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ЕЖЕМЕСЯЧНЫЙ НАУЧНЫЙ ЖУРНАЛ

Медицинские новости Грузии

საქართველოს სამედიცინო სიახლენი

GEORGIAN MEDICAL NEWS

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GMN: Georgian Medical News is peer-reviewed, published monthly journal committed to promoting the science and art of medicine and the betterment of public health, published by the GMN Editorial Board since 1994. GMN carries original scientific articles on medicine, biology and pharmacy, which are of experimental, theoretical and practical character; publishes original research, reviews, commentaries, editorials, essays, medical news, and correspondence in English and Russian.

GMN is indexed in MEDLINE, SCOPUS, PubMed and VINITI Russian Academy of Sciences. The full text content is available through EBSCO databases.

GMN: Медицинские новости Грузии - ежемесячный рецензируемый научный журнал, издаётся Редакционной коллегией с 1994 года на русском и английском языках в целях поддержки медицинской науки и улучшения здравоохранения. В журнале публикуются оригинальные научные статьи в области медицины, биологии и фармации, статьи обзорного характера, научные сообщения, новости медицины и здравоохранения. Журнал индексируется в MEDLINE, отражён в базе данных SCOPUS, PubMed и ВИНИТИ РАН. Полнотекстовые статьи журнала доступны через БД EBSCO.

GMN: Georgian Medical News – საქართველოს სამედიცინო სიახლენი – არის ყოველთვიური სამეცნიერო სამედიცინო რეცენზირებადი ჟურნალი, გამოიცემა 1994 წლიდან, წარმოადგენს სარედაქციო კოლეგიისა და აშშ-ის მეცნიერების, განათლების, ინდუსტრიის, ხელოვნებისა და ბუნებისმეტყველების საერთაშორისო აკადემიის ერთობლივ გამოცემას. GMN-ში რუსულ და ინგლისურ ენებზე ქვეყნდება ექსპერიმენტული, თეორიული და პრაქტიკული ხასიათის ორიგინალური სამეცნიერო სტატიები მედიცინის, ბიოლოგიისა და ფარმაციის სფეროში, მიმოხილვითი ხასიათის სტატიები.

ჟურნალი ინდექსირებულია MEDLINE-ის საერთაშორისო სისტემაში, ასახულია SCOPUS-ის, PubMed-ის და ВИНИТИ РАН-ის მონაცემთა ბაზებში. სტატიების სრული ტექსტი ხელმისაწვდომია EBSCO-ს მონაცემთა ბაზებიდან.

WEBSITE

www.geomednews.com

К СВЕДЕНИЮ АВТОРОВ!

При направлении статьи в редакцию необходимо соблюдать следующие правила:

1. Статья должна быть представлена в двух экземплярах, на русском или английском языках, напечатанная через **полтора интервала на одной стороне стандартного листа с шириной левого поля в три сантиметра**. Используемый компьютерный шрифт для текста на русском и английском языках - **Times New Roman** (**Кириллица**), для текста на грузинском языке следует использовать **AcadNusx.** Размер шрифта - **12**. К рукописи, напечатанной на компьютере, должен быть приложен CD со статьей.

2. Размер статьи должен быть не менее десяти и не более двадцати страниц машинописи, включая указатель литературы и резюме на английском, русском и грузинском языках.

3. В статье должны быть освещены актуальность данного материала, методы и результаты исследования и их обсуждение.

При представлении в печать научных экспериментальных работ авторы должны указывать вид и количество экспериментальных животных, применявшиеся методы обезболивания и усыпления (в ходе острых опытов).

4. К статье должны быть приложены краткое (на полстраницы) резюме на английском, русском и грузинском языках (включающее следующие разделы: цель исследования, материал и методы, результаты и заключение) и список ключевых слов (key words).

5. Таблицы необходимо представлять в печатной форме. Фотокопии не принимаются. **Все цифровые, итоговые и процентные данные в таблицах должны соответствовать таковым в тексте статьи**. Таблицы и графики должны быть озаглавлены.

6. Фотографии должны быть контрастными, фотокопии с рентгенограмм - в позитивном изображении. Рисунки, чертежи и диаграммы следует озаглавить, пронумеровать и вставить в соответствующее место текста **в tiff формате**.

В подписях к микрофотографиям следует указывать степень увеличения через окуляр или объектив и метод окраски или импрегнации срезов.

7. Фамилии отечественных авторов приводятся в оригинальной транскрипции.

