

PATHOLOGICAL CONDITIONS IN THE MUCOUS MEMBRANE OF THE ORAL CAVITY IN CORONAVIRUS INFECTION

Afakova Ma'mura Shuxratovna¹, Ilhomov Asilbek Xurshidovich²

^{1,2}Tashkent State Medical University

Abstract: Outbreaks of viral respiratory and gastrointestinal infections present major public health and economic challenges. The emergence of SARS-CoV-2 highlighted the capacity of coronaviruses to induce secondary systemic inflammatory processes, notably within the oral cavity. While manifestations like ulcers and taste disorders are documented in COVID-19 patients, identifying definitive diagnostic models, transmission reservoirs, and viral persistence limits our comprehension of human coronavirus pathology and oral mucosal alterations. A retrospective single-center study analyzed 120 laboratory-confirmed, moderately severe COVID-19 patients (aged 25–65). Additionally, pathomorphological and virus-immunological features were evaluated in 6 macaques exhibiting spontaneous coronavirus infection to explore comparative human-monkey modeling parameters. Laboratory data of human patients showed elevated C-reactive protein (44.15 ± 31.8 mg/dl) and fibrinogen (7.96 ± 1.6 g/l). Animal observations confirmed persistent coronavirus shedding in feces for 5–20 months, which correlated with antibody titer spikes, respiratory damage, and high mortality from secondary bacterial dysentery. Oral examinations of COVID-19 patients revealed tongue plaque in 88.8%, attached gum pigmentation in 40%, facial xeroderma and angular cheilitis in 13.9%, and hemorrhagic manifestations in 8.7%. Changes in the oral mucosa are secondary manifestations driven by disease progression and antibiotic regimens rather than primary viral causes. Spontaneous monkey infection provides a strong model for human coronavirus progression. Incorporating dental evaluations into standard clinical assessments for COVID-19 is essential due to the diagnostic value of oral mucosal alterations.

Keywords: Coronavirus, SARS-CoV-2, Oral Mucosa, Spontaneous Infection, Animal Model, Pathological Manifestations

Introduction

Numerous attempts were also made to find out the participation of representatives of the b-type group of ECHO and Coxsackie enteroviruses in diseases. Enteroviruses were often detected in the feces of patients with symptoms of gastroenteritis, this was the reason that a number of ECHO and Coxsackie viruses were classified as enteropathogenic. However, the frequent detection of similar types of enteroviruses in healthy people suggests rather that these viruses are concomitant with most acute gastrointestinal diseases [1]. In the long-term studies of G. A. Timofeeva with sovt. / 11 / it is shown that in the conditions of a children's hospital, where children with diarrhea are admitted, viral diarrhea (44%) was the most frequent, followed by bacterial infections (22%) and viral-bacterial infections (15%). Various viruses were detected in patients - adeno (8.5%), ECHO (8.5%), polio (5%), Coxsackie (1%) and untyped viruses (34%). It is noteworthy that in a high percentage of cases, viral agents associated with the disease were not identified. In this review, we have tried to highlight the place and role of coronaviruses in the intestinal and respiratory pathology of humans and monkeys. Coronavirus can cause a number of inflammatory processes in the oral cavity of patients [2]. In particular, they described the occurrence of ulcers and plaques, as well as cracks on the tongue in an elderly patient hospitalized with COVID-19. In addition, infected people may develop a taste disorder, fungus, candidiasis and other pathological conditions in the mouth. Symptoms can be observed as secondary manifestations of infection, as well as as side effects from taking medications, in particular antibiotics. Moreover, dental problems themselves can serve as a risk factor for infection, since they weaken the protective functions of the body. Therefore, it is advisable to include a dental examination in the list of necessary studies for COVID-19 [3].

To study the state of the oral mucosa and substantiate its changes in patients with a laboratory-confirmed diagnosis of SARS-CoV-2 of moderate severity.

Materials and Methods

A retrospective single-center study of patients who were in the infectious diseases department in the period from May to June 2020 with a primary diagnosis at the admission of ICD-X: J18.9: coronavirus infection was conducted. This study included 120 patients aged 25 to 65 years (62 men and 58 women, average age).

