PATHOMORPHOSIS OF EYELID TUMOR PATHOLOGY IN DEMODECTIC INFECTION

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ABSTRACT

Background. Pathological changes in the tissues of the oculo-conjunctival region caused by the activity of the Demodex mite is represented by the development of inflammatory process. On detection of the parasite on eyelashes, the presence of the Demodex mite is diagnosed in half of adult patients seeking ophthalmic care. Pathomorphological descriptions of specific patterns associated with the presence of Demodex infection are practically absent. During pathological examination, in the vast majority of cases it is almost impossible to see the parasite in the test material. There are pathomorphological patterns associated with the presence of the mite as a commensal, not only on the eyelid surface or in the conjunctiva, but also in morphological structures formed against the background of pathological processes in this area.

Aim. To find out the morphological patterns reflecting the pathomorphosis of some tumor processes in the eyelid thickness caused by demodectic invasion, which have not been identified so far in ophthalmopathological studies.

Materials and Methods. We analyzed the archival material from the oculo-conjunctival region submitted to the ocular pathology laboratory within the period of 2020–2023. Surgical and biopsy specimens were processed by standard histologic methods.

Results. One of the pathognomonic patterns of demodecosis are calcifications with fragments of the dead mite and cysts. When a mite rapidly destroys tissue, it leaves the site until it dies without retaining its fragments. Post-demodecosis pathomorphosis in basal cell carcinoma of the eyelids complicates the pathomorphologic diagnosis of the biopsy.

Conclusions. Our results prove the presence of mites in tumor tissues and illustrate their influence on the development of the pathomorphological picture, which should be taken into account in the practical activity of a pathologist.

Keywords: *demodex mite, pathomorphology, ophthalmopathological examination, oculo-conjunctival region.*

Introduction

The idea of the role of Demodex mite in the development of ophthalmic pathology is still limited to the reactive inflammatory process of the eyelids and conjunctiva, usually associated with such clinical conditions as demodectic blepharitis, blepharoconjunctivitis, chalazion, episcleritis, and marginal keratitis. According to the experience of clinical and laboratory diagnosis aimed at detection of the parasite on the eyelashes, at least half of the adult population seeking ophthalmic care can be diagnosed with Demodex mite. Therefore, with such a prevalence of the parasite in the oculo-conjunctival region, it can be expected that the presence of Demodex in the adult population is not limited to an inflammatory response of the conjunctiva and eyelids [1; 2].

However, until recently in ophthalmopathology, all ideas about Demodex-induced morphological changes were limited to the picture of an acute or non-specific chronic inflammatory process. This is largely due to the fact that in ocular patho-

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logy, as in pathomorphology in general, there are virtually no descriptions of specific patterns associated with Demodex infection. This is largely due to the fact that, in contrast to clinical diagnosis during pathological examination, in the vast majority of cases it is almost impossible to see the parasite in biopsy or surgical material [1; 2].

At the same time, as our previous studies [1; 2] have shown, there are a number of pathological patterns associated with the presence of the mite as a commensal, not only on the eyelid surface or in the conjunctiva, but also in the morphological structures formed as a result of pathological processes in this area. The experience of veterinary pathology, where demodecosis is much more common, allows us to pay attention to seemingly insignificant details. It is this experience that has allowed us to link certain details in the histomorphological picture, which are usually ignored as insignificant artifacts, to demodectic infection.

The aim of our work is to find the morphologic patterns reflecting the pathomorphosis of some tumor processes in the eyelid thickness caused by demodectic infection, which have not been identified in ophthalmopathologic studies so far.

Materials and Methods

The clinical and morphologic analysis included cases of demodectic infection detected during histologic examination of clinical biopsy and surgical material received by the Laboratory of Ocular Pathology of Filatov Institute of Eye Diseases and Tissue Therapy of NAMS of Ukraine during the last four years (30 cases with demodex were found among 650 examined biopsies of patients with tumor diseases of the eyelids). The surgical and biopsy material was processed according to the generally accepted histologic methodology with the preparation of paraffin blocks. In each case, 8 to 12 serial hematoxylin-eosin-stained histologic sections were examined.