8. При оформлении и направлении статей в журнал МНГ просим авторов соблюдать правила, изложенные в «Единых требованиях к рукописям, представляемым в биомедицинские журналы», принятых Международным комитетом редакторов медицинских журналов - http://www.spinesurgery.ru/files/publish.pdf и http://www.nlm.nih.gov/bsd/uniform_requirements.html
В конце каждой оригинальной статьи приводится библиографический список. В список литературы включаются все материалы, на которые имеются ссылки в тексте. Список составляется в алфавитном порядке и нумеруется. Литературный источник приводится на языке оригинала. В списке литературы сначала приводятся работы, написанные знаками грузинского алфавита, затем кириллицей и латиницей. Ссылки на цитируемые работы в тексте статьи даются в квадратных скобках в виде номера, соответствующего номеру данной работы в списке литературы. Большинство цитированных источников должны быть за последние 5-7 лет.

9. Для получения права на публикацию статья должна иметь от руководителя работы или учреждения визу и сопроводительное отношение, написанные или напечатанные на бланке и заверенные подписью и печатью.

10. В конце статьи должны быть подписи всех авторов, полностью приведены их фамилии, имена и отчества, указаны служебный и домашний номера телефонов и адреса или иные координаты. Количество авторов (соавторов) не должно превышать пяти человек.

11. Редакция оставляет за собой право сокращать и исправлять статьи. Корректура авторам не высылается, вся работа и сверка проводится по авторскому оригиналу.

12. Недопустимо направление в редакцию работ, представленных к печати в иных издательствах или опубликованных в других изданиях.

При нарушении указанных правил статьи не рассматриваются.

REQUIREMENTS

Please note, materials submitted to the Editorial Office Staff are supposed to meet the following requirements:

1. Articles must be provided with a double copy, in English or Russian languages and typed or compu-ter-printed on a single side of standard typing paper, with the left margin of **3** centimeters width, and **1.5** spacing between the lines, typeface - **Times New Roman** (**Cyrillic**), print size - **12** (referring to Georgian and Russian materials). With computer-printed texts please enclose a CD carrying the same file titled with Latin symbols.

2. Size of the article, including index and resume in English, Russian and Georgian languages must be at least 10 pages and not exceed the limit of 20 pages of typed or computer-printed text.

3. Submitted material must include a coverage of a topical subject, research methods, results, and review.

Authors of the scientific-research works must indicate the number of experimental biological species drawn in, list the employed methods of anesthetization and soporific means used during acute tests.

4. Articles must have a short (half page) abstract in English, Russian and Georgian (including the following sections: aim of study, material and methods, results and conclusions) and a list of key words.

5. Tables must be presented in an original typed or computer-printed form, instead of a photocopied version. **Numbers, totals, percentile data on the tables must coincide with those in the texts of the articles.** Tables and graphs must be headed.

6. Photographs are required to be contrasted and must be submitted with doubles. Please number each photograph with a pencil on its back, indicate author's name, title of the article (short version), and mark out its top and bottom parts. Drawings must be accurate, drafts and diagrams drawn in Indian ink (or black ink). Photocopies of the X-ray photographs must be presented in a positive image in **tiff format**.

Accurately numbered subtitles for each illustration must be listed on a separate sheet of paper. In the subtitles for the microphotographs please indicate the ocular and objective lens magnification power, method of coloring or impregnation of the microscopic sections (preparations).

7. Please indicate last names, first and middle initials of the native authors, present names and initials of the foreign authors in the transcription of the original language, enclose in parenthesis corresponding number under which the author is listed in the reference materials.

8. Please follow guidance offered to authors by The International Committee of Medical Journal Editors guidance in its Uniform Requirements for Manuscripts Submitted to Biomedical Journals publication available online at: http://www.nlm.nih.gov/bsd/uniform_requirements.html
http://www.icmje.org/urm_full.pdf
In GMN style for each work cited in the text, a bibliographic reference is given, and this is located at the end of the article under the title "References". All references cited in the text must be listed. The list of references should be arranged alphabetically and then numbered. References are numbered in the text [numbers in square brackets] and in the reference list and numbers are repeated throughout the text as needed. The bibliographic description is given in the language of publication (citations in Georgian script are followed by Cyrillic and Latin).

9. To obtain the rights of publication articles must be accompanied by a visa from the project instructor or the establishment, where the work has been performed, and a reference letter, both written or typed on a special signed form, certified by a stamp or a seal.

10. Articles must be signed by all of the authors at the end, and they must be provided with a list of full names, office and home phone numbers and addresses or other non-office locations where the authors could be reached. The number of the authors (co-authors) must not exceed the limit of 5 people.

11. Editorial Staff reserves the rights to cut down in size and correct the articles. Proof-sheets are not sent out to the authors. The entire editorial and collation work is performed according to the author's original text.

12. Sending in the works that have already been assigned to the press by other Editorial Staffs or have been printed by other publishers is not permissible.

Articles that Fail to Meet the Aforementioned Requirements are not Assigned to be Reviewed.

ავტორთა საყურადღებოდ!