Viral infections occupy a leading place in the problem of human infectious pathology, which determines the constant interest in them not only by health authorities, but also by representatives of various branches of science [4], [5]. Without a comprehensive study of this problem, it is hardly possible to count on a quick solution to the issues of prevention and control of viral infections, which cause harm not only to human health, but also sometimes cause huge economic damage. It is enough to give examples of the prevalence of viral infections of the upper respiratory tract (influenza and a large group of other viruses), but no less serious problem is gastrointestinal diseases, the cause of most of which are viruses. In recent years, the task of studying a number of viruses that were previously associated with the occurrence of upper respiratory tract diseases, but can also cause intestinal pathology, such viruses include coronaviruses, a group of new and poorly studied viruses. Difficulties in studying representatives of this family are associated with difficulties in cultivating them under experimental conditions, which makes it difficult to successfully solve the problems of diagnosing this infection, especially in humans [6]. If it was possible to endow EHF from patients with a contagious runny nose (OS strains 43, 229E), then attempts to isolate strains from ash with an intestinal form of coronavirus infection were practically unsuccessful, the question of the antigenic relationships of EHF detected in the presence of an unknown clinical pathology of a person remained open, an adequate experimental model of infection was not created. The presented work summarizes the long-term studies of infection with coronaviruses of monkeys, which are unique laboratory animals closest to humans. There is no information in the literature about the isolation of coronavirus from monkeys, and therefore there is no definitive answer to the question of whether monkeys are infected with any strain of human coronavirus or 4 independent species of KB monkeys [7], [8]. Hence, the question remains open about the possibility of modeling coronavirus infection in monkeys, as well as the issues of diagnosis, prevention and treatment of infection; the absence of these data causes the lack of an answer to questions about the reservoirs of infection, the duration of the virus's preservation in the body, etc. All of the above issues determine the relevance of our work.

Results and Discussion

C-reactive protein was elevated in 120 people at admission (44.15 ± 31.8 mg/dl). 55 people had elevated fibrinogen values (the average values of elevated fibrinogen were 7.96 ± 1.6 g / l). The analysis for D-dimer was taken in 65 people (the average value was 287.6 ± 103.68 ng/ml), in 10 people of whom the indicators were elevated (435 ± 24 ng/ml). Hemorrhagic manifestations occurred in 9 (8.7%) patients whose anamnesis was not burdened. Pronounced facial xeroderma and angular cheilitis were detected in 11 (13.9%) patients. In 80 patients (88.8%), there was a white, light yellow and brown plaque on the examination of the mucous membrane of the tongue. Pigmentation in the area of the attached gum on the upper and lower jaw was detected in 26 (40%) patients [9], [10].

Pathomorphologically, 6 macaques with spontaneous coronavirus infection were examined. Two of them died. In both animals, KV was detected in the feces during 6 and 12 months of observation, respectively. Clinically, these monkeys had pneumonia during the first month of their stay in the nursery, one of them was periodically found to have loose stools during observation. The monkeys died from the

associated dysentery colitis, confirmed bacteriologically. In the lungs of these monkeys, there were large hyperchromic formations that looked like ugly conglomerates of nuclei and small lymphocytic infiltrates in the interalveolar septa. Two other monkeys were killed. In one of them, KV in the feces was detected for a period without clinical signs of pneumonia or enterocolitis. During histological examination of the material from this animal, diffuse lymphocytic filtration of the deep parts of the mucous membrane was observed. Morphological signs of infection in the oral cavity and other organs were not found. Thus, for the first time in the literature, we have given a description of spontaneous coronavirus infection in monkeys [11]. A long-term isolation of KV with feces is shown. Approximately half of the 20 long-term infected rhesus macaques and hamadryad baboons were found to have excretion of the virus with feces for 5-20 months, which in most cases was combined with clinical manifestations in the form of diarrhea or pneumonia, as well as changes in the intestines and lungs, which we consider characteristic of coronavirus infection. In the adult half of the animals, the release of the virus had a short-term effect (up to 2 months) and was rarely accompanied by clinical manifestations. The data on the independent infection of groups of monkeys with various strains of EHF OS 43 and 229E are interesting, which may indicate a parallel circulation of different strains of viruses or antigenically related to them among animals. A parallel virus-immunological analysis in groups of monkeys indicates that as the intestinal coronavirus infection spreads, determined by viral excretion with feces, there is an increase in the titers of antibodies to the own strain of KV isolated from macaques, as well as to the strain. Spontaneous HF infection of monkeys is persistent, rotocayushy with damage to the respiratory and/or SOPR, accompanied by eriodic exacerbations, during which clinical manifestations of enterocolitis and / or pneumonia are observed. The death of animals occurs mainly from associated diseases, more often of a bacterial nature. In some cases, the infection proceeds in a manifest form and is, apparently, the cause of the death of animals [12], [13]. For the most part, the monkeys ' gi had a complex of changes indicating a sharp decrease in the immune response (hemoblastosis, the state after irradiation-1st, OSSSHS). The close similarity of the object of our study with a human, as well as positive data indicating a relationship with EHF strains, allow us to extend the data obtained by us during the study of EHF infection of monkeys to humans in the first approximation. We believe that the spontaneous infection of monkeys itself is a good model of the human infection of the same name, the study of which can make a significant contribution to the far-from-developed problems of coronavirus infection. One of the most important tasks of our research was to clarify the question of the etiology and properties of the causative agent of the infection described by us. The establishment of a high infection rate of monkeys of different species with a viral agent morphologically described as a coronavirus brought to the fore the question of detailed characteristics of the properties of this virus [14]. It was important, first of all, to isolate the original virus strains from monkeys, followed by a detailed description of their morphology, molecular biological and biological properties, as well as to establish antigenic relationships with known representatives of the coronavirus family, primarily with prototype human coronavirus strains OS 43 and 229E. The study of these questions would make it possible to establish the species affiliation (or possible independence) of the KV strains isolated from dt monkeys, as well as to answer the question about the similarity or difference between the KV strains isolated from monkeys of different species [15]. The establishment of an antigenic relationship between human and monkey KV strains would solve the problem of currently missing diagnoses, and would allow in the future to consider an experimental monkey soronavirus infection as a suitable model for studying human edno-named infection.

