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Ocular Adnexal Lymphoma: An Ophthalmologist's Perspective from a Single-center Experience

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Abstract

Background/Aim: Lymphomas of the orbit and orbital adnexa are important concerns in ophthalmologic practice; however, due to their nonspecific signs and symptoms, establishing a definitive diagnosis is often challenging. This study aimed to further expand understanding of these entities by assessing the histopathological subtypes and characteristic features of orbital lymphomas in a population undergoing orbital surgery at the Department of Ophthalmology in Katowice.

Patients and Methods: Between 2011 and 2017, a total of 107 orbital surgeries were performed for various orbital tumors. Tissue samples were subjected to histopathological analysis. In all patients, orbital lesions were evaluated using contrast-enhanced magnetic resonance imaging or computed tomography. Additionally, several parameters were measured at baseline and after surgery, including best-corrected visual acuity (BCVA), intraocular pressure (IOP) and associated ocular comorbidities.

Results: Histopathological examination identified B-cell lymphomas in 15 patients (8 women and 7 men; mean age, 65.61 years). Palpable orbital lesions were the most common manifestation of lymphoma (88.89% of cases). No significant changes in BCVA or intraocular pressure were observed postoperatively

Conclusion: Owing to its heterogeneous nature, orbital lymphoma may present with a wide range of clinical symptoms, often mimicking inflammatory conditions. Imaging studies and histopathological examination are essential for establishing the diagnosis and guiding subsequent treatment.

Keywords: Orbital lymphoma, non-Hodgkin lymphoma, exophthalmos, palpable orbital mass.

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Introduction

Orbital tumors comprise histologically diverse neoplasms that affect the orbit and surrounding structures (1, 2). They may originate from any tissue within the orbit – including the nerves, vasculature, glands, soft tissues, or bone – and may be benign or malignant, as well as primary or metastatic. Lymphomas of the orbit and ocular adnexa are relatively rare, representing approximately 1% of all non-Hodgkin lymphomas (3, 4); however, they are the most common primary orbital tumor in adults aged 60 years and older (3).

Orbital lymphoma is classified as *primary* when it arises within the orbit and as *secondary* when it represents metastatic involvement from an extraorbital site (5, 6). Most cases are non-Hodgkin B-cell lymphomas derived from the lymphoid tissue of the ocular adnexa – such as the conjunctiva, lacrimal gland, eyelid soft tissues, or extraocular muscles (6, 7).

Histologically, the vast majority (approximately 97%) are of B-cell origin (3, 8). Among these, extranodal marginal zone B-cell lymphoma of mucosa-associated lymphoid tissue (MALT lymphoma) is the most common subtype (59%), followed by diffuse large B-cell lymphoma (23%), follicular lymphoma (9%), and mantle cell lymphoma (5%) (8). Due to its diverse histology, variable growth patterns, and potential association with systemic diseases, the clinical presentation of orbital lymphoma is highly variable (3, 8).

The aim of this study was to determine the proportion of lymphoma among all orbital tumors based on tissue samples. Owing to the limited number of large cohort studies on this topic in the Polish population, we sought to expand current knowledge and increase the contribution of data from our country.

Patients and Methods

From 2011 to 2017, a total of 107 orbital surgeries were performed in patients with orbital tumor or infiltrative lesions at the Department of Ophthalmology of the Medical University of Silesia in Katowice, Poland. Tissue samples were examined at the Department of Pathomorphology and Molecular Diagnostics of the Medical University of Silesia in Katowice. Histopathological analysis revealed B-cell lymphomas in 15 patients (eight women and seven men) at a mean age of 65.61 years (range=42-85 years). In 12 cases, the tumor was unilateral (eight in the right orbit and four in the left one). Three patients presented with bilateral lesions. Prior to surgery, contrast-enhanced imaging tests were performed in each patient to determine the extent and location of the lesion.

At baseline and after the surgery, the following parameters were assessed: best corrected visual acuity (BCVA), intraocular pressure, signs and symptoms, and other ocular diseases. BCVA was assessed using Snellen charts. Intraocular pressure was measured using a Goldmann applanation tonometer (Haag-Streit, Bern, Switzerland) after topical anesthesia with proxymetacaine solution (Alcaine; Alcon, TX, USA) and tear film staining with fluorescein solution (I-DEW FLO fluorescein strips, Entod Research Cell, London, UK).