რედაქციაში სტატიის წარმოდგენისას საჭიროა დავიცვათ შემდეგი წესები:

1. სტატია უნდა წარმოადგინოთ 2 ცალად, რუსულ ან ინგლისურ ენებზე,დაბეჭდილი სტანდარტული ფურცლის 1 გვერდზე, 3 სმ სიგანის მარცხენა ველისა და სტრიქონებს შორის 1,5 ინტერვალის დაცვით. გამოყენებული კომპიუტერული შრიფტი რუსულ და ინგლისურენოვან ტექსტებში - **Times New Roman (Кириллица)**, ხოლო ქართულენოვან ტექსტში საჭიროა გამოვიყენოთ **AcadNusx.** შრიფტის ზომა – 12. სტატიას თან უნდა ახლდეს CD სტატიით.

2. სტატიის მოცულობა არ უნდა შეადგენდეს 10 გვერდზე ნაკლებს და 20 გვერდზე მეტს ლიტერატურის სიის და რეზიუმეების (ინგლისურ, რუსულ და ქართულ ენებზე) ჩათვლით.

3. სტატიაში საჭიროა გაშუქდეს: საკითხის აქტუალობა; კვლევის მიზანი; საკვლევი მასალა და გამოყენებული მეთოდები; მიღებული შედეგები და მათი განსჯა. ექსპერიმენტული ხასიათის სტატიების წარმოდგენისას ავტორებმა უნდა მიუთითონ საექსპერიმენტო ცხოველების სახეობა და რაოდენობა; გაუტკივარებისა და დაძინების მეთოდები (მწვავე ცდების პირობებში).

4. სტატიას თან უნდა ახლდეს რეზიუმე ინგლისურ, რუსულ და ქართულ ენებზე არანაკლებ ნახევარი გვერდის მოცულობისა (სათაურის, ავტორების, დაწესებულების მითითებით და უნდა შეიცავდეს შემდეგ განყოფილებებს: მიზანი, მასალა და მეთოდები, შედეგები და დასკვნები; ტექსტუალური ნაწილი არ უნდა იყოს 15 სტრიქონზე ნაკლები) და საკვანძო სიტყვების ჩამონათვალი (key words).

5. ცხრილები საჭიროა წარმოადგინოთ ნაბეჭდი სახით. ყველა ციფრული, შემაჯამებელი და პროცენტული მონაცემები უნდა შეესაბამებოდეს ტექსტში მოყვანილს.

6. ფოტოსურათები უნდა იყოს კონტრასტული; სურათები, ნახაზები, დიაგრამები - დასათაურებული, დანომრილი და სათანადო ადგილას ჩასმული. რენტგენოგრამების ფოტოასლები წარმოადგინეთ პოზიტიური გამოსახულებით **tiff** ფორმატში. მიკროფოტოსურათების წარწერებში საჭიროა მიუთითოთ ოკულარის ან ობიექტივის საშუალებით გადიდების ხარისხი, ანათალების შეღებვის ან იმპრეგნაციის მეთოდი და აღნიშნოთ სურათის ზედა და ქვედა ნაწილები.

7. სამამულო ავტორების გვარები სტატიაში აღინიშნება ინიციალების თანდართვით, უცხოურისა – უცხოური ტრანსკრიპციით.

8. სტატიას თან უნდა ახლდეს ავტორის მიერ გამოყენებული სამამულო და უცხოური შრომების ბიბლიოგრაფიული სია (ბოლო 5-8 წლის სიღრმით). ანბანური წყობით წარმოდგენილ ბიბლიოგრაფიულ სიაში მიუთითეთ ჯერ სამამულო, შემდეგ უცხოელი ავტორები (გვარი, ინიციალები, სტატიის სათაური, ჟურნალის დასახელება, გამოცემის ადგილი, წელი, ჟურნალის №, პირველი და ბოლო გვერდები). მონოგრაფიის შემთხვევაში მიუთითეთ გამოცემის წელი, ადგილი და გვერდების საერთო რაოდენობა. ტექსტში კვადრატულ ფჩხილებში უნდა მიუთითოთ ავტორის შესაბამისი N ლიტერატურის სიის მიხედვით. მიზანშეწონილია, რომ ციტირებული წყაროების უმეტესი ნაწილი იყოს 5-6 წლის სიღრმის.

9. სტატიას თან უნდა ახლდეს: ა) დაწესებულების ან სამეცნიერო ხელმძღვანელის წარდგინება, დამოწმებული ხელმოწერითა და ბეჭდით; ბ) დარგის სპეციალისტის დამოწმებული რეცენზია, რომელშიც მითითებული იქნება საკითხის აქტუალობა, მასალის საკმაობა, მეთოდის სანდოობა, შედეგების სამეცნიერო-პრაქტიკული მნიშვნელობა.

10. სტატიის ბოლოს საჭიროა ყველა ავტორის ხელმოწერა, რომელთა რაოდენობა არ უნდა აღემატებოდეს 5-ს.

