The ocular adnexa

The ocular adnexa include the eyelids, the conjunctival sac, the lacrimal drainage system, the lacrimal gland, and the orbital contents except for the eye and optic nerve. Many of the lesions that involve the adnexa are similar to those seen in other areas of the body and general surgical pathologists may feel that there is nothing special about this area of the head and neck. Experienced ophthalmic pathologists are, however, only too familiar with the diagnostic errors and inadequate interpretations rendered by surgical pathologists on tissue samples from this region. Proper care of patients with adnexal lesions, particularly in a referral center, requires the collaboration of a specialist ophthalmic pathologist with oculoplastic surgical colleagues in clinicopathological correlation. This issue of the journal is devoted to the interface between oculoplastic surgery and ophthalmic pathology.

With the death of Dr. Frederick Jakobiec on November 14, 2020, the world of Ophthalmology and Ophthalmic Pathology lost one of its outstanding practitioners and a leading exponent of clinicopathological correlation. His colleagues in eye pathology everywhere will always remember his diagnostic skill and his insights into the pathogenesis of many of the lesions he described, always set out in the most erudite language. Those of us who knew him personally will never forget his impish sense of humor and the respectful way in which he would disagree with another pathologist’s diagnosis. Toward the end of his distinguished career, Dr. Jakobiec served as Director of the David G. Cogan Laboratory of Ophthalmic Pathology at the Massachusetts Eye and Ear Infirmary in Boston. In this issue, we are fortunate to have a personal perspective on his numerous contributions from his successor in that position, Dr. Anna Stagner. This review will remind all who practise ophthalmic pathology how much we owe him.

The review by Dr. Hind Alkatan and coauthors of the different biopsy techniques used to obtain tissue samples from the orbit should be read by all trainees in oculoplastic surgery. The authors discuss the indications for, and the advantages and disadvantages of, fine-needle aspiration biopsy, core-needle biopsy, incisional biopsy, and excisional biopsy. The importance of not crushing the tissue, especially if a lymphoma is in the differential diagnosis, is emphasized and I have found the use of iris forceps with small adnexal biopsies to be helpful in avoiding “crush artifact.”

Furthermore, in this issue, we are fortunate to have a review of Merkel cell carcinoma of the eyelid by Dr. Noreen Walsh, a respected Canadian dermatopathologist and international authority on this tumor, which will be of practical value to ophthalmic pathologists. In addition to a presentation of the clinical and pathological diagnosis of Merkel cell carcinoma, Dr. Walsh discusses the significance of Merkel cell polyomavirus in its pathogenesis and natural history. That oncocytic lesions occur in the ocular adnexa has long been recognized. The nature of the oncocyte, as a transformed epithelial cell with increased numbers of abnormal mitochondria, has also been appreciated for several decades and, in most cases, pathological diagnosis of a swelling in the ocular adnexa as an oncocyteoma is a source of satisfaction, since these neoplasms are almost always benign. What is generally ignored in pathological case studies is any discussion of how these tumors arise and why they are usually benign. This topic is covered in a review of oncocytic lesions of the ocular adnexa. The pathogenesis of oncocytomas reflects abnormalities in both the nuclear and mitochondrial genomes, as well as in mitochondrial metabolism and bioenergetics. The basic science underlying these abnormalities is complex and not fully understood, but the review presents a simplified description of some of the molecular events that characterize these fascinating lesions.

The classical textbooks of ophthalmic pathology have paid little attention to the lacrimal drainage system and much of this has been focussed on neoplasms of the lacrimal sac. The inclusion in this issue of several articles on inflammatory processes within both the lacrimal sac and canaliculus is welcome. Despite the frequency of chronic dacryocystitis in clinical practice, pathological specimens from the lacrimal sac are relatively uncommon in the laboratory and many surgical pathologists are uncomfortable with their interpretation. As pointed out in the review of oncocytic lesions, oncocytic metaplasia of the surface and crypt epithelium is a recognized feature of biopsies in chronic dacryocystitis. Goblet cell hyperplasia is another feature that may be seen, in addition to lymphoplasmacytic infiltration that may or may not reflect immunoglobulin G4 (IgG4)-related disease. Biopsy of the sac mucosa should be given strong consideration when a dacryocystorhinostomy (DCR) has failed and is being repeated, but biopsy of apparently normal sac mucosa at primary DCR has a generally low yield of specific pathological diagnoses (<1%) and is not routinely undertaken. The most common diagnoses include lymphoma, papilloma, and sarcoidosis, the latter manifesting as non-caseating granulomatous inflammation. Although sarcoid granulomas are usually not associated with a heavy lymphocytic infiltrate, this may not be the case in the lacrimal sac and a history of systemic sarcoidosis should be sought. It has long been recognized that, in the context of orbital inflammatory disease, non-caseating granulomas will likely reflect sarcoidosis but idiopathic isolated granulomatous inflammation may also...
Most orbital lesions present as space-occupying masses and there is an understandable tendency of both ophthalmic pathologists and general surgical pathologists to focus on neoplasms rather than inflammatory and vascular lesions that may elude definitive diagnosis. However, over the past decade, there has been considerable interest in the ophthalmic manifestations of IgG4-related disease, particularly the orbitopathy. Cruz et al. have now reviewed published cases of other orbital lesions that may show a high ratio of IgG4-positive to IgG-positive plasma cells, a defining feature of IgG4-related disease. In twenty reports of such inflammatory lesions they found most to be cases of adult-onset xanthogranuloma, Wegener’s granulomatosis, necrobiotic xanthogranuloma, or Rosai-Dorfman disease. The significance of the IgG4-positive plasma cells in these conditions remains unclear but given the unusual nature of this class of antibody, it may serve to down-regulate the immune response.