After assessment by an anesthesiologist, the surgery was performed under either local or general anesthesia. First, an incision was made in the skin (or in the conjunctiva in two cases) over the lesion. Three patients underwent tumor excision – two under general anesthesia and one under local anesthesia owing to advanced age and ineligibility for general anesthesia.

The remaining 12 patients underwent biopsy. Local anesthesia with lignocaine and bupivacaine was used in 11 cases, while one patient received general anesthesia due to the depth of tumor invasion. After the surgery, sutures were put on the incision site, and a rubber drain was left in the orbit for 24 h.

Patients remained at the Department of Ophthalmology for one day after surgery for the evaluation of the local and general condition. An antibiotic ointment was ordered to be applied to the suture site for 10 days. Antiglaucoma treatment was continued in patients with glaucoma. During the follow-up visit, the results of the histopathological examination were verified. Patients with the diagnosis of lymphoma were referred to the Department of Hematology for further treatment.

The tissue specimens were fixed in 10% formaldehyde, measured, described, and embedded in paraffin blocks. Then, the blocks were sliced and routinely stained with hematoxylin and eosin. Stained sections were evaluated by a pathomorphology specialist. The most common pathologies included in the differential diagnosis of ocular and periocular tumors were basal cell carcinoma, squamous cell carcinoma, choristoma, lipodermoid, neuroblastoma, hemangioma, cyst, and inflammatory lesions. A uniform tumor, monomorphic lymphoid cells, and infiltration of the adipose tissue, blood vessels, and central nervous system suggest the diagnosis of non-Hodgkin lymphoma. Based on microscopic tumor features, additional immunohistochemical staining was performed, with the following antibodies: CD20, CD79a, CD3, CD5, CD43, CD10, cyclin D1, CD23, CD38, CD138 bcl-6, bcl-2, CD15, CD30, PAX-5, CD15, MUM-1, Tdt, and CK. In all cases, ki-67 staining was used to determine the tumor growth fraction. Specimens were classified according to World Health Organization criteria (9).

Results

At baseline, the mean BCVA was 0.73±0.33 and mean intraocular pressure was 17.29±4.34 mmHg. In three patients, intraocular pressure was higher than 21 mmHg because of massive orbital infiltration, stasis, and eyeball compression. Two patients used topical drops for previously diagnosed glaucoma. The characteristics of the study group are shown in Table I.

The mean BCVA remained stable after the surgery (0.77±0.34). During follow-up, none of the patients showed deterioration in BCVA, while improvements of 0.4, 0.3, and 0.2 were observed in one patient each. The remaining patients showed either an increase in BCVA of 0.1 or no change. The mean intraocular pressure after the surgery was 15.76±2.05 mmHg. Among three patients with elevated intraocular pressure at baseline, a reduction in pressure values was observed after surgery. The two patients with glaucoma continued topical treatment after the surgery.

Table I. *Characteristics of the study group.*

Number of patients	15 (8 women, 7 men)
Age, years, range (mean)	42-85 (65.61)
BCVA, mean±SD (range)	0.73±0.33 (0.02-1.0)
Intraocular pressure, mmHg, mean±SD (range)	17.29±4.34 (10-28)
Number of eye sockets, n	18
Unilateral tumor, n	
Right orbit	8
Left orbit	4
Bilateral tumor, n	3
Biopsy, n	15
Complete tumor excision, n	3
Presence of glaucoma, n	2

BCVA: Best corrected visual acuity; SD-standard deviation; n-number.

None of the patients presented with the typical symptoms of orbital lymphoma, and the clinical picture suggested nonspecific inflammation. The most common findings were a palpable mass lesion (n=16), exophthalmos (n=2), motility disturbances (n=2), diplopia (n=1), reduced visual acuity (n=2), pain (n=4), lacrimation (n=4), palpebral fissure distortion (n=4), and elevated intraocular pressure (n=3). The photographs of selected cases are presented in Figure 1.

Each patient underwent contrast-enhanced imaging testing. Magnetic resonance imaging was performed in 11 patients, and computed tomography, in four. Tumor growth patterns ranged from diffuse lesions with infiltration of adjacent anatomical structures to well-demarcated masses. One patient had a well-defined tumor, while in two patients the infiltrates formed hard nodules or plaques. The remaining patients presented with diffuse lesions. Clinical evaluation and imaging findings did not allow to differentiate between lymphoma and nonspecific inflammation. The final diagnosis was established based on a pathomorphological analysis (Figure 2).