11. რედაქცია იტოვებს უფლებას შეასწოროს სტატია. ტექსტზე მუშაობა და შეჯერება ხდება საავტორო ორიგინალის მიხედვით.

12. დაუშვებელია რედაქციაში ისეთი სტატიის წარდგენა, რომელიც დასაბეჭდად წარდგენილი იყო სხვა რედაქციაში ან გამოქვეყნებული იყო სხვა გამოცემებში.

აღნიშნული წესების დარღვევის შემთხვევაში სტატიები არ განიხილება.

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THE INFLUENCE OF THE DEMODEX MITE ON THE MORPHOLOGICAL PICTURE OF EYELID PAPILLOMA

Artemov O.V[1], Lytvynenko M.V[2], Chumachenko I.V[3], Bondarenko A.V[4], Dotsenko N.V[3], Ostapchuk K.V[2], Koshelnyk O.L[2], Gargin V.V[4,5].

[1]*State University "Institute of Eye Diseases and Tissue Therapy named after V.P. Filatov National Academy of Sciences of Ukraine", Odessa, Ukraine.*

[2]*Odessa National Medical University, Odessa, Ukraine.*

[3]*OM Beketov National University of Urban Economy, Kharkiv, Ukraine.*

[4]*Kharkiv National Medical University, Kharkiv, Ukraine.*

[5]*Kharkiv International Medical University, Kharkiv, Ukraine.*

Abstract.

Aim: The aim of work is description of new observations related to the participation of demodex in tumor morphogenesis with goal to study the example of eyelid papilloma, imagine the connection between the presence of the demodex mite and certain changes in the typical histomorphological picture of the neoplasm.

Materials and methods: Histomorphological examination covers biopsy and operative material of eye pathology with diagnosis of neoplasm (eyelid papilloma and actinic keratosis (senile keratosis, senile keratoma, solar keratosis)) were selected, with special attention paid to the presence of horn cysts. Agile methodologies were employed to manage the research workflow effectively.

Results: As a result of the conducted histomorphological examination, in 24 cases (48%), patterns pathognomonic for demodectic infection were found. Such patterns, which could indicate the presence of a demodex mite, were cystic formations, as well as fragments of a dead parasite. We noted their presence not only in the tumor tissue, but also in the adjacent hair follicles, sebaceous glands, and subepidermal stroma. It is no coincidence that the authors who previously noted the presence of pigmented elements in keratopapillomas or seborrheic keratomas could not explain their origin, resorting to putting forward such fantastic assumptions as the presence of "symbiosis of melanoblasts and epithelial cells, which ensures the transfer of pigment from the first to the second".

Conclusions: Histomorphological study of serial sections allows us to see the successive stages of transformation of cavity intratissue defects created by the activity of the mite into horn cysts. Cavity defects are the main evidence of demodectic infestation. They occur in basal cell and squamous cell carcinomas, xanthomas, sebaceous adenomas, etc. tumors of the eyelids, but only in keratoacanthomas and senile keratomas they can turn into corneal cysts, which can be assumed to be due to the differentiating potential of these neoplasms.

Key words. Demodex, papilloma, tumor, morphogenesis, Agile.

Introduction.

The experience of pathomorphological work with biopsy material of domestic animals (cats, dogs) made it possible to pay attention to some pathomorphological patterns associated with ectoparasites generally and demodicosis [1-3] partly. These changes in human pathology, as a rule, are underestimated or ignored as artifacts, the consideration of which is optional when establishing a diagnosis with variable presents of invasive agents [4,5].

Unlike humans, demodectic infection in animals is often accompanied by gross tumor-like changes in the skin. Therefore, such pathological conditions often become objects of pathomorphological research. In humans, demodectic skin changes encountered by dermatologists and dermatovenerologists, as a rule, do not require a biopsy. As a result, there is insufficient knowledge about the consequences of demodectic infection in human pathology [3,6].

As for ophthalmopathology, here the main method of diagnosing demodectic infection is the clinical diagnostic study of the native material - the removed eyelash under a low magnification microscope. Thus, detection of a mite with a characteristic picture of blepharitis or blepharoconjunctivitis becomes sufficient for diagnosis [7]. Based on this practice, the belief was formed that demodectic infection is limited only to acute and chronic inflammatory processes with a characteristic clinical picture, which in most cases does not require pathomorphological confirmation [8,9].

