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PECULIARITIES OF THE DIFFERENTIAL DIAGNOSIS OF DIFFERENT TYPES OF CEREBRAL SINUS AND VEIN THROMBOSIS IN PATIENTS WITH ENT ORGANS INVOLVEMENT

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Ключові слова: *центральный венозный тромбоз, асептический тромбоз кавернозного синуса, дифференциальная диагностика тромбозів*

Ключевые слова: *центральный венозный тромбоз, асептический тромбоз кавернозного синуса, дифференциальная диагностика тромбозов*

Abstract. *Peculiarities of the differential diagnosis of different types of cerebral sinus and vein thrombosis in patients with ENT organs involvement. Lamza N.V., Kovtunenکو O.V., Morgachova G.K., Tereschenko L.A., Lyschenko D.V., Zaitsev A.V., Fannan A. The paper is devoted to the problems of diagnosis of septic and aseptic forms of central venous thrombosis. The aim of the study was to study the clinical manifestation and lesions of the ear, nose and throat, in patients with aseptic central venous thrombosis in order to increase the efficiency of differential diagnosis of various forms of thrombosis and to determine the tactics of further treatment of patients with this disease. Variants of manifestation of lesions of Lesions of the ear, nose and throat were studied in 14 patients with aseptic central venous thrombosis who were hospitalized for the period from 2016 to 2019, the results of their ophthalmological and neurological examination, as well as laboratory studies are given. It was found that among patients with cerebral venous thrombosis in most cases (82.4%) various changes in otolaryngological status were detected, of which 21.4% of cases – with septic lesions of the ENT organs, 78.6% of cases – with aseptic changes. During the examination, the character of these pathological changes in otolaryngology status in non-purulent lesions of the ENT organs (swelling of the soft tissues of the face, sinus mucosa or their necrosis, dysfunction of the pharyngeal muscular system, neurosensory deafness) were formulated, which could be explained by secondary ischemic tissue changes and impaired venous outflow of the soft tissues of the face. Also, the absence of a primary purulent focus of infection and septic changes in peripheral blood and cerebrospinal fluid in patients with a clinically confirmed diagnosis of CVT, confirmed the aseptic (primary) form of the disease. Patients with aseptic CVT are assigned direct anti-coagulant therapy and symptomatic therapy depending on the presence of cerebral and focal neurological symptoms, which is radically different from the therapeutic tactics used by patients with septic CVT. Thus, when conducting a differential diagnosis of different forms of CVT, for the choice of therapeutic strategy, in addition to the standard algorithm of examination of the patient should take into account the nature of changes in otolaryngological status.*

Реферат. *Особенности дифференциальной диагностики разных видов тромбозу мозговых синусов и вен у пациентов с поражением ЛОР-органов. Н.В. Ламза, О.В. Ковтуненко, Г.К. Моргачова, Л.А. Терещенко, Д.В. Лищенко, А.В. Зайцев, А. Фаннан. Статья посвящена проблеме диагностики септической и асептической форм центральных венозных тромбозов. Методу цього дослідження було вивчення клінічних проявів ураження ЛОР-органів у пацієнтів з асептичним центральним венозним тромбозом для підвищення ефективності дифференциальної діагностики різних форм тромбозів і визначення тактики подальшого лікування пацієнтів. Вивчено варіанти проявів ураження ЛОР-органів у 14 пацієнтів із септичним центральним венозним тромбозом (ЦВТ), які перебували на стаціонарному лікуванні за період з 2016 до 2019 р., наведені результати їх офтальмологічного й неврологічного обстеження, а також лабораторних досліджень. Було виявлено, що серед пацієнтів з церебральним венозним тромбозом у більшості спостережень (82,4%) визначаються різні зміни в отоларингологічному статусі, з них у 21,4% спостережень – із септичним ураженням ЛОР-органів,*