Results

Our understanding of the pathognomonic histomorphologic patterns of demodecosis was based on the experience of tissue examination of demodectic infections in veterinary medicine. It is in domestic animals that various manifestations of demodectic infection are most often detected, which, unlike in humans, often become the object of surgical intervention and, consequently, subsequent histologic examination. Thus, veterinary practice has allowed us to understand and evaluate the histomorphologic patterns that are pathognomonic for this parasitic infection, which we have noted in the study of a number of ophthalmic pathologic processes.

As a result of histomorphologic examination of surgical and biopsy material of the eyelids, the above patterns that are pathognomonic for demodicosis infection were detected in 30 cases, which is about 5% of the total number of studies for this period.

First of all, such patterns are cystic cavities, which are most often seen in direct contact with the skin appendages, especially the sebaceous glands. It is the destruction of the sebaceous glands that explains the appearance of these cysts (*Fig. 1*). However, the origin of such cavities is not obvious to the pathologist without appropriate experience.

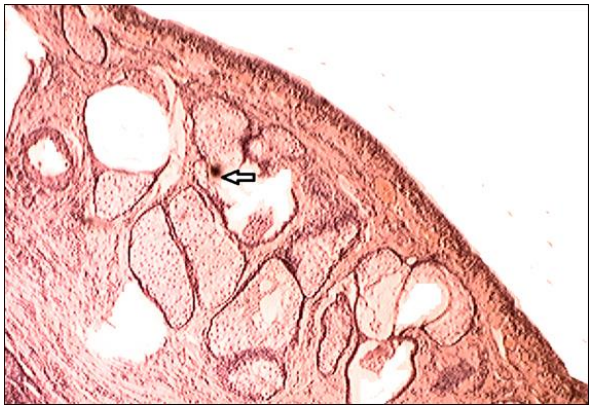

Fig. 1. Adenoma of the sebaceous gland near the lower lid margin with a large number of glands destroyed by the mite. *A calcified fragment of a dead mite is visible in one of the cavities (arrow). ×100*

Therefore, it is not surprising that such patterns are ignored, as well as many other artifacts caused by mechanical damage to histologic sections. For this reason, for a long time in ocular pathology, when examining biopsy and surgical material from eyelid tissues, no attention was paid to the characteristic patterns of demodecosis.

In veterinary practice demodectic infection is usually associated with acute, chronic or granulomatous inflammation, in which cystic cavities are usually found, as a result of the mite devouring the parenchyma of glands, mainly sebaceous glands.

An important pathognomonic pattern of demodecosis are foci of calcification, which, like the aforementioned cysts, are usually interpreted as trivial dystrophic calcifications (*Fig. 2*). Only a specific examination of these calcifications reveals their unusual nature due to the fact that they are based on fragments of a dead mite in the form of keratinous debris [3–7].

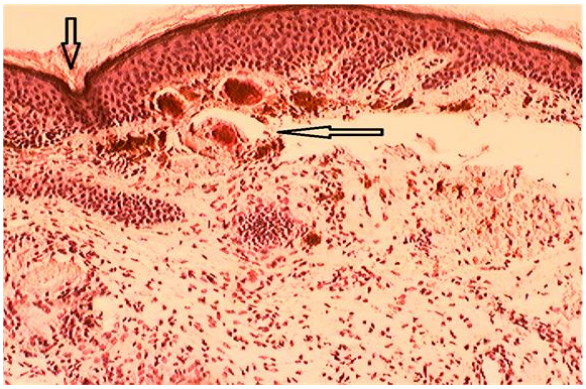

Fig. 2. Numerous foci of calcified mite fragments under the epidermis (horizontal arrow). *The upper part shows the presumed site of mite penetration through the epidermis (vertical arrow). ×100*

