**Characterization of all surgical specimens provided by a Portuguese Department of Ophthalmology, over 13 years activity**

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**Title for header**

Characterization of ophthalmic surgical specimens

**C****haracterization of all surgical specimens provided by a Portuguese Department of Ophthalmology, over 13 years activity.**

**Abstract**

Purpose: We intend to evaluate clinically, topographically and morphologically all specimens sent by a Department of Ophthalmology of Hospital de Braga to same venue Department of Pathology.

Methods: Two hundred and fifty eight surgically obtained specimens, from the
Department of Ophthalmology of Hospital de Braga, analysed in same venue
Department of Pathology, during the period from January 2002 to June 2015,
were characterized. Data was arranged according to year, age, sex, topography and morphological diagnosis according SNOMED ® coding system.

Results: Mean age at time of diagnosis was 54,6 years old; 52,3% were male subjects. The number of specimens oscillated little until the year 2010, with a significant increase between 2011 and 2013. Most frequent topography was eyelid (54,7%), followed by conjunctiva (26,7%); and most frequent morphological diagnosis was malignant epithelial lesions (22,48%), followed by melanocytic tumours (22,09%) and benign epithelial lesions (17,05%).

Discussion: The results are distinct from previous publications presumably because of differences between the populations submitted to analysis.

Conclusion: This is the first indexed publication characterizing ophthalmic specimens of a Department of ophthalmology in Portugal; moreover, it also includes an extensive review over world wide ophthalmic specimens epidemic data.

Keywords: SNOMED; ocular pathology.

**Caracterização de todas as amostras biológicas colhidas num Serviço de Oftalmologia Português durante 13 anos de atividade**

Objetivo: Pretende-se avaliar clínica, topográfica e morfologicamente todos as amostras biológicas enviadas pelo Serviço de Oftalmologia do Hospital de Braga para o Serviço de Anatomia Patológica do mesmo Hospital.

Métodos: Duzentas e cinquenta e oito amostras biológicas obtidas cirurgicamente pelo Serviço de Oftalmologia do Hospital de Braga e analisadas pelo Serviço de Anatomia Patológica (Hospital de Braga), no período de janeiro de 2002 a junho de 2015. Os dados foram organizados de acordo com o ano, idade, sexo, topografia e diagnóstico morfológico de acordo com sistema de codificação SNOMED ®.

Resultados: A idade média dos doentes à altura do diagnóstico foi de 54,6 anos, sendo 52,3% destes indivíduos do sexo masculino. O número de amostras oscilou pouco até ao ano 2010, verificando-se um aumento importante entre 2011 e 2013. A maioria das amostras biológicas enviadas foram de pele de pálpebra (54,7%), seguida de conjuntiva (26,7%); os diagnósticos morfológicos mais comuns foram as lesões epiteliais malignas (22,48%), seguido pelos tumores melanócitos (22,09%) e as lesões epiteliais benignas (17,05%).

Discussão: Os resultados são distintos das publicações anteriores, presumivelmente devido a diferenças entre as populações analisadas.

Conclusão: Esta é a primeira publicação indexada caracterizando as amostras biológicas de um Serviço de Oftalmologia em Portugal; além disso, inclui uma extensa revisão de dados epidemiológicos sobre amostras biológicas oftalmológicas a nível global.

Palavras chave: SNOMED; patologia ocular.

**Introduction**

The data of diagnosis coming from ophthalmic surgically
obtained specimens have been published since long time. In 1998, Spraul et al. [1] reported a retrospective long term (55 years) and large (24.444 specimens) study, providing relative frequencies of specimens submitted to a Department of Pathology that exclusively evaluated these ophthalmic specimens. After this, many consecutive large studies have been published accounting relative frequencies of morphological diagnosis and/or histological examination of specific tissues; however, none of them have had analysed all ophthalmic surgical specimens obtained by a single Department of Ophthalmology.

In this study, characterization of all the ophthalmic surgical specimens examined by the Department of Pathology of the same hospital was performed, over a 13 year period of time.

**Materials and methods**

In this study, it’s reported everlasting cases of specimens submitted from the Department of Ophthalmology of Hospital de Braga to same venue Department of Pathology, corresponding to the period between January 2002 and June 2015. Year of surgery, year of diagnosis, age, sex and SNOMED Topography and Diagnostic Codes for Ophthalmic Pathology of all specimens were introduced in a database. No phacoemulsification or vitrectomy fluid aspirations were evaluated. All specimens were histologically analysed with light microscopy.

