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ANALYSIS OF THE RESULTS OF TREATMENT OF 93 PATIENTS WITH POST-COVID THROMBOSIS OF THE CAVERNOUS SINES IN THE CONDITIONS OF THE DEPARTMENT OF PURULENT SURGERY

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Abstract*. Complications of the transferred COVID-19 are accompanied by the development of such complications as cavernous sinus thrombosis. The paper analyzes the results of treatment of 93 patients treated in the Department of Purulent Surgery and Surgical Complications of Diabetes Mellitus. The analysis showed that only in 31.2% of cases, patients were discharged with positive dynamics for further treatment and observation on an outpatient basis, while more than half of the patients 62 (66.7%) were taken home. It is necessary to revise the tactics of managing patients with post-covid manifestations of cavernous sinus thrombosis. Recommendations should reflect specific criteria for when expectant management is needed and when emergency surgery is needed, as another outbreak of the virus with its new mutating strains is not ruled out, where specialists should be ready to manage these patients.*

Аннотация. *Осложнения перенесенного COVID-19, сопровождаются развитием таких осложнений, как тромбоз кавернозного синуса. В работе проанализированы результаты лечения 93 пациентов, находящихся на лечении в отделении гнойной хирургии и хирургических осложнений сахарного диабета. Анализ показал, что только в 31,2% случаев больные выписаны с положительной динамикой для дальнейшего лечения и наблюдения в амбулаторных условиях, при этом более половины больных 62 (66,7%) взяты дом. Необходим пересмотр тактики ведения пациентов с постковидными проявлениями тромбоза кавернозного синуса. Рекомендации должны отражать конкретные критерии того, когда необходима выжидательная тактика, а когда необходима экстренная операция, т.к. не исключена еще одна вспышка вируса с его новыми мутирующими штаммами, где специалисты должны быть готовы вести этих пациентов.*

Izoh. *O'tkazilgan COVID-19 asoratlaridan - kavernöz sinus trombozi kabi asoratlarning rivojlanishi bilan kuzatilishi mimkin. Maqolada, qandli diabetning yiringli jarrohlik va jarrohlik asoratlari bo'limida davolanayotgan 93 nafar bemorni davolash natijalari tahlil qilingan. Tahlillar shuni ko'rsatdiki, faqat 31,2% hollarda bemorlar ambulator sharoitda keyingi davolanish va kuzatuv uchun ijobiy dinamika bilan chiqarildi. Kavernoz sinus trombozining postkovid ko'rinishlari bo'lgan bemorlarni davolash taktikasini qayta ko'rib chiqish kerak. Tavsiyalar kutilayotgan davolash zarur bo'lganda va shoshilinch jarrohlik zarur bo'lganda aniq mezonlarni aks ettirishi kerak. Mutaxassislar ushbu bemorlarni boshqarishga tayyor bo'lishi kerak bo'lgan yangi mutatsiyaga uchragan shtammlari bilan virusning yana bir epidemiyasi inkor etilmaydi.*

Keywords: *COVID-19; SARS-CoV- 2; invasive mucormycosis ; rhino -sino-orbital mucormycosis ; diabetes; thrombosis of the cavernous sinus; infection; treatment;*

Doing. Humanity faced a new challenge when, in December 2019, severe acute respiratory syndrome coronavirus 2 (SARSCoV-2) was identified as the cause of an outbreak of pneumonia cases in Wuhan, a city in the Chinese province of Hubei. In the first few months of 2020, infection with this new coronavirus led to a global pandemic that affected every country in the world, with more than 21 million cases by August 2020 [1]. Although coronavirus disease 2019 (COVID-19) primarily presents as a lung infection with symptoms ranging from mild upper respiratory infection to severe pneumonia and acute respiratory distress syndrome, other multisystem manifestations of

the disease and its associated complications are increasingly common. [2 , 3].