Cases in which pathomorphologic diagnosis revealed patterns that are pathognomonic for demodectic infection were usually clinically manifested as benign tumor processes: atheromas, sebaceous gland adenomas, fibrolipomas, nevi, xanthelasma. Fig. 2 shows the histomorphologic picture of a clinically diagnosed xanthelasma of the eyelid. However, it is very difficult to confirm this diagnosis on the basis of pathological examination, since most of the cell parenchyma of the tumor is destroyed, and mainly calcified fragments of the mite and its cavities are visible. Only the projection of the characteristic clinical manifestations of eyelid xanthelasma on the histomorphological picture, in which individual xanthoma cells are visible, allows to draw a conclusion about the post-demodecosis pathomorphosis of this tumor process. This pathomorphosis is most pronounced in adenomas of the sebaceous glands, which were often represented exclusively by cavities in the absence of glandular structures (*Fig. 3*).

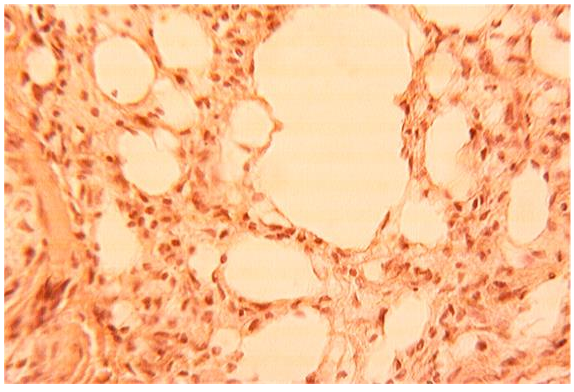

Fig. 3. Post-demodecosis pathomorphosis of a sebaceous adenoma with total destruction of the glands, leaving only cavities made by the mite. *×100*

As portrayed, concerning post-demodecosis pathomorphosis there are sometimes situations when the diagnosis of sebaceous adenoma is made without the adenomatous tissue itself, mainly on the basis of the previous clinical picture. Moreover, with such a total destruction of the tumor tissue, sometimes even fragments of the mite may not be detected. This is due to the fact that with a sufficiently rapid destruction of the cellular array available to the mite, it leaves the area before death without preserving its fragments.

This situation is more typical of sebaceous adenomas, which are usually small in size. In addition, it should be noted that after the death of a mite under normal conditions, almost complete destruction occurs within 2–3 hours, which can be observed directly on a native clinical diagnostic preparation. Therefore, it is not surprising that in most cases only small fragments of the mite body or calcium-impregnated microfragments, keratin debris, are found. The parts of the mite that have not undergone calcification are lost in the histologic specimen. Therefore, the absence of mite fragments cannot be considered a contraindication in the presence of other characteristic pathological patterns. However, even when such calcified fragments are preserved, they rarely contain elements of the parasite body. Only in one case we did find a head part that had the characteristic chelicerae of the parasite almost completely preserved (*Fig. 4*).

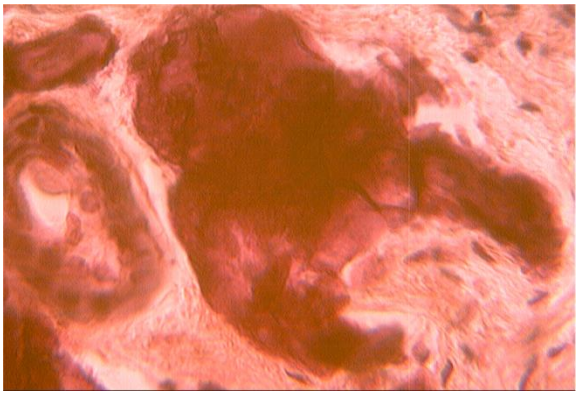

Fig. 4. A unique calcified fragment of the mite head with chelicerae preserved away from the epidermis. *×400*

It is interesting to note that in some cases, as a result of mite activity, the morphological picture of the pathological process changes so much that it can be difficult to diagnose. In this regard, the demodectic infection in basal cell carcinoma, which was detected in 10 cases on biopsy material, is of particular interest.