**Results:**

Two hundred and fifty eight cases were reviewed, corresponding to a period of 12,5 years (150 months), from January 2002 to June 2015. The number of specimens, which had been stable until 2010, increased between the period from 2011 to 2013, remaining stable until today (Figure 1).

Figure 1 – Number of specimens distributed by year.

Age and sex were recorded in all cases. Ages ranged from 8 month-old to 97,4 year-old, and its distribution is shown in Figure 2; mean age was 54,6 year-old and its standard deviation was 24,5 year-old. There were 135 (52,3%) males and 123 females (47,7%); all were caucasians.

Figure 2 - Distribution of specimens by patients’ age.

The relative frequency of topographic locations with histologic diagnosis is presented in Figure 3. The most common was eyelid (n=141), followed by conjunctiva (n=69), orbit (n=23), enucleation (n=13), cornea (n=5), lacrimal gland (n=3), caruncula (n=2) and other (ciliary body and choroid, n=2).

Figure 3 - Relative frequency of topographic locations of specimens

Eyelid specimens were the most common (Table 1). Mean age was 60,7 year-old and female gender was the most affected (n=79; 56,03%). Malignant epithelial lesions comprised the most frequent lesions.

**TABLE 1 - FREQUENCY OF SPECIMENS FROM EYELID**

|  |  |  |  |
| --- | --- | --- | --- |
| Eyelid | Number  | %  | Mean age  |
| Miscellaneous lesions | **7** | **4,96%** | **64** |
| Cutaneous Calcinosis | 1 | 14,29% | 79 |
| Fibrosis  | 3 | 42,86% | 65,33 |
| Other | 3 | 42,86% | 57,67 |
| Inflammation  | **9** | **6,38%** | **49,44** |
| Chronic Inflammation, unspecific | 8 | 88,89% | 53,75 |
| Granulation tissue proliferation | 1 | 11,11% | 15 |
| Infeccious Diseases | **3** | **2,13%** | **18,33** |
| *Molluscum contagiosum* | 1 | 33,33% | 6 |
| Wart  | 2 | 66,67% | 24,5 |
| Benign Epithelial Lesions  | **30** | **21,28%** | **54,17** |
| Epithelial Cysts  | 11 | 36,67% | 35,73 |
| Squamous Cell Papilloma  | 3 | 10,00% | 55 |
| Hyperkeratosis | 1 | 3,33% | 40 |
| Seborrheic Keratosis | 12 | 40,00% | 70,33 |
| Keratoacanthoma | 1 | 3,33% | 40 |
| Hyperplasia  | 2 | 6,67% | 71,5 |
| Precancerous Epithelial Lesions  | **2** | **1,42%** | **81,5** |
| Actinic Keratosis  | 2 | 100,00% | 81,5 |
| Malignant Epithelial Tumours | **51** | **36,17%** | **74,69** |
| Basal Cell Carcinoma  | 45 | 88,24% | 74,07 |
| Squamous Cell Carcinoma  | 6 | 11,76% | 79,33 |
| Melanocytic Tumours  | **31** | **21,99%** | **52,16** |
| Blue Nevus  | 2 | 6,45% | 51,5 |
| Juncional Nevus  | 2 | 6,45% | 38 |
| Compound Nevus  | 8 | 25,81% | 51,63 |
| Dermal Nevus  | 19 | 61,29% | 53,95 |
| Tumours of the Pilar Structures of the Eyelid  | **1** | **0,71%** | **9** |
| Pilomatrixoma  | 1 | 100,00% | 9 |
| Vascular Tumours  | **6** | **4,26%** | **51,83** |
| Capillary Hemangioma  | 2 | 33,33% | 67,5 |
| Cavernous Hemangioma  | 3 | 50,00% | 58,33 |
| Hemangioendothelioma  | 1 | 16,67% | 1 |
| Lymphoid Disorders | **1** | **0,71%** | **76** |
| Lymphoma  |  |  |  |
| Diffuse Large B-cell Lymphoma  | 1 | 100,00% | 76 |
| Total  | **141** |  |  |

The second tissue most commonly analysed was conjunctiva (Table 2). Mean age was 46,1 year-old, and male gender was the commonest (n=44; 63,7%). Melanocytic tumours were the most frequent diagnosis.