Speaking of post-COVID complications, the development of thrombosis of the cavernous sinuses is alarming. Cavernous sinus thrombosis (CST) is a single cerebral vein and sinus thrombosis that causes a characteristic clinical syndrome. It usually has an infectious cause. Cavernous sinus thrombosis is a rare disease, although the exact frequency of its occurrence is unclear. The incidence of cerebral vein thrombosis is 13 cases per 1,000,000 per year [4]. The cavernous sinus is the least frequent localization of cerebral vein thrombosis [5,6]. Moreover, in the pre- antibiotic period, it was accompanied by high mortality [7]. The outcome of this condition has greatly improved since the advent and widespread use of antibiotics, but it still depends on timely diagnosis and treatment. Possible treatments include antibiotics, anticoagulants, and corticosteroids, as well as surgical treatment of the infection [8]. On the one hand, the main cause of cavernous sinus thrombosis may be a remote focus with sepsis, which can lead to cavernous sinus thrombosis. On the other hand, the infection can spread from the facial areas *through the* facial venous vessels and ophthalmic veins, or from the sphenoid sinus directly into the adjacent cavernous sinus [9]. Among the most common causes contributing to this condition, a nasal furuncle is mentioned (50%), accompanied by ethmoid or sphenoid sinuses (30%) and dental infections (10%) [10, 11]. The tonsils, soft palate, middle ear, mastoid process, and orbit are some of the most common major areas of infection. The venous system of the paranasal sinuses with a high degree of anastomosis allows the infection to spread retrogradely into the cavernous sinus through the superior and inferior ophthalmic veins [12,13].

And if earlier bacteria dominated in the etiology of cavernous sinus thrombosis, then in patients with COVID-19, the starting point is the presence and progression of fungal microflora, which manifests itself as rhino-sino-orbital mucormycosis - RCOM. RSOM is the most common manifestation, causing approximately two-thirds of all cases of mucormycosis [14, 15]. The spores enter the nasopharynx, and tissue invasion, thrombosis, and necrosis progress from the nose to the cavernous sinuses. Prior to the pandemic, prevalence was estimated at 0.005–1.7 per million population worldwide [16 , 17]. In COVID-19, the incidence of secondary bacterial or fungal infections is 8%, with aspergillosis and candida being the most common fungi [18, 19]. The current wave of COVID-19 has caused a surge in mucormycosis . COVID-19 creates a hypoxic environment with high glucose, high ferritin, and reduced leukocyte phagocytic activity due to immunosuppression by the virus itself and the corticosteroids used in treatment. Such an environment is very conducive to the germination and reproduction of fungal spores [16]. Unhygienic practices, prolonged hospital stay with the possibility of nosocomial infection, use of immunosuppressants, and comorbidities are other risk factors associated with an increase in the incidence of COVID-19-associated ROM. According to published data, 76% of patients with COVID-19-associated rhino - sino-orbital mucormycosis were given a history of systemic corticosteroids [16]. Irrational or thoughtless use of corticosteroids may be a possible cause of POCM. Corticosteroids have been criticized for their role in increasing susceptibility to mucormycosis , and this claim is not entirely unfounded. A cumulative dose in excess of 600 mg of prednisone and 2–7 g of methylprednisolone has been found to predispose immunocompromised patients to mucormycosis [20]. Long-term administration of high doses of systemic corticosteroids for more than 3 weeks is considered a risk factor for the development of mucormycosis [21]. Literature Review of Existing Global Singh Data *et al.* [16] and Hoenigl *et al.* [22] showed that rhino -sino-orbital mucormycosis develops in 80% of cases in patients with diabetes mellitus.

Summing up this review, a number of questions remain unresolved, in particular, in what terms the development of cavernous sinus thrombosis is possible and what is the starting point, where patients with this pathology should be treated and the criteria for their recovery.

The purpose of this work was to analyze the results of treatment of patients with cavernous sinus thrombosis in conditions of purulent

surgery, with the definition of tactics for their treatment.