78,6% випадків – з асептичними змінами. У ході обстеження були сформульовані характеристики зазначених патологічних змін в отоларингологічному статусі при не гнійному ураженні ЛОР-органів (набряк м'яких тканин обличчя, слизової оболонки пазух або їхній некроз, порушення функції м'язового апарату глотки, нейросенсорна туговухість), які могли бути пояснені вторинними ішемічними змінами тканин і порушенням венозного відтоку м'яких тканин голови. Також відсутність первинного гнійного вогнища інфекції й септичних змін у периферичній крові та спинномозковій рідині у хворих з клінічно підтвердженим діагнозом ЦВТ підтверджувала асептичну (первинну) форму цього захворювання. Пацієнтам з асептичним ЦВТ була показана терапія прямими антикоагулянтами й симптоматична терапія залежно від наявності загально мозкової та осередкової неврологічної симптоматики, що кардинально відрізняється від терапевтичної тактики, застосовуваної пацієнтам із септичною формою ЦВТ. Таким чином, проводячи диференціальну діагностику різних форм ЦВТ для вибору терапевтичної стратегії, крім стандартного алгоритму обстеження пацієнта, слід брати до уваги характер змін в отоларингологічному статусі.

Cerebral venous and venous sinus thrombosis is a relatively rare cerebrovascular disease, accounting for not more than 1-2% of all cerebrovascular diseases and occurring more frequently in young adults. The incidence in adults is 0.2-1.8 cases per 100,000 population in different countries. During pregnancy and the postpartum period, the prevalence of cerebral venous and venous sinus thrombosis increases to 12 cases per 100,000 women annually [6]. Without treatment, the prognosis is unfavorable in 15% of cases, the lethality can reach 10%, but even with severe neurological disorders, complete spontaneous recovery is possible [7].

The cause of septic central venous thrombosis (CVT) is an infectious process in the area of venous drainage: cavernous sinus thrombosis – in facial infections, sigmoid sinus – in middle ear infections, sagittal sinus – in scalp infections [4]. Due to the widespread use of antibiotics, the incidence of septic thrombosis as a complication of ENT organ infections has significantly decreased (down to 8% of observations) and the problem of aseptic central venous thrombosis (ACVT) has become more relevant. Clinical manifestations of ACVT are non-specific and variable, which leads to difficulties in timely diagnosis on the one hand and difficulties in differential diagnosis between different forms of CVT - on the other hand. This is an important issue, since the form of thrombosis determines the tactics of treatment of patients with this pathology. If, in case of septic thrombosis, timely curing of the primary focus of infection, including antibacterial therapy, detoxification and, in some cases – corticosteroid therapy is necessary, in aseptic thrombosis the therapy is fundamentally different [2,3].

According to standard recommendations, the treatment of aseptic sinus thrombosis should start with heparin, then switch to indirect anticoagulants, as well as symptomatic therapy, depending on the presence of general hemorrhagic and focal neurological symptoms. On-time onset of therapy and duration of each stage are extremely important to prevent fatal outcomes and relapses [5].

The clinical picture of aseptic thrombosis can be very diverse and variable with the regard to the dynamics, duration and intensity of symptoms. According to different authors, the most frequent of them is headache, which occurs in 80-90% of patients, which may have its own features due to the degree of thrombosis severity, the patient's age, the time passed since the onset of the disease [7]. Focal neurological deficit syndrome is the next most frequent, it happens in 39-60% of observations, and as an initial symptom – in 15%. Completing the triad of the most constant syndromes in patients with ACVT is the ophthalmic syndrome, which most often manifests as edema of the optic disc and vision loss – up to 50% of observations [8].

Currently, the diagnosis of ADVC is based on the confirmation of clinical data by the results of neuroimaging studies (computed tomography, magnetic resonance imaging (MRI), MR venography) [9]. But even these diagnostic methods are not absolutely sensitive for this pathology. Thus, normal CT images are found in 10-20% of cases with proven central cerebral sinus thrombosis and in 50% of patients with isolated intracranial hypertension syndrome, which is usually a consequence of CVT. Visualization of high density thrombus in the lumen of cavernous sinus is possible only in 25% of cases. T1 and T2 MRI is also not a reliable diagnostic criterion, as it depends on the stage of thrombus formation – the signal may be both absent and intensified [9]. MR venography has a greater diagnostic value.

