orbital exenteration surgeries were performed per year (Kuo, 2011), while in Turkey, the number was around 6.8 per year in 2010 (Soysal, 2010) and 1.5 per year in 2014 (Karabekmez, 2014). In India, the rate was around 1.5 surgeries per year (Maheshwari, 2010), while in France, it was 1.73 per year (Qassemeyar, 2014). In southern Brazil, the rate was approximately 2.63 surgeries per year (Rech, 2012). In comparison, FCECON had a rate that was five times higher than the national and international occurrences reported in the literature.

Other comparisons are shown in Table 2.

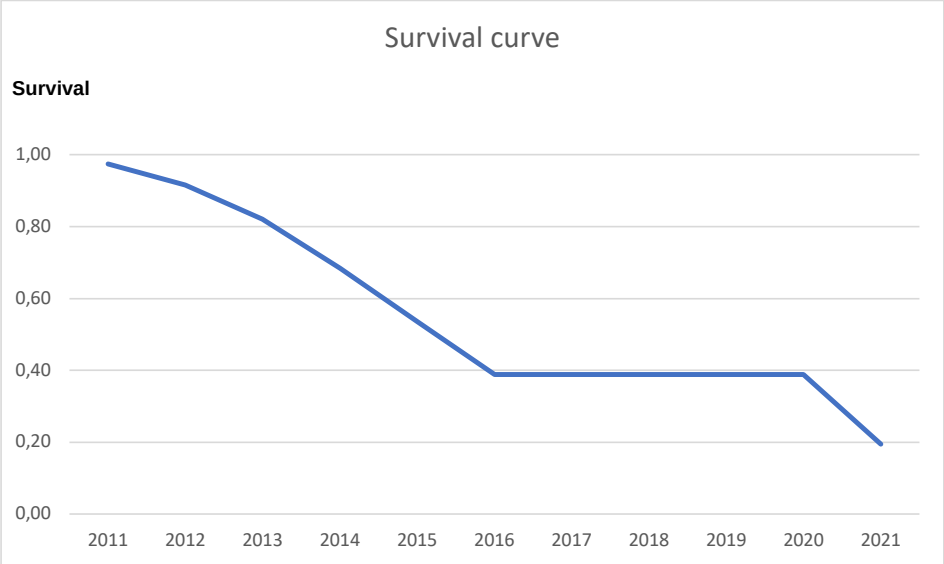

Figure 2. Survival curve of patients treated with radical eye surgery at FCECON, Amazonas state, Brazil, according to Kaplan–Meier survival curve

The most common malignant disease in this study was squamous cell carcinoma, similar to what was reported in Australian, Turkish and other two Brazilian studies (KUO, 2011; SOYSAL, 2010; RECH, 2012; ATIQUE-TACLA, 2006). However, studies done in Frence and England reported Basal cell carcinoma as the tumor that mostly required exenterations (NASSAB, 2007; QASSEMYAR, 2014; RAHMAN, 2005). In India, sebaceous gland carcinoma was more prevalent (MAHESHWARI, 2010) and a study from Scotland identified malignant melanoma as the most common tumor that was treated with radical orbital surgery (TAYLOR, 2006).

In our study, 14 patients (35%) died before one year past surgery. These patients had advanced retinoblastoma (4 cases), squamous cell carcinoma (4 cases), fusocellular sarcoma (2 cases), chondroblastic osteosarcoma (1 case), maxillary sinus adnexal microcystic carcinoma (1 case), malignant melanoma (1 case) and multiple myeloma (1e case), which represents twice the number of different countries (KUO, 2011; SOYSAL, 2010; NEMET, 2007).

This higher number of radical surgical procedures and mortality rate, if compared with numbers reported in studies done in other countries, can be explained by many reasons. The Amazon region presents geographical limitations and logistical difficulties, worsened by poor and expensive transportation that restrains patients timely access to

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treatment. Some cities are more than 14-days away by boat trip from the state capital, where our hospital is located. These facts contribute to delay in diagnosis and by the time these patients receive treatment at FCECON, the disease is in an advanced stage (T3/T4). The high rate of aggressive surgeries among the patients treated at the Head and Neck Surgical Department at FCECON can be explained by the absence of a public Ophthalmologic Centre specialized in eye-oncology in the Amazonas that could properly diagnose the diseases in the early stages and give the proper treatment. That is why head and neck surgeons mostly perform retinoblastoma surgery in the Northern region of Brazil.

In addition, the number of specialist physicians in the region often does not meet the high demand of patients, resulting in long waiting times for surgical procedures and extended pre- and post-operative control consultations. This delay may compromise the treatment of recurrences leading to greater morbidity and premature death.