The histopathological examination of the tumor samples revealed B-cell lymphoma in all 15 cases, including extranodal marginal zone B-cell lymphoma (n=7), small B-cell lymphoma (n=3), diffuse large B-cell lymphoma (n=3), follicular lymphoma (n=1), and mantle cell lymphoma (n=1). Key histopathological findings are presented in Figure 3, Figure 4, Figure 5, and Figure 6.

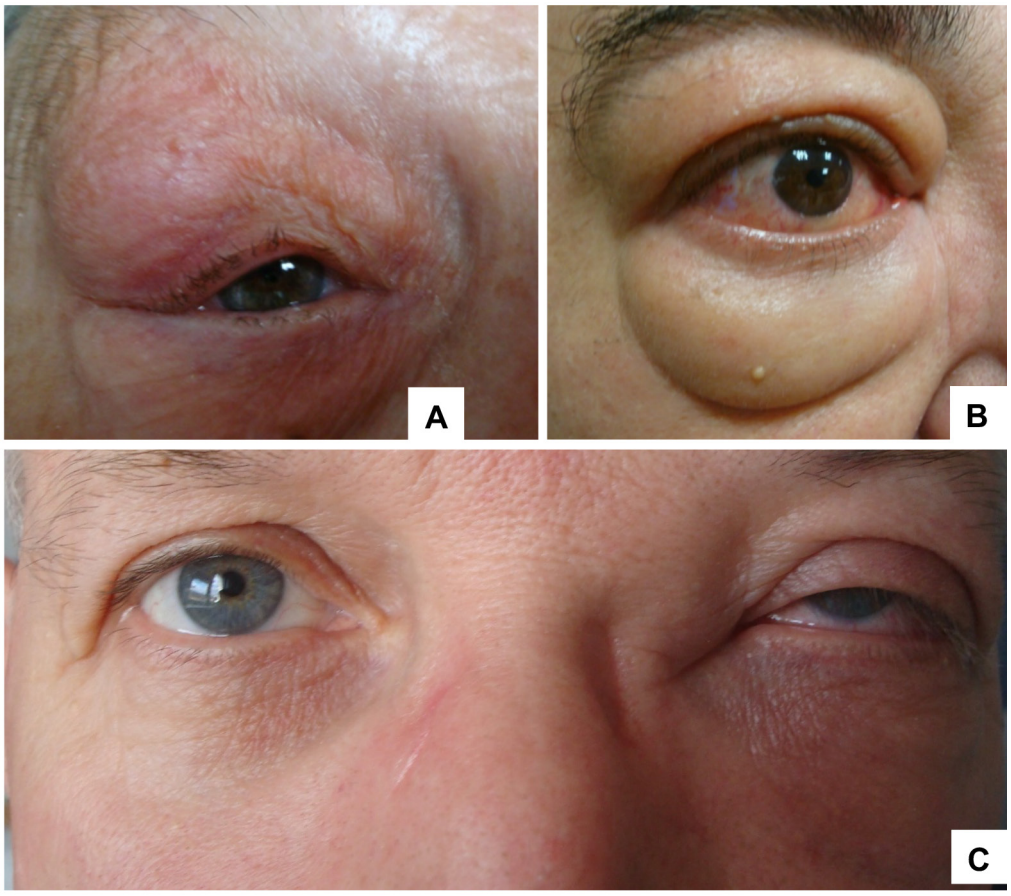

Figure 1. *Orbital lesions with exophthalmos (A) and palpebral fissure distortion (B, C).*

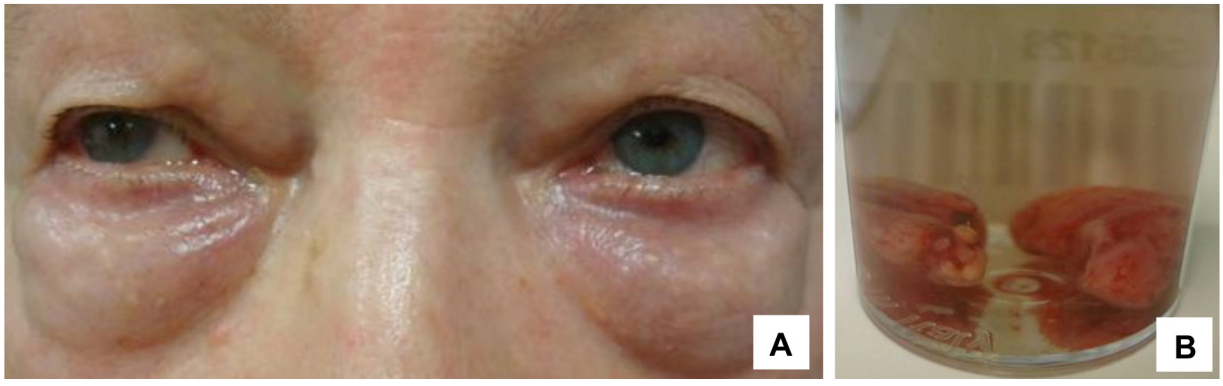

Figure 2. *Primary cutaneous diffuse large B-cell lymphoma in a 75-year-old woman (A); a biopsy specimen (B).*