In spite of the fact that progress in the development of neuroimaging techniques and the expansion of ideas about the etiology and pathogenesis of CVT contributed to the improvement of its diagnosis, the relevance of differential diagnosis of various forms of this disease for choosing the appropriate management tactics for patients with this pathology remains. In view of the above the Purpose of our research is to study the variants of ENT-organ lesions manifestation in patients with aseptic central venous thrombosis in order to improve the efficiency of differential diagnostics of various forms of

thrombosis and to determine the tactics of further treatment of patients with this pathology.

MATERIALS AND METHODS OF RESEARCH

Under our clinical observation there were 17 patients on inpatient treatment in Dnepropetrovsk regional clinical hospital named after Mechnikov, in the otolaryngological departments, as well as the departments of neurology, vascular neurosurgery and septic intensive care units during the period from 2016 to 2019 with CVT syndrome at the age of 32 to 65 years. There were 11 male patients, accounting for 64.7% of observations, and 6 female patients (35.3% of cases). All patients underwent endoscopic otolaryngological examination and tone audiometry, the results of ophthalmological and neurological examinations were studied [8]. In addition, the following laboratory examinations were performed: general and biochemical blood tests, coagulation test, determination of D-dimer parameters, and cerebrospinal fluid (CSF) analysis [5, 9]. Neuroimaging methods included magnetic resonance imaging (MRI) and computed tomography (CT) with contrast medium. The study was performed on a Toshiba Alexion tsx-032a and GE optima ct660 [4, 6]. During CT there were determined following signs of CVT: an increasing of the X-ray density (hyperdensity) of cerebral veins and sinuses (direct sign), or ischemic changes that either do not fit the arterial pool of blood supply, or being located in the immediate vicinity of the venous sinus (indirect signs). CVT on the CT with contrast medium was detected by the presence of a symptom called "empty delta" – a hypodense area of the venous sinus amid the background of hyperdense collateral veins of the sinus wall. CT venography made it possible to diagnose a CVT by a defect in the accumulation of cerebral veins and/or sinuses [4, 6].

The following criteria were taken into account to include patients to the research:

1. Thrombosis of the central venous sinuses, established on the basis of the clinic, laboratory and diagnostic studies, confirmed by neuroimaging data [4]

2. The presence of pathological changes in the otolaryngological status on the basis of endoscopic examination, audiometry and neuroimaging data [4, 10]

3. The age of the patients is from 18 to 70 years.

The criteria for excluding patients to the research were:

- Other (non-vascular) diseases of the central nervous system

- Concomitant diseases in the decompensation stage.

CVT in patients was determined by the presence of some prevailing syndromes: isolated intracranial

hypertension (headache), focal neurological deficit syndrome, ophthalmological syndrome, neuroimaging data [4, 9].

The main diagnostic signs that are distinguishing septic (secondary) CVT from aseptic (primary) were the presence of an infectious purulent focus in the area of the external nose, soft tissues of the face, paranasal sinuses, acute (or fulminant) onset, febrile fever, neutrophilic leukocytosis in general clinical blood analysis, neutrophilic cytositis in the CSF, as well as the presence of pathogenic microflora in the contents of the focus of infection, in the blood and cerebrospinal fluid during bacteriological examination [4].

The criteria for aseptic CVT were the absence of a purulent focus of infection in the ENT organs, subacute disease progression, the presence of various risk factors associated with the development of CVT (craniocerebral trauma, long-term use of steroids or contraceptives, hereditary predisposition, etc.).

Given the small number of observations, we applied nonparametric statistical methods [1]. Quantitative parameters were described as median [25th; 75th] percentiles. Comparison of quantitative indicators in two independent samples was carried out using the Mann-Whitney test. Statistical data processing was carried out using the R program (version 3.6.3.), For citation -R Core Team (2020). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. URL <https://www.R-project.org/>. The critical level of p for testing statistical hypotheses was taken <0.05

The materials and figures presented in the paper totally comply with the principles of ethics set out in the Declaration of Helsinki "Ethical Principles of Medical Research with Human Participation" developed by the World Medical Association, the "Universal Declaration on Bioethics and Human Rights (UNESCO)", the order of the Ministry of Health of Ukraine "On Approval of the Procedure for Conducting clinical trials of medicinal products and examination of materials of clinical trials and model regulations on the Commission on Ethics "No. 690 of 23.09.2009.