Our latest observations allowed pay attention and characterized number of pathognomonic patterns associated with the presence of the demodex mite, based on the study of biopsy and surgical material of tumor processes, thanks to which the peculiarities of the pathomorphosis of some eyelid tumors were revealed as morphological research [10-12]. Moreover, the dynamic nature of studying demodicosis, which involves rapid changes in observations and findings, necessitates a flexible and adaptive approach to research. Implementing Agile methodologies can significantly enhance the efficiency and responsiveness of research teams dealing with such intricate medical conditions. Agile transformation is becoming increasingly popular among medical institutions as it promotes innovation and enhances efficiency in complex adaptive healthcare systems. This method fosters sustainable innovations focused on clients and helps manage rapid personnel changes and resource redistribution efficiently, ensuring that medical teams can respond promptly to emerging challenges. These studies, which we considered as preliminary, provide not only examples of the presence of the mite in tumor tissues, but also show its influence on the histomorphological picture of the pathological process in some cases [8]. The application of Agile methodologies in our research allowed us to promptly identify and analyze these patterns, improving our overall efficiency and adaptability during the study [13,14].

A methodology has been devised to enable Agile redistribution of human resources within medical settings, employing a donor-acceptor interaction approach and considering options for functional preservation when forming or reorganizing project

teams within the medical environment. This Agile resource redistribution method has been tailored for use in a multi-project medical environment, aiming to allocate resources effectively while adhering to principles of resilience, adaptability, and functional preservation. Implementing this method will enable the management of human resources to adapt to the dynamic nature of changes and requirements within medical facilities [13]. Specialists in dermatology, ophthalmology, pathology, laboratory diagnostics, oncology could be involved in diagnostics and management of the Demodex of eyelid tissue and Agile method directed to optimize their efforts.

In this work, we present new observations related to the participation of demodex in tumor morphogenesis with goal to study the example of eyelid papilloma, imagine the connection between the presence of the demodex mite and certain changes in the typical histomorphological picture of the neoplasm. Furthermore, we aim to illustrate how Agile methodologies can be applied to adaptively manage research processes and resources in the study of demodicosis and its effects on tumor pathology.

Materials and Methods.

Histomorphological examination covers biopsy and operative material of eye pathology for the last four years. Biopsy and operative material, including more than one and a half thousand eyelid tumors, was retrospectively reviewed. Among this array, 50 neoplasms with a diagnosis of eyelid papilloma and actinic keratosis (senile keratosis, senile keratoma, solar keratosis) were selected, with special attention paid to the presence of horn cysts.

The material was processed according to the traditional histological method with the preparation of paraffin blocks. In each case, at least 8 serial histological sections stained with hematoxylin-eosin were examined. Agile methodologies were employed to manage the research workflow effectively. By utilizing iterative cycles and continuous feedback, our team was able to quickly adapt to new findings and adjust our focus as necessary [15,16]. This approach facilitated the efficient allocation of resources and personnel, ensuring that each stage of the research was conducted with optimal responsiveness to emerging data.

Results and discussion. As a result of the conducted histomorphological examination, in 24 cases (48%), patterns pathognomonic for demodectic infection were found, which we drew attention to in previous studies [8]. 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; acute, chronic or granulomatous inflammation, in which cystic cavities are usually found; foci of calcification; fragments of a dead mite in the form of keratinous debris.

So, such patterns, which could indicate the presence of a demodex mite, were cystic formations, as well as fragments of a dead parasite. We noted their presence not only in the tumor tissue, but also in the adjacent hair follicles, sebaceous glands, and subepidermal stroma. It should be noted that, unlike cyst-like formations, fragments of the parasite are found much less often. Thus, in our material, these fragments were in 18 cases out of 24, and, usually, as so-called keratin debris - shapeless pigmented particles in the stroma with a size of no more than 2-5 microns. These scattered pigmented pits cannot be attributed as elements of the parasite without knowledge of other factors. It is no coincidence that the authors who previously noted the presence of pigmented elements in keratopapillomas or seborrheic keratomas could not explain their origin, resorting to putting forward such fantastic assumptions as the presence of "symbiosis of melanoblasts and epithelial cells, which ensures the transfer of pigment from the first to the second" [17]. Only viewing a large number of serial sections allows one to find, in most cases, next to the keratin debris, the structured fragments of the parasite, which are demonstrated below.

Fixing the presence of the demodex mite in keratopapillomas and seborrheic keratomas, we drew attention to two histomorphological patterns of these neoplasms: horn cysts and cellular polymorphism. The latter was considered by some authors as a sign of malignancy. However, taking into account the clinically proven benign nature of these tumors, most researchers associate the presence of these patterns with "irritation" of the tumor tissue or with a violation of differentiation. However, observing similar patterns in keratopapillomas and senile keratomas, we did not notice any connection between cellular polymorphism and atypia with the inflammatory component. However, in all cases where similar changes in the structure of these tumors occurred, we were able to see the presence of demodex.

At the same time, it should be taken into account that after the death of the tick, its almost complete destruction occurs within a few hours. This can be verified by leaving the native drug in normal conditions for only one day. Therefore, it is not surprising that in most cases only small fragments of the tick are found, which are doubtful in terms of its identification. Therefore, here we will illustrate those cases where structures are visible that can definitely be correlated with the parasite observed on the removed eyelash (Figures 1 and 2).