In most cases, the pathomorphosis taking place after demodecosis was limited to the formation of cysts in certain areas of the tumor with preservation of the typical pattern of basal cell carcinoma. In two cases, however, the changes were so pronounced that repeated review of the histopathologic specimens was required for correct verification of the tumor pathology (*Fig. 5*).

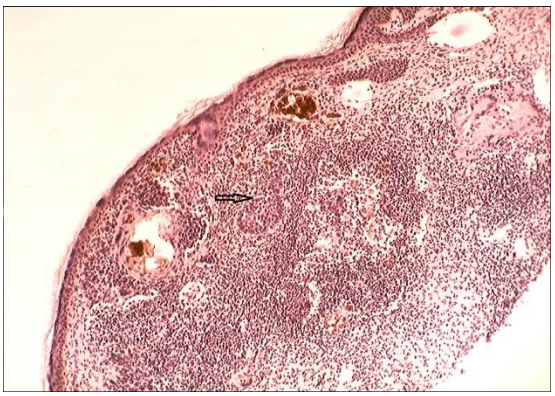

Fig. 5. The typical tumor pattern is severely disturbed: only a solid complex with a barely preserved palisade is visible (arrow). *Several cavities and areas of discharge can be seen beneath the epidermis due to the presence of Demodex, calcified fragments of which are also present near the epidermis. ×100*

The tumor was mostly represented by polymorphic cells situated randomly, without the tendency to form complexes characteristic of basal cell carcinoma, as can be seen in *Fig. 6*. This picture dominated the initial examination. It was not until 12 serial sections were examined that some of them showed the picture of Fig. 5, with only a single complex characteristic of basal cell carcinoma.

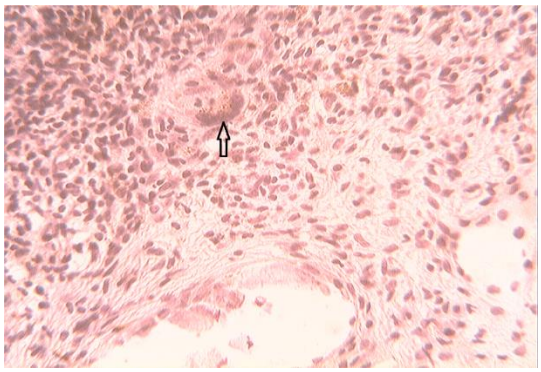

Fig. 6. Fragment of the previous tumor: cells are randomly distributed against a background of cavities, characteristic solid complexes are absent. *A calcified fragment of the parasite is seen in the upper part of the picture (arrow). ×200*

It should also be noted that the patient had two tumors removed with the same clinical diagnosis: basal cell carcinoma. The second tumor had a histomorphologic structure typical of basal cell carcinoma, which facilitated the targeted search and detection of the corresponding solid complexes in the other tumor.

It should be noted that malignant tumors of the eyelid skin are usually not completely removed, and after biopsy and diagnosis, local cryodestruction is performed, sometimes followed by radiotherapy. Therefore, the biopsy material is often small in volume and only some superficial layers of tumor tissue are present. Underestimating these circumstances can lead to difficulties in pathologic diagnosis, as illustrated by the case shown in Fig. 7.