TABLE 2 - FREQUENCY OF SPECIMENS FROM CONJUNCTIVA

|  |  |  |  |
| --- | --- | --- | --- |
| Conjuntiva  | Number  | %  | Mean age  |
| Miscellaneous lesions | **10** | **14,49%** | **52,6** |
| Hemorrhage  | 1 | 10,00% | 84 |
| Fibrosis  | 1 | 10,00% | 28 |
| Other | 8 | 80,00% | 51,75 |
| Inflammation  | **8** | **11,59%** | **34,63** |
| Inflammation, unspecific | 2 | 25,00% | 44 |
| Chronic Inflammation, unspecific | 3 | 37,50% | 26 |
| Granulation tissue proliferation | 3 | 37,50% | 37 |
| Degenerative Lesions | **4** | **5,80%** | **57,25** |
| Pinguecula  | 4 | 100,00% | 57,25 |
| Benign Epithelial Tumours  | **4** | **5,80%** | **51,5** |
| Epithelial Cysts  | 1 | 25,00% | 22 |
| Squamous Cell Papilloma  | 3 | 75,00% | 61,33 |
| Precancerous Epithelial Lesions  | **6** | **8,70%** | **60** |
| Actinic Keratosis  | 6 | 100,00% | 60 |
| Malignant Epithelial Tumours | **7** | **10,14%** | **72,43** |
| Basal Cell Carcinoma  | 1 | 14,29% | 74 |
| Squamous Cell Carcinoma  | 6 | 85,71% | 72,17 |
| Melanocytic Tumours  | **25** | **36,23%** | **35,76** |
| Lentigo  | 2 | 8,00% | 57,5 |
| Juncional Nevus  | 1 | 4,00% | 29 |
| Compound Nevus  | 15 | 60,00% | 24,93 |
| Dermal nevus  | 7 | 28,00% | 53,71 |
| Vascular Tumours  | **2** | **2,90%** | **16,5** |
| Pyogenic Granuloma  | 1 | 50,00% | 30 |
| Cavernous Hemangioma  | 1 | 50,00% | 3 |
| Lymphoid Disorders | **2** | **2,90%** | **34,5** |
| Lymphoid Hiperplasia  | 1 | 50,00% | 14 |
| Lymphoma  |  |  |  |
| Marginal Zone B-cell Lymphoma | 1 | 50,00% | 55 |
| Normal Tissue  | **1** | **1,45%** | **61** |
| Total  | **69** |  |  |

Orbit was the third most common specimen (Table 3). Mean age was 40,7 year-old and male was the most common gender (n=12; 52,2%). Benign epithelial lesions were the most frequent diagnosis.

TABLE 3 - FREQUENCY OF SPECIMENS FROM ORBIT

|  |  |  |  |
| --- | --- | --- | --- |
| Orbit  | Number  | %  | Mean age  |
| Miscellaneous lesions | **4** | **17,39%** | **53,75** |
| Other | 4 | 75,00% |  |
| Inflammation  | **3** | **13,04%** | **38,67** |
| Chronic Inflammation, unspecific | 3 | 100,00% |  |
| Benign Epithelial Tumours  | **7** | **30,43%** | **13** |
|  Epithelial Cysts  | 7 | 100,00% |  |
| Lipomatous Tumours | **2** | **8,70%** | **62** |
| Lipoma  | 2 | 100,00% |  |
| Meningeal Tumours  | **1** | **4,35%** | **59** |
| Meningioma  | 1 | 100,00% |  |
| Peripheral Nerve Sheath Tumours  | **1** | **4,35%** | **58** |
| Neurilemoma  | 1 | 100,00% |  |
| Fibroblastic/Myofibroblastic Tumours  | **1** | **4,35%** | **62** |
| Inflammatory Myofibroblastic Tumour | 1 | 100,00% |  |
| Lymphoid Disorders | **2** | **8,70%** | **77** |
| Lymphoma  |  |  |  |
| Follicular Lymphoma  | 1 | 50,00% | 76 |
| Marginal Zone B-cell Lymphoma | 1 | 50,00% | 78 |
| Normal Tissue  | **2** | 100,00% | **29** |
| Total  | **23** |  |  |

The fourth most common specimen were enucleated eyes (Table 4). Mean age was 52,5 year-old and male was the most frequent gender (n=11; 84,6%). Melanoma was the most frequent morphological diagnosis.