In those cases where there were no signs of the presence of demodex, the tumor retained a typical structure. This allows us to say that structural atypia in keratopapillomas and senile

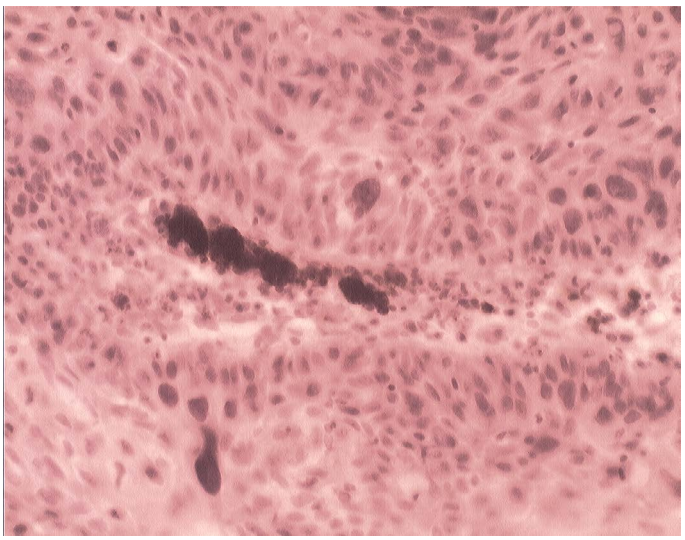

Figure 1. *A partially preserved parasite with visible fragment of the main part of the tick among the parenchyma of a senile keratoma with atypia and cellular polymorphism. Staining with hematoxylin and eosin, magnification x200.*

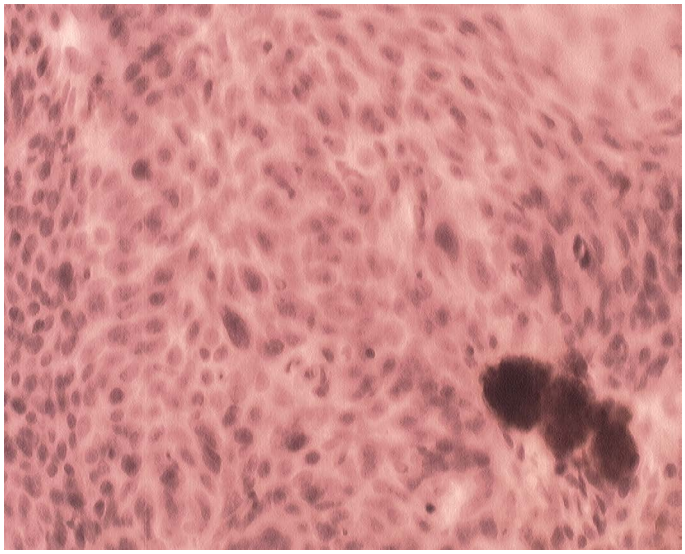

Figure 2. *A clearly visible fragment of the main part of the tick. Cellular polymorphism and atypia in the parenchyma of keratopapilloma. Staining with hematoxylin and eosin, magnification x400.*

keratomas may be caused not by their malignancy, but by the destructive effect of the demodex mite. In any case, such a conclusion is legitimate when, against the background of structural atypia, there are elements of a dead tick.

We have already noted a similar manifestation of the mite's destructive activity on the example of ball cell carcinomas. Thus, the presence of a mite in these tumors is accompanied not only by the formation of cavities in the tumor parenchyma, but also sometimes by complete discomplexation of solid complexes, which in some places resembles the picture of undifferentiated carcinoma and, as we have shown earlier, can represent a problem in making a diagnosis [8].

As for cysts, they are the main element associated with the vital activity of the tick and are most often observed in connection with the parenchyma of the sebaceous glands. However, and this is confirmed by our previous observations, the absorption of cellular elements of the sebaceous glands is not related to some mythical attraction of the mite to the lipids contained in these glands, but only to the availability of these structures.

Indeed, once on the surface of the skin, the mite cannot penetrate the cytoplasmic structures, other than along the hair shaft. On this path, only the sebaceous gland can become the only available cell array. At the same time, in the area of the eyelids, especially at the junction of the skin and nonkeratinized epithelium, in the presence of the conjunctival cavity, exceptionally favorable conditions for the mite to live are created.

Such conditions do not exist on the keratinized epidermis of the skin, which is much rougher than at the margin of the eyelids, and even more so in the area of the lacrimal meatus. This is the only place where the appendages of the skin are under a thin layer of non-keratinized epithelium, which itself can be a source of nutrition for the tick, as well as by penetrating the appendages.