Research methods. Due to the increase in the number of patients with post- COVID complications, in particular, thrombosis of the cavernous sinuses, on August 28, 2021, under No. multidisciplinary TMA clinic, in the surgical block of specialized beds for patients with various manifestations of cavernous sinus thrombosis. The beds were created in the department of the Center for Purulent Surgery and Surgical Complications of Diabetes Mellitus, where 93 patients were treated from September to December.

In all patients, the clinical picture developed after suffering SARS-CoV-2, while we conditionally divided the patients into anatomical zones (Table No. 1).

Table No. 1

Distribution of patients

Nosology	**Total**	
	n	**%**
TCS, with eye involvement	26	27.9
TCS, with sinus involvement	34	36.6
TCS, with the defeat of the maxillofacial area	33	35.5
Total	93	one hundred

The analysis showed that an isolated lesion of one anatomical region was not observed in patients, mainly a combined lesion dominated, however, we divided the patients according to prevailing signs. Most often, patients had damage to the paranasal sinuses and maxillofacial region, which was detected in 36.6% and 35.5% of cases, respectively. At the same time, the involvement of the eyes in the process was manifested by the orbital fissure syndrome, manifested by ophthalmoplegia, ptosis, exophthalmos and enophthalmos, of varying severity. It was detected in 26 patients (27.9%).

The distribution of patients by sex and age showed that the incidence in males and females was almost the same, amounting to 53.7% and 46.3%, respectively (table No. 2). The average age of the patients was 56.1 ±3.8 and I would like to note that patients of working age and the elderly prevailed. Thus, 39.8% of patients were aged 51-60 years and 33.3% - 61-70 years.

Table number 2

Distribution of patients by age and sex

Groups		**Number of patients (n =93)**	
		n	**%**
Age groups	up to 30 years	one	1.1
	31-40 years old	7	7.5
	41-50 years old	nine	9.7
	51-60 years old	37	39.8
	61-70 years old	31	33.3
	71-80 years old	7	7.5
	over 80 years	one	1.1
Average age, years		56.1 ±3.8	
Floor	Male	fifty	53.7
	Female	43	46.3

A study of the nature of the appealability of patients showed that the main contingent were patients from Tashkent - 11 and Tashkent region - 21. Patients from Namangan and Surkhandarya regions also prevailed, which accounted for 11.8% and 13.9%. All patients were secondary, i.e. at the initial stage, they were treated at the place of stay (lost **time)**, and only when the clinical picture worsened, they were sent to the TMA clinic (table No. 3).

Table No. 3

Distribution of patients by regions

Localization	**Main**	
	n	**%**
Tashkent	eleven	11.8
Tashkent region	21	22.6
Andijan region	4	4.3
Jizzakh region	five	5.4
Kashkadarya region	five	5.4
Navoi region	one	1.1
Namangan region	eleven	11.8
Samarkand region	five	5.4
Surkhondarya region	13	13.9
Sirdarya region	8	8.6
Fergana region	7	7.5
Khorezm region	2	2.2
Total	93	one hundred

After analyzing the timing of the appearance of the clinical picture of thrombosis of the cavernous sinuses after suffering COVID 19, it was revealed that they most often manifest themselves in terms of 7 to 14 days, in our study, there were 63 such patients, which is 67.7%, in second place is the manifestation occurred after 14 days, accounting for 20.4%. Less commonly, clinical manifestations occur up to 7 days after suffering COVID 19.

Table No. 4

Characteristics of patients according to the terms of hospitalization after undergoing COVID

Time of treatment before hospitalization	**Total**	
	n	%
up to 7 days	eleven	11.9
7 – 14 days	63	67.7
over 14 days	19	20.4
Total	93	one hundred

Taking into account the main contingent of patients, which was represented by patients of working age and the elderly, we analyzed the presence of comorbidities in these patients. 81.7% of patients had a history of diabetes mellitus, while they had type II diabetes mellitus and all of them received insulin, of various durations of action. In 59 patients (63.4%), hypertension was diagnosed and in 48.4% of cases, patients had coronary heart disease (table No. 5).