RESULTS AND DISCUSSION

During the observation of patients with CVT in order to verify the purulent focus, we paid attention to the fact that pathological changes in the otolaryngological status were detected in the majority of patients with CVT. At the same time, clinical manifestations of these changes differed significantly in different patients in their nature (septic, aseptic), course and degree of severity. According to the established ideas, the presence of any pathological changes in the pharynx, paranasal sinuses,

and middle ear cavities was evaluated as a septic focus leading to the development of CVT, which was an indication to start antibacterial therapy and surgical elimination of the primary focus of infection. In a number of cases, in the absence of the patient's primary purulent source of infection, antibiotic therapy was ineffective, and only against the background of direct anticoagulants, patients showed positive dynamics. Such experience in the observation of patients with CVT created the need to analyze and systematize pathological changes in the otolaryngological status in this group of patients, which may have sufficient diagnostic value.

As a result of our examination, among 17 patients with central venous sinus thrombosis, 14 (82.4%) had changes in the otolaryngological status. According to the nature of pathological changes of ENT organs these patients were divided into 2 groups: Group 1 – 3 patients (21.4% of observations) with septic lesion of ENT organs, Group 2 – 11 (78.6%) patients with aseptic changes in otolaryngological status.

Otolaryngological examination of Group 1 patients revealed the following diagnoses: purulent maxillary sinusitis (MS), purulent ethmoid sinusitis (ES) – 1 patient, external nasal fornix – 1 patient, and closed fracture of the nasal back, left-sided hem sinus complicated by left-sided purulent MS and ES in 1 patient. All patients complained of headaches of moderate intensity and noted a decrease in pain syndrome after the start of treatment (drainage of purulent focus, anti-inflammatory therapy). In addition, all patients had febrile hyperthermia in the debut of the disease, during the ophthalmological examination edema of the optic nerve, edema of periorbital tissues, ptosis and

corneal opacity were detected in one patient and another patient had exophthalmos. Syndrome of neurological deficit in the 1st group patients was manifested as exophthalmos, ophthalmoplegia due to affection of III, IV and VI pairs of CN – in 2 patients, impaired function of V pair of cranial nerves (CN) (I branch) – in 1 patient (Table 1).

The data of laboratory studies showed that all Group 1 patients had absolute neutrophilic leukocytosis and elevated sedimentation rate in the detailed blood count. Biochemical blood tests (Table 3) showed a slight decrease in the mean values of PV and AEF, as well as an increase in the mean values of fibrinogen (3.6 g/l) and D-dimer (0.6 µg/ml) ($p > 0.05$). CSF analysis in these patients was characterized by elevated CSF pressure, averaging up to 220 mm a.v., and moderate cytos, averaging up to 15 cl/µL ($p < 0.05$).

Results of spiral CT revealed decreased pneumatization of the sinuses due to the presence of pathological content in the maxillary and ethmoid paranasal sinuses on one side with Hounsfield density +40 HU – 2 cases. In all patients, CT signs of thrombosis of the cavernous sinus were obtained, including in 1 patient – the superior sagittal sinus (Table 1).

During the therapeutic and diagnostic puncture of the paranasal sinuses, purulent contents were obtained in the maxillary sinuses in 2 patients and in 1 – upon opening the furuncle of the vestibule of the nose.

Based on the clinical and laboratory findings, Group 1 patients were diagnosed with secondary cavernous sinus thrombosis (septic form). This group of patients underwent antibacterial and detoxification therapy with drainage of purulent focus of infection.

Table 1

Results of examination of Group 1 patients

No.	Gender/age	Location of thrombosis	ENT status	Ophthalm. status	Neurolog. status	Data of CT/CT venography	Bacterial examination
1	m/34	CS	External nose abscess	Swelling of the optic nerve, paraorbital fiber	Disorder of the V pair of FMN, mening. s-m function	CS thrombosis	Focus - S. aureus, Blood-neg. Liquor-neg.
2	m/47	CS	Purulent MS, ES	Swelling of the optic nerve, paraorbital fiber exophthalmos	Ophthalmoplegia (III, IV, VI mening. s-m lesion)	MS, ES, CS thrombosis	Focus - S. aureus, St.pyogenes Blood-neg. Liquor-neg.
3	m/41	CS, SSS	Hem sinus, purulent MS, ES	Swelling of the optic nerve, paraorbital fiber Corneal opacity	Ophthalmoplegia (III, IV, VI mening. s-m lesion)	MS, ES, CS thrombosis, SSS	Focus - S. aureus, Blood-neg. Liquor-neg.