Conclusions

In COVID 19 (SARS-CoV-2), changes in the COPD are not the primary cause, but are manifested as a result of drug treatment and the progression of the disease, despite the fact that the oral cavity is one of the sources of the entrance gate for infection.

REFERENCES

- [1] Yu. G. Belotserkovskaya, A. G. Romanovskikh, and I. P. Smirnov, "COVID-19: Respiratory infection caused by a new coronavirus: new data on epidemiology, clinical course, patient management," *Consilium Medicum*, no. 3, pp. 12-20, 2020.
- [2] E. V. Vakhrushina, "Clinical and laboratory substantiation of immunocorrective therapy of patients with recurrent aphthous stomatitis," Abstract of Ph.D. dissertation, Cand. Med. Sci., Moscow, Russia, 2012, 21 p.
- [3] Ya. A. Lavrovskaya, I. G. Romanenko, O. M. Lavrovskaya, and I. S. Pridatko, "Candidiasis of the oral mucosa with dysbiotic changes," *Crimean Therapeutic Journal*, no. 3, pp. 27-30, 2017.
- [4] S. V. Morozova and I. Yu. Meitel, "Xerostomia: causes and methods of correction," *Medical Advice*, no. 1, pp. 124-128, 2016.
- [5] V. V. Nikiforov, T. G. Suranov, A. Yu. Mironov, and F. G. Zabozaev, *New coronavirus infection (COVID-19): etiology, epidemiology, clinical features, diagnosis, treatment and prevention*. Moscow, Russia, 2020, 48 p.
- [6] R. V. Ushakov, N. B. Eliseeva, N. P. Polevaya, et al., *Modern methods of diagnosis, elimination and prevention of halitosis: a textbook*. Russian Medical Academy of Postgraduate Education, Moscow, Russia, 2016, 81 p.
- [7] B. Iranmanesh, M. Khalili, R. Amiri, H. Zartab, and M. Aflatoonian, "Oral manifestations of COVID-19 disease: A review article," *Dermatologic Therapy*, vol. 34, no. 1, p. e14570, Jan. 2021.
- [8] J. Amorim Dos Santos, et al., "Oral manifestations in patients with COVID-19: A 14-case series," *Field Actions Science Reports*, vol. 22, no. 2, pp. 111-119, 2020.
- [9] N. Huang, et al., "SARS-CoV-2 infection of the oral cavity and saliva," *Nature Medicine*, vol. 27, no. 5, pp. 892–903, May 2021.
- [10] Biadsee, A. Biadsee, F. Kassem, O. Djaiani, S. Masarwa, and Z. Ormianer, "Olfactory and gustatory symptoms, and xerostomia in hospitalized COVID-19 patients," *Journal of Clinical Medicine*, vol. 9, no. 9, p. 2977, Sep. 2020.
- [11] M. Salehi, et al., "Opportunistic fungal infections in the oral cavity of COVID-19 patients," *Frontiers in Medicine*, vol. 8, p. 719231, Aug. 2021.
- [12] B. Rockx, et al., "Comparative pathogenesis of COVID-19, MERS, and SARS in a nonhuman primate model," *Science*, vol. 368, no. 6494, pp. 1012-1015, May 2020.
- [13] V. J. Munster, et al., "Respiratory disease in rhesus macaques inoculated with SARS-CoV-2," *Nature*, vol. 585, no. 7824, pp. 268–272, Sep. 2020.
- [14] P. Zhou, et al., "A pneumonia outbreak associated with a new coronavirus of probable bat origin," *Nature*, vol. 579, no. 7798, pp. 270–273, Mar. 2020.
- [15] S. F. Sia, et al., "Pathogenesis and transmission of SARS-CoV-2 in golden hamsters," *Nature*, vol. 583, no. 7818, pp. 834–838, Jul. 2020.