Even wider possibilities of penetration to parenchymal cellular elements appear in the conditions of tumor growth, when the mite gets the opportunity to penetrate not only to the sebaceous glands, but also to the tumor parenchyma

Thus, based on previous observations, we turned to the analysis of the characteristic pattern of keratopapilla and senile keratos - horn cysts. As you know, cysts occur in acanthotic growths of the epidermis, both in deep layers and near the surface. Their appearance is explained by the ability of tumor cells to keratinize, as a result of which foci of hyperkeratinization appear, which gradually transform into horn cysts [17].

However, this explanation does not contradict only the statement about the ability of tumor cells to keratinize. A similar ability can be observed, for example, in basal cell and squamous cell carcinomas, but at the same time, horn cysts are not formed. T should also be noted, that based on topographic relationships (homeomorphism), keratinization centers cannot transform into such a cavity structure, which is represented by horn cysts. After all, in corneal cysts, the formation of the stratum corneum proceeds from the periphery to the center, which is accompanied by a certain stratification in the direction from spiny cells to keratinized cells.

In other words, the organizing factor may not be individual cells, but the surface, where the stratum corneum may arise as a result of successive differentiation of cells. The center of keratinizing cells can transform into pearls, horny masses, etc. This explanation of the mechanism of formation of horn cysts is confirmed by our observations (Figures 3-5).

So, we can prove literature data that Demodex folliculorum and Demodex brevis are ectoparasites that inhabit the skin of humans. They have been related to alterations in the ocular surface, such as, dysfunction of Meibomian glands, blepharitis, chalazion, etc. Ocular demodicosis is characterised by the pathognomonic presence of cylindrical dandruff at the base of the eyelashes, and various symptoms including, among others, itching, lacrimation, and hyperaemia [9]. Hyperkeratotic spicules are rare cutaneous lesions associated with underlying systemic illnesses. In more recent times, facial spinulate demodicosis has been suggested as an etiological factor. Demodicosis is a common dermatological condition characterized by the presence of Demodex mites in the pilocutaneous follicles [6]. Simultaneously, diagnostic difficulties of pathology with fasial localization are famous

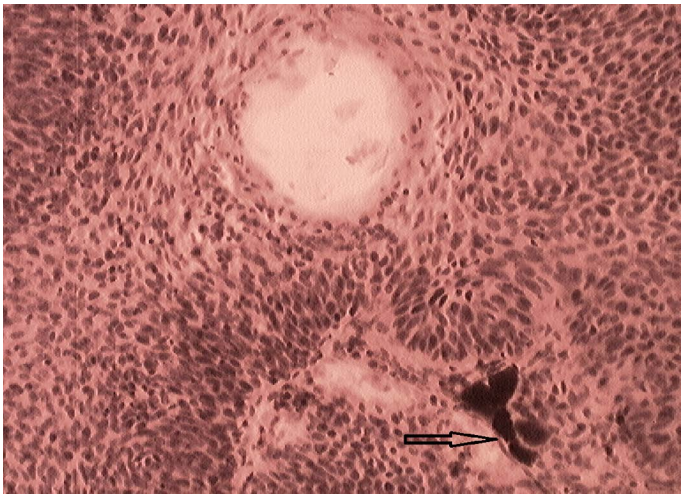

Figure 3. *The cyst is practically without signs of keratinization, not far visible fragments of the mite (arrow). Staining with hematoxylin and eosin, magnification x100.*

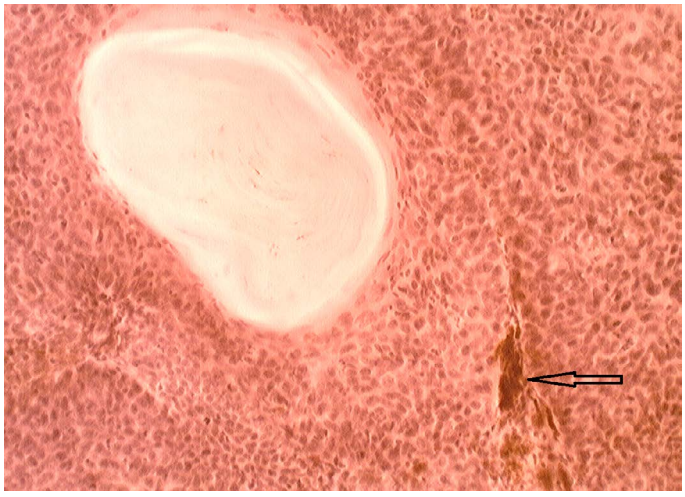

Figure 4. *A cyst with initial signs of keratinization, fragments of a destroyed tick are visible nearby (arrow). Staining with hematoxylin and eosin, magnification x200.*