Notes: CS – cavernous sinus, SSS – superior sagittal sinus.



There were also revealed changes in the otolaryngological status in the 2nd observation group: 11 patients (79% of observations) with clinical manifestations of CVT. As a result of a thorough clinical examination, the presence of a purulent focus of infection in these patients was ruled out. Local changes in ENT organs in patients of the 2nd group had aseptic character of the lesion and were manifested as soft tissue edema, mucous membrane or (and) its necrosis, impairment of any organ function. This fact led us to the assumption of the primary genesis of thrombosis development.

To reveal provoking factors of CVT we collected the anamnesis of patients and found out that 3 patients (27.2% of cases) took corticosteroid drugs, including oral contraceptives for a long period of time, 2 patients (18.1% of observations) were followed up because of the type II diabetes, 2 patients (18.1% of observations) had a history of cranio-cerebral trauma, and one of them (9%) had a closed trauma of the facial skeleton followed by rhinoseptoplasty 5 years ago. One patient noted a case of central cerebral sinus thrombosis in a family history (9%), and factors contributing to CVT were not identified in 3 patients (27.2% of observations).

Analyzing the clinical picture, we found that 6 patients (54.5%) had persistent intense headache,

which was evaluated by the VAS scale (visual analog scale) – 9 points, not relieved by analgesics, and half of them had headache characterized by a gradual increase in intensity over a long period of time (up to 1 year). In the remaining patients, the headache was not constant and scored 4 by the VAS scale.

In the course of the otolaryngological examination, in 10 patients (90.9%) was revealed a pronounced one-sided pitting edema of the soft tissues of the face in the area of the maxillary sinus projection, combined with pain during palpation of this area. This symptom appeared at the onset of disease and disappeared on its own. At the same time, in 1 patient (9.1%), this symptom was combined with pain during palpation and pitting edema in the area of the projection of the frontal sinus. One patient (9.1%) had progressive necrotic changes in the hard palate mucosa on one side (Fig. 1). Also, 1 patient had a decrease in the sensitivity of half of the tongue (due to paresis of the intermediate nerve) with subsequent necrosis on the affected side and 1 patient (9.1%) had one-sided pharynx asymmetry combined with the inability to swallow solid food due to one-sided paralysis of the stylopharyngeus muscle innervated by the IX pair of CN.



Fig. 1. Necrotic changes in the hard palate with a clear line of necrosis in a patient with ACTT

In addition, due to neurological examination there are diagnosed – ophthalmoplegia, due to the

defeat of III, IV and VI pairs of FMN – in 8 patients (72.7%), in one patient (9.1%) – dysfunction of the

V pair of FMN (I branch), as well as impaired mobility of the upper and lower extremities by the type of hemiparesis (alternating variant) in 1 patient (9.1%). Ophthalmological examination of patients of the 2nd group showed the presence of edema of the optic nerve and edema of the paraorbital tissues – 10 patients (90.9%) (Table 2).

Using audiometric examination 6 patients (54.5% of cases) from the 2nd group were diagnosed with

unilateral neurosensory hearing loss with a progressive course.

These neurological changes, in our opinion, could be explained by secondary ischemic changes in the brain tissue, since CVT leads to an increase in venous and capillary pressure, cerebral hypoperfusion develops, and, as a consequence, ischemic damage. Clinically it may present with focal neurological symptoms characteristic of non-infectious CVTs [4].