Table 2. Literature review of orbital exenteration, including author, year of publication, country, period of retrospective study, mean number of radical orbital surgeries done per year and most common malignant disease.

Author	Year	Country	Study period	Orbital exenteration(n)	N per year	Most commom tumor
Kuo, et al	2010	Australia	15 years	38	2.53	Squamous cell carcinoma
Taylor, A.	2006	Scotland	11 years	14	1.27	Malignant melanoma
Maheshwari	2010	India	10 years	15	1.5	Sebaceous gland carcinoma
Rahman, et al	2005	England	13 years	68	5.23	Basal cell carcinoma
Atique-Tacla, et al	2006	Brazil (São Paulo)	5 years	21	4.2	Squamous cell carcinoma
Soysal, et al	2010	Turkey	10 years	68	6.8	Squamous cell carcinoma
Nassab, et al	2007	England	20 years	32	1.6	Basalcell carcinoma
Nemet, et al	2007	Australia	15 years	38	2.53	Basal cell carcinoma
Rech, et al	2012	Brazil (Rio Grande do Sul)	8 years	21	2.63	Squamous cell carcinoma
Qasseymar et al	2014	France	15 years	26	1.73	Basal cell carcinoma
Karabekmez et al	2014	Turkey	6 years	9	1.5	Squamous cell carcinoma
Present study	2014	Brazil (Amazonas)	2 years	32	16	Squamous cell carcinoma

Most patients were European-Amerindian descendant, however the national and international literature indicates that orbital tumors are more frequent among Caucasians (ROCHE, 2012; TYERS, 2006; MAHESHWARI, 2010; RAHMAN, 2005; SOYSAL, 2010; RECH, 2012; ATIQUE-TACLA, 2006; TAYLOR, 2006; NEMET 2007). In the Amazonas State, European-Amerindian descendants represents 77.2% of the population (IBGE, 2010), they are the miscegenation between Amerindians and Europeans that staretd in the 19th century (IBGE, 2010). Most studies report that skin tumors are more common in Caucasians, but due to the high incidence of sunlight near the equator, skin tumors are very frequent in Northern Brazil in the European-Amerindian descendants and Afro-descendants.

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Two cases of orbital meningioma were found in the present study, with an orbital enucleation and an orbital exenteration being performed due to an aggressive tumor growth associated with local infection and loss of ocular function.

Retinoblastoma is a tumor that has a genetic basis and is the most common eye cancer in children (PARK, 2014; PALAZZI, 2013). Five of 40 patients (12.5%) who underwent radical orbital procedures in this study were patients with retinoblastoma. Two patients were one-year-old, two patients were three-years-old and one patient was two-years-old, two were females and three were males. The prevalence among male children and the early ages of tumor appearance are in accordance with the national and international literature data (PARK, 2014; PALAZZI, 2013). One case underwent orbital exenteration as treatment for a cancer in its initial stages one underwent orbital exenteration as a rescue treatment and three cases underwent eye enucleation as initial treatment. Also, in the present study 4 out of 5 retinoblastoma patients (80%) died before one year past surgery. Park et al (2014) reported 7.9% of mortality in Korean children with retinoblastoma (PARK, 2014), which agrees with the international average, while Palazzi (2013) in Brazil reported a mortality of 21% (PALAZZI, 2013). Therefore, the mortality rate observed in the present study is aligned with both international and national literature data.

It is understood that a single specialized center would not be enough to treat all orbital tumors in the Amazon region. The possibility that genetic factors may plpay a role in the genesis of tumors is raised. This hypothesis deserves further investigation. The T3 and T4 stage tumors distribution among young people is also to be pointed out because its proper treatment, the radical eye surgery, can be a more painful and detrimental act. In these cases, a multidisciplinary care in order to support patients to restores their physical and psychological health is required.

In the northern region of Brazil there is no public orbital reconstruction service to esthetically rehabilitate enucleated or exenterated patients. Thus, the patient needs to have the orbital prosthesis done through research initiatives at local public universities or even through their own and paid means.

5. Conclusion

Delayed diagnosis of eye tumors can lead to continuous invasion of the orbit and a poor prognosis for patients. In some cases, this can result in the need for eye enucleation or orbit exenteration, which can have a significant impact on a patient's quality of life.

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Disclosure

This is an original study not being considered by any other journal. The author(s) and reviewers did not report any conflict of interest during their review. Therefore, the journal Scientia Amazonia holds the copyright, has the approval and permission of the authors to disseminate this article by electronic means. The authors have no financial disclosures.

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