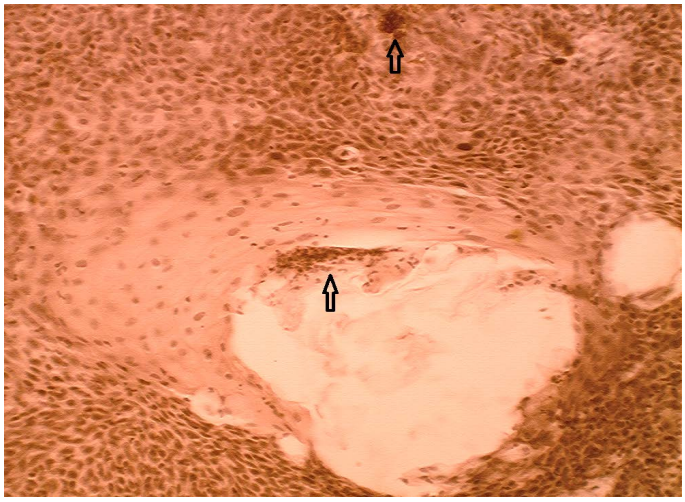

Figure 5. *Cyst with partial keratinization, fragments of a tick - keratin debris (arrows). Staining with hematoxylin and eosin, magnification x200.*

[18]. The pathogenetic mechanism by which Demodex mites influence tumor growth could be connected with constant tissue injury due to parasite presence, chronic inflammation with proliferation activation, and disturbed regenerative process.

As we said above, application of Agile methodologies in our research allowed us to promptly identify and analyze these patterns, improving our overall efficiency and adaptability during the study. In wartime conflicts, epidemics, or pandemics, significant challenges arise, such as rapid reductions in medical personnel, quick changes in the specialization of medical workers considering local conditions, difficulties in accessing workplaces, and the formation of brigades considering medical personnel transportation capabilities. Integrating Agile methodologies into our research process demonstrated significant benefits in managing the dynamic aspects of studying demodicosis. This approach ensured effective resource allocation, rapid problem-solving, and the ability to swiftly adapt to new findings, ultimately enhancing the quality and efficiency of our histomorphological examinations. Implementing this method will enable the management of human resources to adapt to the dynamic nature of changes and requirements within medical facilities. To standardize and streamline management processes, an Agile resource redistribution process model (IDEF0) has been developed. A scenario-based approach has been proposed to ensure Agile resource redistribution, taking into account constraints, regulatory requirements, and organizational culture. Furthermore, an IDEF3 model of the resource redistribution process, based on scenario-based approaches, has been created. Agile transformation can address these challenges through strategic flexibility and organizational resilience with involvement of different medical staff [19] when morphological diagnosis is important [20,21]. That is especial important in skin pathology [22-26]. Adequate implementation of Agile methodology could implement classical [27] and new created methods [28,29] of investigation medical images and processes

Correct measures of demodex diagnostic require the expertise of dermatologists, ophthalmologists, clinical laboratorians, pathologists, and systems analysts in partnering with software-engineering consultants to design and implement a solution. Concurrently, Agile software-building best practices could be formulated, which may be emulated for scalable and cost-effective laboratory-authored measures in ophthalmological organizations [30].

The presented series shows how a cavity formed by a mite can turn into a horn cyst. We noted the presence of similar cysts, but without keratinization, in basal cell and squamous cell carcinomas, nevi, and xanthelasma. However, only in keratopapillomas and senile keratomas, where the tumor cells retain the differentiating potentials of the epidermis, the cavities formed by the tick can turn into horn cysts. The experience of pathomorphological studies in veterinary medicine is useful in studying the consequences of demodectic infection in humans. Knowledge of patterns pathognomonic for demodicosis allows one to pay attention to the role of demodicosis in the cytomorphosis of tumorous skin diseases. This is especially relevant for tumor pathology of the eyelids, where there are the most favorable conditions for the tick to exist, which ensures its constant presence in the majority of the adult population

Conclusion.

The detection of patterns associated with the presence of demodex in keratopapillomas and senile keratomas made it possible to show that the cause of cellular polymorphism and atypia, which are often found in these tumors and simulate malignancy, may be the vital activity of the demodex mite, which penetrates into the tumor parenchyma and causes destructive changes.

Histomorphological study of serial sections allows us to see the successive stages of transformation of cavity intratissue defects created by the activity of the mite into horn cysts. Cavity defects are the main evidence of demodectic infestation. They occur in basal cell and squamous cell carcinomas, xanthomas, sebaceous adenomas, etc. tumors of the eyelids, but only in keratoacanthomas and senile keratomas they can turn into corneal cysts, which can be assumed to be due to the differentiating potential of these neoplasms.

Integrating Agile methodologies into our research process demonstrated significant benefits in managing the dynamic aspects of studying demodicosis by different specialists. This approach ensured effective resource allocation, rapid problem-solving, and the ability to swiftly adapt to new findings, ultimately enhancing the quality and final efficiency of histomorphological examinations.

Conflict of interest.

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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