Table 2

Results of examination of patients of the 2nd group

No.	Gender /age	Location of thrombosis	ENT status	Ophthalm. status	Neurolog. status	Data of CT / CT venography	Bacter. examination
1	m/45	CS, SSS, TS	Pastosity soft tissues in MS projection, necrosis of the hard palate	Swelling of the optic nerve, paraorbital fiber	Ophthalmoplegia (lesion of III, IV, VI) hemiparesis, paresis of IX pair of FMN	MS, ES, CS thrombosis, SSS, TS	Focus – neg. Blood-neg. Liquor-neg.
2	f/32	CS	Pastosity soft tissues in MS projection, NHL	Swelling of the optic nerve, paraorbital fiber	Ophthalmoplegia (lesion of III, IV, VI)	No signs of CVT detected	Focus – neg. Blood-neg. Liquor-neg.
3	m/61	CS	Pastosity of soft tissues in MS projection, unilateral oropharyngeal necrosis, NHL	Swelling of the optic nerve, paraorbital fiber	Ophthalmoplegia (lesion of III, IV, VI), paresis of the intermediate nerve	MS, ES, CS thrombosis	Focus - S. aureus, Blood-neg. Liquor-neg.
4	m/54	CS	Pastosity of soft tissues in MS projection, unilateral necrosis of the nasal cavity, NHL	Swelling of the optic nerve, paraorbital fiber	Ophthalmoplegia (lesion of III, IV, VI)	MS, ES, CS thrombosis	Focus - neg. Blood-neg. Liquor-neg.
5	f/39	CS	Pastosity of soft tissues in MS projection, NHL	Swelling of the optic nerve, paraorbital fiber	Ophthalmoplegia (lesion of III, IV, VI)	No signs of CVT detected	Focus – neg. Blood-neg. Liquor-neg.
6	f/50	CS	Pastosity of soft tissues in MS projection	Swelling of the optic nerve, paraorbital fiber	Ophthalmoplegia (lesion of III, IV, VI)	No signs of CVT detected	Focus – neg. Blood-neg. Liquor-neg.
7	f/45	CS	Pastosity of soft tissues in MS projection	Swelling of the optic nerve, paraorbital fiber	Ophthalmoplegia (lesion of III, IV, VI)	CS thrombosis	Focus – neg. Blood-neg. Liquor-neg.
8	f/49	CS	Pastosity of soft tissues in MS projection	Swelling of the optic nerve, paraorbital fiber	Disorder of function of the V pair of FMN	No signs of CVT detected	Focus – neg. Blood-neg. Liquor-neg.
9	m/65	CS	Pastosity of soft tissues in MS projection	Swelling of the optic nerve, paraorbital fiber		CS thrombosis	Focus – neg. Blood-neg. Liquor-neg.
10	m/36	CS	NHL	-	Ophthalmoplegia (lesion of III, IV, VI)	No signs of CVT detected	Focus – neg. Blood-neg. Liquor-neg.
11	m/56	CS	Pastosity of soft tissues in MS projection, NHL	Swelling of the optic nerve, paraorbital fiber		CS thrombosis	Focus – neg. Blood-neg. Liquor-neg.

Notes: *TS - transverse sinus, SSS – superior sagittal sinus, CS – cavernous sinus, TS – transverse sinus.

The laboratory research showed that in all patients of the 2nd group, no changes were found in the full blood count. Analysis of CSF parameters showed average values of CSF pressure ($p>0.05$) and the absence of cytositis ($p<0.05$), while in 4 patients (36.4% of observations) the pressure in the CSF was increased (Table 3). In the 1st group of patients, the results of the CSF analysis showed

moderate cytositis ($p<0.05$) in all patients and increased pressure. Our results confirmed that the pathological process in patients of the 2nd group had an aseptic nature, the results of a biochemical blood test (PT, APTT, fibrinogen, D-dimer) in the 2nd group patients did not fundamentally differ from the same indicators in group 1 patients ($p>0.05$).