Some patients presented with lesions in the lacrimal gland (n=3, 16.67%), conjunctiva (n=3, 16.67%), and eyelid (n=3, 16.67%). In six patients (33.33%), extraocular muscles were involved. Selected cases of orbital lesions at baseline and after the surgery are shown in Figure 7. The most common tumor site was the upper-lateral quadrant

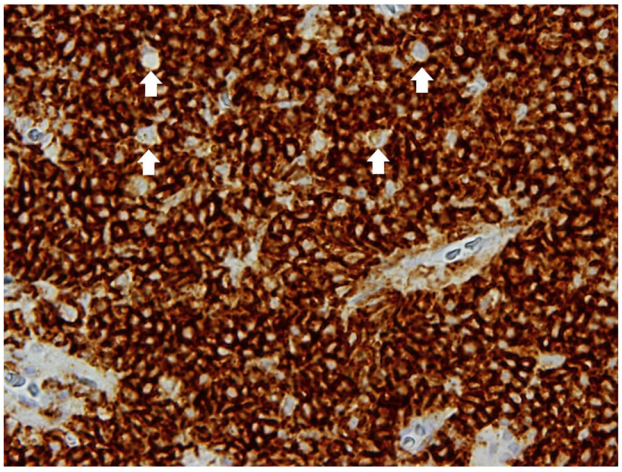

Figure 3. *Immunohistochemical staining for CD20 (magnification 40×). Neoplastic B-cells show positive staining (CD20+); macrophages are negative (CD20-; arrows): mucosa-associated lymphoid tissue lymphoma.*

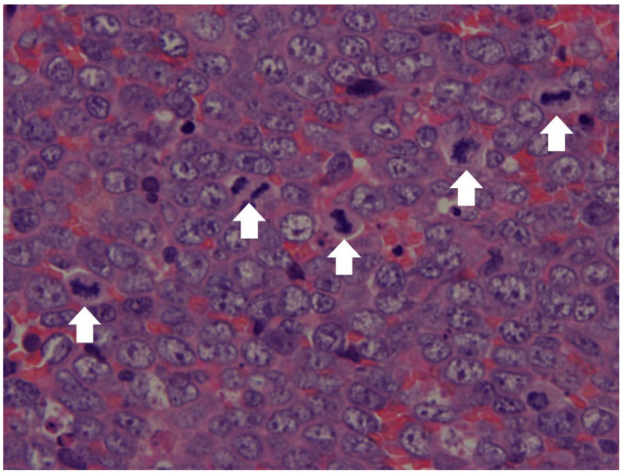

Figure 5. *Diffuse large B-cell lymphoma: hematoxylin and eosin staining (magnification 40). Large tumor cells with a significant degree of nuclear atypia, distinct nucleoli, and very high mitotic activity (arrows).*

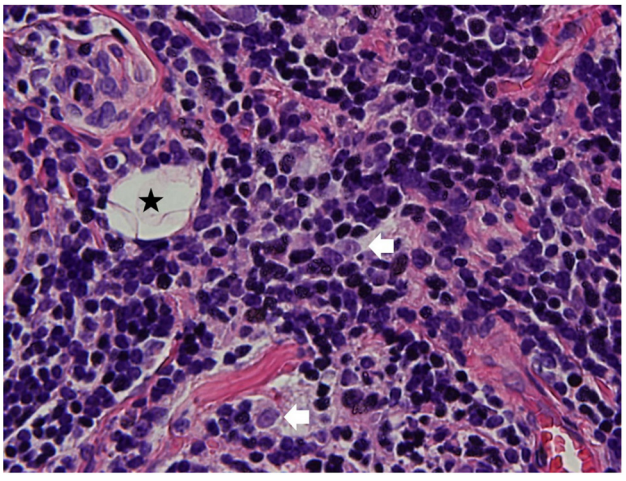

Figure 4. *Mucosa-associated lymphoid tissue lymphoma: hematoxylin and eosin staining (magnification 40×); orbital fat (star) infiltration by a population of monomorphic small tumor cells with clear cytoplasm. Among them, a few larger macrophages (arrows) are found with abundant cytoplasm and distinct nucleoli.*