TABLE 4 - FREQUENCY OF SPECIMENS FROM ENUCLEATION

|  |  |  |  |
| --- | --- | --- | --- |
| Enucleation  | Number  | %  | Mean age  |
| Miscellaneous lesions | **5** | **38,46%** | **39,00** |
| Other | 5 | 100,00% |  |
| Melanoma  | **8** | **61,54%** | **60,86** |
| Total  | 13 |  |  |

Cornea was only the fifth most common tissue, accounting for 5 cases (Table 5). Mean age was 54,6 year-old, and female gender (n=3; 66,7%) was the most affected. All specimens were obtained immediately after trauma events.

TABLE 5 - FREQUENCY OF SPECIMENS FROM CORNEA

|  |  |  |  |
| --- | --- | --- | --- |
| Cornea  | Number  | %  | Mean age  |
| Miscellaneous lesions | **2** | **40,00%** | **48** |
| Other | 2 | 100,00% |  |
| Inflammation  | **1** | **20,00%** | **81** |
| Acute Inflammation | 1 | 100,00% |  |
| Normal Tissue  | **2** | **40,00%** | **48,5** |
| Total  | **5** |  |  |

Lacrimal gland was the sixth most frequent location of specimens (Table 6). Female gender was predominant (n=2; 66,7%). Mean age was 73 year-old. Two cases were diagnosed as benign epithelial tumours. The other was a follicular lymphoma.

TABLE 6 - FREQUENCY OF SPECIMENS FROM LACRIMAL GLAND

|  |  |  |  |
| --- | --- | --- | --- |
| Lacrimal gland  | Number  | %  | Mean age  |
| Benign Epithelial Tumours  | **2** | **66,67%** | **71,5** |
| Epithelial Cysts  | 2 | 100,00% |  |
| Lymphoid Tumours  | **1** | **33,33%** | **82** |
| Lymphoma  | 1 | 100,00% |  |
| Total  | **3** |  |  |

Caruncula was the less frequent topography, accounting only for two cases, in males (Table 7). Mean age was 44 year-old. First case was a benign epithelial lesion and second was a melanocytic tumour.

TABLE 7 - FREQUENCY OF SPECIMENS FROM CARUNCULA

|  |  |  |  |
| --- | --- | --- | --- |
| Caruncula  | Number  | %  | Mean age  |
| Benign Epithelial Tumours  | **1** | **50,00%** | **29** |
| Squamous Cell Papilloma  | 1 | 100,00% |  |
| Melanocytic Tumours  | **1** | **50,00%** | **59** |
| Dermal Nevus  | 1 | 100,00% |  |
| Total  | 2 |  |  |

**Discussion**

Department of Pathology of Hospital de Braga was founded only in 1990 and received its first ophthalmic specimen in January 2002. Municipal investment, local medical school and, most important of all, updates on local health policy, turned Hospital de Braga into a tertiary center for many specialities since 2009, assisting more than 1.2 million people today.

We studied retrospectively all specimens obtained by the Department of Ophthalmology of Hospital de Braga, which were evaluated by the same venue Department of Pathology. There was no specimen analysed outside this institution. All specimens were obtained in surgeries exclusively performed by ophthalmologists.

The number of specimens analysed through 13 years must be divided in 3 periods. From 2002 to 2010, the average number of specimens was 8 per year, according to the level of differentiation, smaller number of physicians and target population. Between 2011 and 2013, specimens significantly increased to 38 per year, as National Health Policies endorsed programs to reduce surgery waiting list. The number of assistants of all kind of ophthalmic subspecialties increased and the department was also selected for residency programs. Since 2014 to June 2015, a higher number of specimens – average of 4 specimens per month / overall average of 48 per year – has been analysed.

Specimens from the eyelid were the most frequent. This is significantly different from the only study found reporting a largest number of ophthalmic specimens. In Spraul’s study, cornea was the most common topographic area (39,3%); eyelid was only the fifth (8,0%) [1]. In this study, no characterization was made on location (for example, superior or inferior eyelid). Malignant epithelial tumours were the most common diagnosis, accounting for 36,17% cases, different from 17,0% on Spraul’s. Basal cell carcinoma was the most common subtype, with 88,24% of cases; in remaining literature, we found this to range from 14,3% to 86% [2-9]. Mean age for malignant epithelial tumours (74,6 year-old) was different from other publications [7-8]. Melanocytic tumours (21,99%) and benign epithelial lesions (21,28%) were the second and the third commonest diagnosis. In Deprez study, melanocytic and benign epithelial lesions were all considered as “benign tumours”, and accounted for 84% of specimens, and “malignant tumours” were responsible for 16% [3].