Chronic inflammation and antigenic stimulation, accompanied by acquired genomic changes, has been proposed as a causative mechanism of clonal expansion of lymphocytes in ocular adnexal lymphoma (OAL). Mucosa-associated lymphoid tissue resulting from chronic inflammation transforms into extranodal marginal zone lymphoma, the most common type of OAL. Although much information has been gained from recent international multi-centre studies, a retrospective study from a single institution, where diagnosis and management may be more consistent, is also useful. The largest review of this type has now been published in this issue by Fernandez et al., who assessed the diagnosis and management of 133 patients at the Wills Eye Hospital.

Other studies of orbital neoplasms in this issue include a series of six cases of nasopharyngeal carcinoma that presented with ophthalmic complaints before the primary neoplasm was identified. Four presented with disturbed ocular motility, with or without loss of vision and orbito-facial pain. Most were undifferentiated or poorly differentiated squamous cell carcinoma. Renal cell carcinoma is notorious for producing metastases in unexpected locations, although metastases to the ocular adnexa are rare. Magan et al. reviewed the cases of ocular adnexal metastases reported in the literature and found only 44 well-documented cases, although seven of these represented secondary extension from the paranasal sinuses rather than true metastases. The ocular adnexal metastases were frequently the initial manifestation of the primary renal cell carcinoma (41% of cases), the remainder occurring in the setting of known stage IV disease.

The collection of articles covering a wide range of topics in this issue of the Saudi Journal of Ophthalmology offers much to stimulate interest and research into the pathology and clinical management of the various diseases that involve the ocular adnexa.

John G. Heathcote
Department of Pathology, Dalhousie University, Halifax, Nova Scotia, Canada

Address for correspondence: Dr. John G. Heathcote, Department of Pathology, Dalhousie University, Halifax, Nova Scotia, Canada. E-mail: godfrey.heathcote@dal.ca

Submitted: 07-Mar-2022
Accepted: 07-Mar-2022
Published: 18-Apr-2022

References

1. Stagner AM. In memoriam: Frederick A. Jakobiec, M.D., D.Sc., the “king of cysts” and so much more. Saudi J Ophthalmol 2021;35:170-3.
2. Alkatan HM, Alyousef NA, Alsahabi NS, Aljasser IH. A comprehensive review of biopsy techniques for oculoplastic and orbital surgeons from ophthalmic pathologists’ perspective. Saudi J Ophthalmol 2021;35:174-8.
3. Walsh NM. Merkel cell carcinoma of the eyelid and periocular skin: A review. Saudi J Ophthalmol 2021;35:186-92.
4. Heathcote JC, Archibald CW, Valenzuela AA. Oncocytic lesions of the ocular adnexa: A review of the histopathology with a brief discussion of the pathogenesis. Saudi J Ophthalmol 2021;35:179-85.
5. Tanenbaum M, Nicholson NA, Davis EB. Oncocytes in chronic dacryocystitis. Chibret Int J Ophthalmol 1986;4:10-2.
6. Takahashi Y, Takahashi E, Nishimura K, Kakizaki H. Immunoglobulin G4-related dacryocystitis. Can J Ophthalmol 2017;52:e188-90.
7. Al-Yacoubi R, Canan H, Sizmaz S, Bal N, Pelit A, Akova YA. Nasolacrimal duct obstruction: Clinicopathologic analysis of 205 cases. Orbit 2010;29:254-8.
8. Mombaerts I, Schlingemann RO, Goldschmeding R, Koornneef L. Idiopathic granulomatous orbital inflammation. Ophthalmology 1996;103:2135-41.
9. Singh S, Gandhi A, Modiwala Z. Isolated non-carcinomatous granulomatous inflammation of the lacrimal sac masquerading as a malignancy. Saudi J Ophthalmol 2021;35:269-72.
10. Bothra N, Ali MJ. Orbital involvement in lacrimal drainage disorders. Saudi J Ophthalmol 2021;35:204-8.
11. Heathcote JC. Changing patterns in orbital pathology. Saudi J Ophthalmol 2018;32:1-2.
12. Cruz AA, Camacho MA, Cunha BS, Alkatan H, Xavier NF. Plasma cell IgG4 positivity in orbital biopsies of non-IgG4-related conditions. Saudi J Ophthalmol 2021;35:193-7.
13. Sjö LD, Heegaard S, Pruse JU, Petersen BL, Pedersen S, Rafklaer E. Extranodal marginal zone lymphoma in the ocular region: Clinical, immunophenotypical, and cytogenetical characteristics. Invest Ophthalmol Vis Sci 2009;50:516-22.
14. Kirkegaard MM, Rasmussen KP, Coupland SE, Esmaeli B, Finger PT, Graue GF, et al. Conjunctival lymphoma – An international multicenter retrospective study. JAMA Ophthalmol 2016;134:406-14.
15. Fernandez CA, Henry RK, Shields CL, Bilyk JR, Lally SE, Eagle RC, et al. Ocular adnexal lymphoma: A single-institution retrospective study. Saudi J Ophthalmol 2021;35:230-9.
16. Alrashed SH, Alkatan HM, Alfaraj M, Alnahdi MA, Almehari NZ, Almutairi FJ, et al. Nasopharyngeal carcinoma (NPC) in the ophthalmic practice: A serious neoplasm presenting initially to ophthalmologists.
17. Magan T, Pradeep T, Tuluc M, Bilyk JR, Milman T. Ocular adnexal metastases from renal cell carcinoma: An update and comprehensive literature review. Saudi J Ophthalmol 2021;35:209-16.