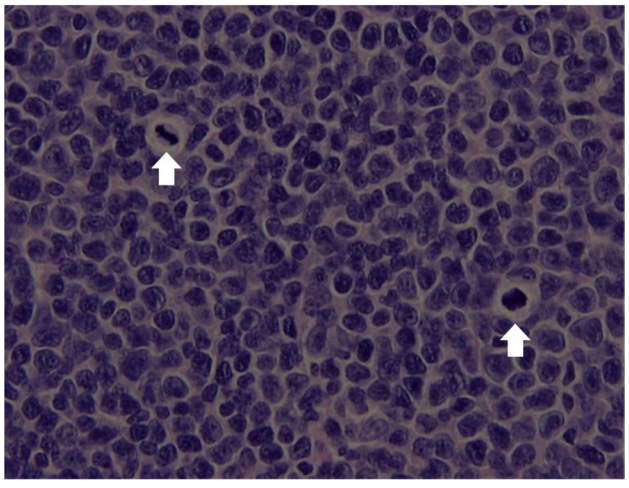

Figure 6. *Mantle cell lymphoma: hematoxylin and eosin staining (magnification 40×). Small tumor cells with angular nuclei and sparse cytoplasm; few mitotic figures (arrows).*

(n=5, 27.78%). The distribution of lesions in individual quadrants is presented in Table II.

Discussion

The results of our study expand the current knowledge and are consistent with numerous published articles, including the major 2018 analysis (8). Furthermore, they substantially contribute to the characterization of the Polish population, highlighting that ophthalmologists are often the first specialists to initiate the diagnostic process for orbital lymphoma.

In terms of histological subtypes, the most common was extranodal marginal zone B-cell lymphoma of mucosa-

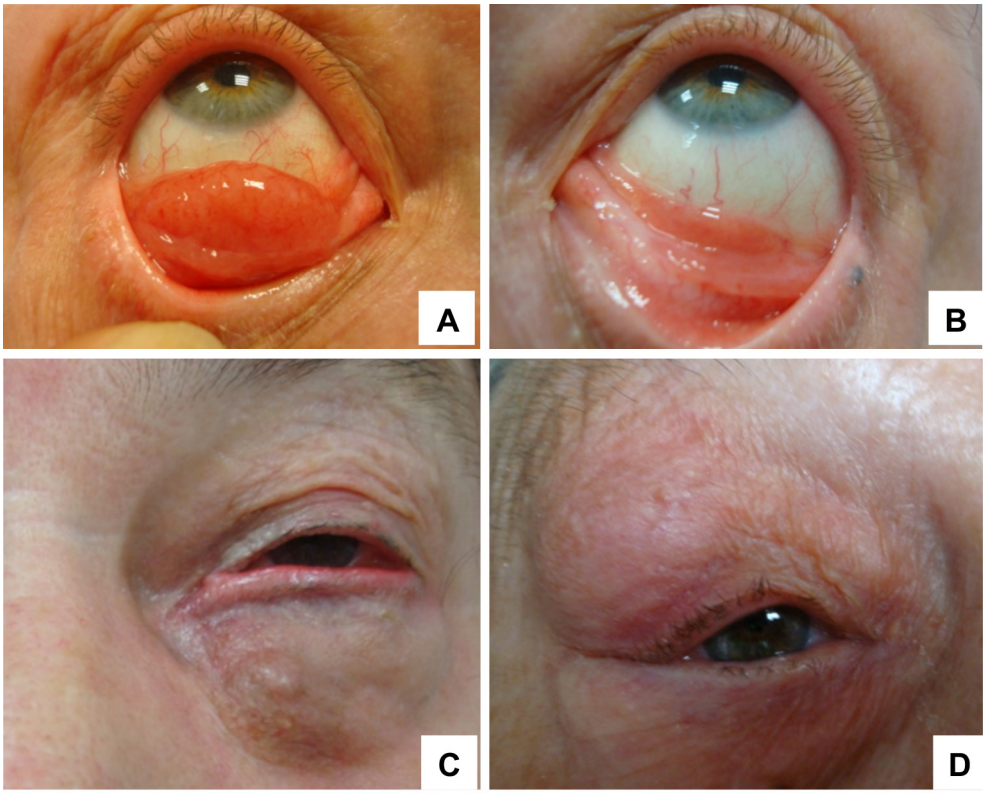

Figure 7. *Examples of orbital lesions before (A, C) and after (B, D) surgery.*

associated lymphoid tissue (MALT), followed by diffuse large B-cell lymphoma and several less frequent subtypes.