Table 3

Primary biochemical blood test indicators (prothrombin time (PT), activated partial thromboplastin time (APTT), Fibrinogen, D-dimer), CSF (pressure and cytositis) of studied patients

Patients	Pressure (mm H ₂ O)	cytositis (cells / μ l)	PT (sec)	APTT (sec)	Fibrinogen (g/L)	D-dimer (μ g FEU/ml)
1-st group						
1	150	20	9.4	20.5	3.8	0.6
2	220	13	10.2	19.6	3.6	0.62
3	230	15	11.6	21.5	3.2	0.54
Average	200	16	10.4	20.53	3.53	0.587
2-nd group						
1	250	5	13.2	23.6	2	0.45
2	220	3	11.2	23.5	2.4	0.25
3	240	3	12.1	24.3	1.9	0.45
4	240	2	11.6	22.1	3.4	0.32
5	100	5	13.2	21.2	2.9	0.54
6	120	1	11.4	20.1	3.6	0.57
7	150	2	11.2	19.8	3.7	0.61
8	100	3	10.5	21	3.7	0.72
9	150	4	11.2	20.7	3.8	0.75
10	130	2	10.3	20.1	3.6	0.62
11	140	2	10.6	20.4	3.7	0.59
Average values	167.273	2.909	11.5	21.527	3.155	0.534
P value	0.43	0.01	0.16	0.39	0.53	0.58

Note. $p < 0.05$ in comparison to the original data.

The results of spiral computed tomography in patients of the 2nd group identified signs of unilateral hemisinusitis (maxillary, ethmoidal) with a Hounsfield density +10 HU in 3 patients (27.3% of cases) and 1 patient (9.1%) had the presence of pathological contents in the sphenoid sinus with a

Hounsfield density +15 HU (Fig. 2). CT examination in 6 patients (54.5%) showed the accumulation of contrast agent in the cavernous sinus area (Fig. 3a, 3b), including signs of thrombosis of the superior sagittal and transverse sinus in 1 patient (Table 2).

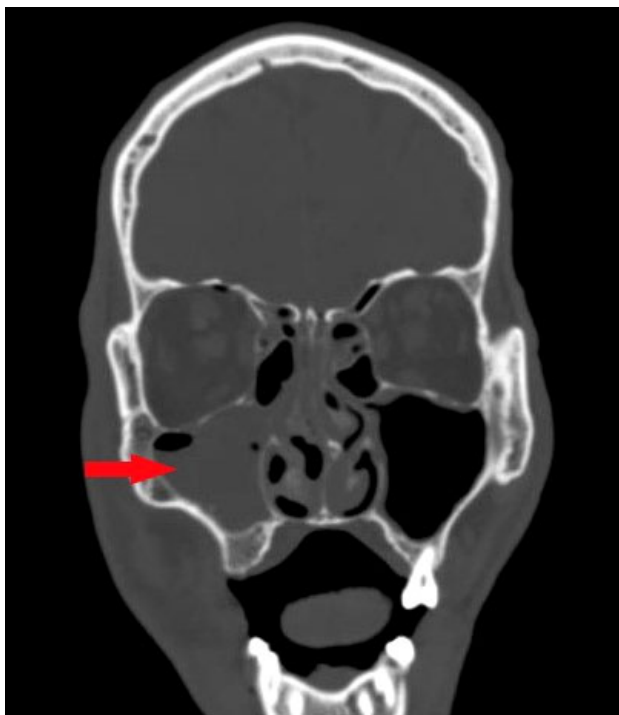


Fig. 2. CT of head (coronal view). Decreased maxillary sinus pneumatization on the right in a patient with ACTT

The results of the therapeutic and diagnostic puncture of the paranasal sinuses showed the absence of pathological discharge in these patients, and the increase in tissue density in the cavities of the paranasal sinuses was explained by the presence of parietal edema of the mucous membrane.



Fig. 3a. CT of head with amplification in axial projection, an accumulation of contrast agent in the area of right cavernous sinus

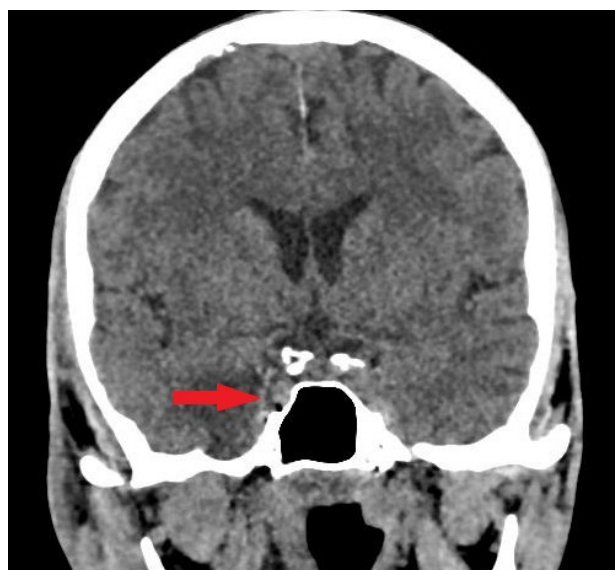


Fig. 3b. CT of head with amplification in coronal projection. Accumulation of contrast agent in the area of the cavernous sinus on the right