Conjunctiva was the second most frequent topography (26,7%). As eyelid, it is significantly different from Spraul’s study (7,7%) [1]. In this study, melanocytic tumours were the most common, accounting for 36,23% of cases, followed by miscellaneous tumours (14,49%), inflammation (11,59%) and malignant epithelial lesions (10,14%). These results are different from some previous important reports: in some, inflammatory, acquired epithelial and degenerative lesions were the most common [10]. Compound nevi were the commonest conjunctival nevi subtype in Alkatan study, such as in this [11]. Shield, a world reference in conjunctiva, claims that squamous cell carcinoma is one of the most frequent non-melanocytic neoplastic lesions, which have an important incidence in our study [12]. Also, his results on conjunctiva lesions from children were also similar to our study [13]. In 1/4 of cases, the pathological diagnoses were different from the clinical diagnosis, making legitimate to recommend a systematic pathological analysis [14].

Orbit was the third most common topography (8,9%). The most common subtype was benign epithelial lesions, accounting for 30,43% of cases. There was a small number of cases, restraining comparison to other surveys. Malignant lesion was the most common subtype in Spraul’s (46,4%) as in other studies [1;15]. Many surveys confine their studies to tumours of orbit. Orbital tumour malignancy ranged from 36 to 63% [16-18]. Surveys concerning all space-occupying lesions reported 45% of malignant tumours in adults [19], and 22% to 57% malignant tumours in children [19,20]. In this study, only 5 cases were paediatric cases – all epithelial cysts. These results are similar to some literature [21] concerning Mediterranean countries.

The number of enucleation specimens was reduced: only 13. Melanoma was the most common diagnosis. This survey is too short to be significantly compared with other studies, some of those with thousands of patients or with different target population [22-37]. In the same way, our experience regarding cornea, lacrimal gland and caruncula is almost insignificant. It was only collected 5 specimens from cornea, all collected after trauma events. The Department of Ophthalmology has no of authorization for cornea transplantation. At Spraul’s study, cornea was the most common specimen, and its most frequent diagnoses were keratitis and bullous keratopathy [1]. It was not possible to find studies similar to Spraul’s. Some publications describe only indications for penetrating keratoplasty [38-42] but, we didn’t found evidence of histological diagnosis (instead of clinical diagnosis) and percentages were different, with a higher prevalence of dystrophies. Lacrimal gland counted for 1,2% cases of this study, similar to those 1,4% from Spraul’s [1]. Again, it is too short for comparison with any reliable series. According to literature, inflammatory specimens tend to be the most common (25,0% - 64,0%), followed by tumours (12,3% - 37,5%), lymphoid tumours (9,2% - 27,1%) and miscellaneous lesions (6,0% - 21,5%) [1; 43-45]; the exception was Von Holstein’s study, in which malignant tumours were the most frequent [46]. Polito et al. identified in his study that adenoid cystic carcinoma was the most common malignant tumour [44]. Lastly, we had 0,8% cases of caruncula. At Spraul’s, caruncula corresponded to 1,0% of specimens [1]. In 2009, Levy et al. published a review with his survey, comparing it to other similar seven studies; nevus ranged from 16,8% to 59,5%; cysts from 5,1% to 34,6%; and papilloma from 4,7% to 31,6% [47].

**Conclusion:**

This research let local physicians understand that eyelid and conjuntiva were the most common specimens submitted to surgery and pathological characterization. The rates of corneal specimens and enucleation were specially low when compared to other centers in the world; the latter is because our center has no authorization for corneal transplantation; and the last, because there are Portuguese “reference centers” regarding ophthalmic oncology (Centro de Responsabilidade Integrada em Oftalmologia, Hospitais Univeristários de Coimbra, Coimbra, Portugal; IPO-Porto, Porto, Portugal), where specialized teams take care of this kind of pathology. Lastly, it can be concluded that frequency of specimens is the expected given the broad assistance that is intended to be provided for a department like this, reaching 1,2 millions people, from urban and non-urban areas.

This is the first publication, at a Pubmed indexed journal, regarding characterization of ophthalmic specimens in a Portuguese Department of Ophthalmology. It covers data from the begging of activity and extends through more than 10 years period, in order to get a significant outlook over this matter. An extensive bibliography review was done. This also performs the first known bibliography review, since Spraul’s study, dated almost 20 years ago.

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