Orbital lymphoma has a wide array of clinical manifestations (3, 10). As noted by Słoniewski *et al.* (11), symptom diversity likely reflects the limited orbital volume and the large number of anatomical structures within the orbit. This variability and lack of specificity in clinical presentation are widely emphasized in the literature and are considered contributing factors to delayed diagnosis. Patients may present with multiple symptoms, with proptosis being the most commonly reported manifestation of orbital lymphoma worldwide (8). In our population, the most common presenting sign was a palpable orbital mass, observed in 88.89% of patients. Other symptoms included diplopia, pain, excessive lacrimation, eyelid ptosis, changes in visual acuity, and ocular motility disorders, all of which have been reported in other studies (12-17).

Table II. *Distribution of tumors.*

Orbital quadrant	No. of cases
Superior	1
Superior lateral	5
Superior medial	1
Inferior	2
Inferior lateral	2
Inferior medial	3
Posterior	2
Anterior medial	1
All	1

Currently, orbital lesions can be well visualized with diagnostic imaging techniques -with magnetic resonance imaging (MRI) and computed tomography (CT) being equally useful (15, 18-20). In our study, patients underwent MRI (n=11) or CT (n=4).

Orbital lymphomas are predominantly unilateral (15, 17, 21-23). Any part of the orbit may be involved, with the superolateral (or "extraconal") aspect of the orbit being most commonly affected (72%) (8, 24). The majority cases show also involvement of the lacrimal gland (51% of all orbital B-cell lymphomas) (8).

In immunocompetent individuals, lymphomas typically appear as relatively homogeneous highly cellular infiltrates that mold to surrounding structures rather than destroying them (4, 5, 10, 25).

To establish a diagnosis of lymphoma in accordance with the World Health Organization classification, the immunophenotype of tumor cells should be determined using immunohistochemical testing. In selected cases, molecular studies may also be required. Diagnosis can be challenging, and the quality of the biopsy material is crucial (3, 4). Typically, a tissue sample of the tumor is obtained for analysis, while complete tumor excision is performed less frequently (3). It is well established that tissue biopsy or core needle biopsy remain the mainstay of diagnosis, providing the most reliable material (3).

In our study, tumor excision was performed in three cases with limited, solitary lesions, whereas in the remaining cases only a biopsy was taken for further examination.

Samples were carefully obtained directly from the tumor, which is typically firmer than the surrounding healthy tissue. Subsequently, they were stored in paraffin blocks and remain available for future reference should new diagnostic or therapeutic approaches become available.

Fine-needle aspiration (FNA) biopsy is not recommended when lymphoma is suspected due to its low sensitivity, inability to allow immunophenotyping, and low concordance with the final diagnosis. FNA is particularly ineffective in Hodgkin lymphoma, where neoplastic cells may constitute only a small fraction of the infiltrate, reducing the likelihood of obtaining diagnostic material. Thus, FNA may delay diagnosis and treatment (8, 26, 27).

Conclusion

Lymphomas are heterogeneous and may be misdiagnosed as inflammation or other tumors; diagnosis is challenging and requires a comprehensive diagnostic workup. This study provides insight into the appearance and prevalence of orbital lymphoma in the Polish population. Extranodal marginal zone B-cell lymphoma was the most common subtype in our cohort, consistent with global data. The most frequent clinical manifestation in our population was a palpable orbital mass. Detailed diagnostic imaging and histopathological examination of tissue samples are essential for establishing the diagnosis. The mainstay of diagnosis remains tissue or core-needle biopsy; FNA is not recommended.

Conflicts of Interest

The Authors declare no competing interests in relation to this study.

Authors' Contributions

Conceptualization: DPW, IKB; Methodology: DPW, MHS, AK; Formal analysis: DPW, IKB, KGG; Investigation: DPW, MHS, AK; Resources: DPW, MHS, AK; Data curation: DPW, MHS; Writing – original draft: DPW, IKB, KGG; Writing – review & editing: IKB, KGG; Supervision: DPW, IKB.

Artificial Intelligence (AI) Disclosure

No artificial intelligence (AI) tools, including large language models or machine learning software, were used in the preparation, analysis, or presentation of this manuscript.

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