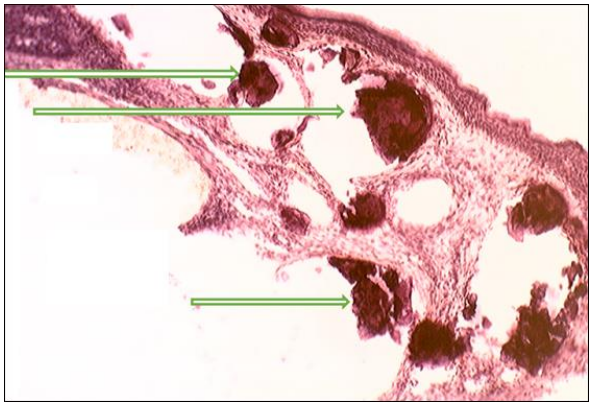

Fig. 7. Destruction of parenchyma by mites. *The biopsy shows numerous cavities that are passages of the Demodex mite with a large number of calcified parasite fragments (arrows). ×100*

The above picture in the biopsy seems to clearly indicate demodecosis. Despite the clinical diagnosis of basal cell carcinoma, no tumor elements were found in the 10 serial sections examined. However, when referring to the clinical data, it was noted that the tumor nodule at the lid margin measured 10×6 mm and macroscopically corresponded to a typical basal cell carcinoma, which was effectively cryodestructed after biopsy.

The analysis of these circumstances made it possible to realize that the examined biopsy, measuring of 2×0.5 mm, in this situation cannot reflect the entire structure of the pathological process. In addition, it is necessary to understand what cellular material was destroyed by the mite during the formation of a large number of cysts under the epidermis, especially since in this fragment there were no hair follicles with which sebaceous glands could be associated. Thus, the cysts

shown in the previous photo were most likely formed as a result of the mite's destruction of the tumor parenchyma. This was confirmed by the following observation.

On re-examining this biopsy material, special attention was paid to a small cluster of cells at the periphery of one of the cysts (Fig. 7, left part). Under high magnification, one of the sections showed a certain resemblance of the cells of this complex to basalioma (*Fig. 8*).

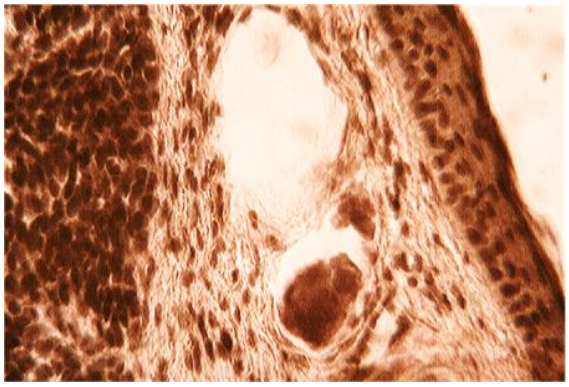

Fig. 8. A partially disrupted microcomplex at the periphery of a biopsy specimen of basal-like cells, but without a characteristic palisade. *×400*

Post-demodecosis pathomorphosis in basal cell carcinoma of the eyelids complicates the pathomorphologic diagnosis of the biopsy.

Conclusions

Based on the experience of studying biopsy material in veterinary medicine, in our study the attention was first drawn to the features of hypertrophic forms of chronic demodecosis, the morphologic manifestations of which had not been previously recorded in ocular pathology.

Subsequent observations performed in order to systematize a number of patterns that are pathognomonic for demodectic infection allowed, based on the study of biopsy and surgical material, to expand the understanding of pathological changes in eyelid tissues associated with the presence of Demodex mite and to draw attention to the pathomorphosis of some eyelid tumor processes.

In general, the current study should be considered as preliminary, since the concept of tumor pathomorphosis caused by the presence of the Demodex mite previously did not exist. At the same time, the examples presented by us not only prove the presence of the mite in the tumor tissue, but also show its significant influence on the pathomorphologic picture, which should be taken into account in diagnostic work.

DECLARATIONS:

Disclosure Statement

The authors have no potential conflicts of interest to disclosure, including specific financial interests, relationships, and/or affiliations relevant to the subject matter or materials included.

Statement of Ethics

The authors have no ethical conflicts to disclosure.

Data Transparency

The data can be requested from the authors.

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Consent for publication

All authors give their consent to publication.

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