Table number 5

The presence of comorbidities

Pathology	**n**	**%**
Diabetes	76	81.7
Hypertonic disease	59	63.4
Coronary artery disease	45	48.4

The manifestation of clinical signs and the main complaints of patients were as follows. Almost all patients had headaches and nasal congestion of varying severity, which was in 84 patients (90%), in second place was the presence of sinus necrosis, in our patients it was in 76% of cases (71 patients). Necrosis of the upper palate was in 19 patients, and the intensity of necrosis at the time of treatment in patients was different, from the initial, in the form of limited cyanosis, to the formed one. At the same time, patients did not have limited necrosis (the presence of a demarcation line). Manifestations of the orbital fissure syndrome, such as visual impairment, ophthalmoplegia, diplopia, ptosis, exophthalmos were observed in 28 patients, which is 30%.

Table No. 6

The frequency of occurrence of rhino-sino-cerebral complications

No.	Complications	**n**	**%**
1	Necrosis of the nasal mucosa and paranasal sinuses	71	76.3
2	Eye complications	61	65.6
3	Meningeal complications	twenty	21.5
4	Cerebral circulation disorders	nine	9.6

The study of the development of rhino-sino-cerebral complications of cavernous sinus thrombosis showed that 71 patients had necrosis of the nasal mucosa and paranasal sinuses, 65.6% had ocular complications of varying severity, and 9.6% of patients had cerebrovascular accidents (table number 6).All patients underwent a histological examination of the material, while mucormycosis was detected in all patients

The tactics of medical and diagnostic measures included multislice computed tomography, taking clinical and laboratory tests and surgical intervention. The choice of surgical treatment tactics included FESS - functional endoscopic sinus surgery, the volume of which was different (table No. 7).

Table number 7

The nature and number of operations performed

Operation name	**n**	**%**
necrectomy	4	4.3
Maxillary sinusectomy + necrectomy	29	31.2
Sequestrectomy	10	10.6
Opening of soft tissue abscess	2	2.2
Puncture of the maxillary sinus	one	1.1
Cancellation of the operation	2	2.2
without surgery	45	48.4
Total	93	one hundred

As can be seen from the presented table, operative interventions of various nature were performed in half of the treated patients. In 31.2% of cases sinustomy with necrectomy was performed, in 10 (10.6%) patients sequestrectomy was performed. Against the background of the development of necrotic manifestations of the nasal mucosa in 2 patients, the process progressed with the transition to the face and the development of phlegmon of the facial area. In the presence of clear indications for surgical intervention, two patients refused operations. 48.4% of patients did not undergo surgical interventions. The reasons for their failure were the severity of the condition of the patients, the extent of the lesion and the refusal of relatives to perform the operation. This indicator is reflected in the results of treatment.

Table number 8

Distribution of patients depending on the results of treatment

	n	**%**
Discharged for outpatient treatment	29	31.2
Transfer to another medical institution	2	2.1
Taken home	62	66.7
Total	93	one hundred

Analyzing the results of treatment of patients, it can be seen that only in 31.2% of cases, patients were discharged with positive dynamics for further treatment and observation on an outpatient basis, while more than half of the patients 62 (66.7%) were taken home. The reasons for this were the serious condition of the patients, the refusal to perform surgery, the deterioration of the condition after the surgical operation. Two patients were transferred to the Department of Neurology due to the progression of the clinical picture of acute cerebrovascular accident.

Thus, the study showed that it is necessary to revise the tactics of managing patients with post- covid manifestations of cavernous sinus thrombosis. It would seem that the stopped state of acute respiratory syndrome caused by coronavirus 2 (SARSCoV-2) gives a formidable complication in the form of thrombosis of the cavernous sinuses with rhino -sino-orbital mucormycosis. In our opinion, an in-depth study of this pathology is necessary, with the development of guidelines for the management of such patients, the definition of dominant specialists in the department of which these patients should be located in order to exclude the development of cross-infection. Recommendations should reflect specific criteria for when expectant management is needed, and when emergency surgery is needed, because. another outbreak of the virus with its new mutating strains is not ruled out, where specialists should be ready to manage these patients.

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