After analyzing the results obtained, we noted a number of clinical features that distinguish patients of the 1-st and 2-nd study groups. So, one of the defining factors that make it possible to differentiate various forms of CVT is the nature of pathological changes in the local otolaryngological status of patients with a confirmed diagnosis of CVT. If the changes in the ENT-organs in patients have a septic nature, such as soft tissue swelling, tissue necrosis, or neurological damage, which took place in patients of the 2-nd group, it can be assumed that such patients have primary CVT. The next sign that makes it possible to differentiate the types of thrombosis is the difference between the provoking factors in the medical history. In the 1-st group, as a rule, the cause was acute purulent diseases of the nose or paranasal sinuses, with the subsequent acute development of the CVT clinical picture, and in the 2-nd group – the absence of obvious causes of the onset of the disease with a gradual increase in CVT symptoms, as well as the presence of anamnestic data in the form of long-term use of corticosteroid drugs, endocrine diseases, traumatic brain injury. In addition, we noted different dynamics of headache between patients of the 1-st and 2-nd groups. The headache quickly enough regressed in patients of the 1st group after the start of antibiotic therapy, on the contrary, in the 2-nd group the headache in half of the patients did not respond well to treatment and was characterized by a gradual increase. Analysis of the neurological status also allowed us to determine the difference in the manifestation of neurological disorders between patients of both groups, namely,

focal neurological symptoms were more pronounced in the 2-nd group of patients, and cerebral symptoms – in the 1-st group.

CSF analysis indicators can also be used as a criterion for differential diagnosis between septic and aseptic CVT. In the absence of cytolysis against the background of increased CSF pressure, the septic nature of the pathological process can be excluded. At the same time, the indicators of biochemical blood tests (PT, APTT, fibrinogen, D-dimer), according to our study, can only indicate the presence of thrombosis, but cannot be used as a differential diagnosis between its various forms. Bacteriological studies of blood and cerebrospinal fluid were not informative as a differential diagnosis in our study. Only 2 patients of the 1st group were found to have pathogenic microflora in the contents of the focus of infection.

Thus, the absence of a primary purulent focus of infection and septic changes in the peripheral blood and CSF in patients with a clinically confirmed diagnosis of CVT, we assumed a variant of the aseptic (primary) form of this disease. This was an indication for starting therapy with direct anticoagulants and symptomatic therapy, depending on the presence of cerebral and focal neurological symptoms.

CONCLUSIONS

1. Among patients with cerebral venous thrombosis in 82.4% of cases, various changes in the otolaryngological status are revealed, of which 21.4% of cases – with septic lesions of the ENT organs, 78.6% of cases – with aseptic changes.

2. According to our observations, with aseptic (primary) form of central venous thrombosis, patho-

logical changes in the otolaryngological status appeared in the form of non-suppurative lesions of the ENT organs (edema of the soft tissues of the face, sinus mucosa or necrosis, dysfunction of the muscular apparatus of the pharynx, neurosensory hearing loss), the non-infectious nature of which was confirmed by clinical data, the results of laboratory and instrumental research methods.

3. When conducting differential diagnostics of various CVT forms, in order to choose a therapeutic strategy, in addition to the standard algorithm of examining the patient, the nature of changes in the otolaryngological status, the presence of factors provoking thrombosis in the history and the nature of neurological changes should be taken into account.

Contributors:

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REFERENCES

- Holovanova IA, Byelikova IV, Lyakhova NO. [Fundamentals of medical statistics: textbook. Way. For graduate students and clinical residents]. Poltava; 2017. p. 113. Ukrainian.
- Maksimova MYu, Dubovitskaya YuI, Sharov MN, Prokofieva YuS. [Headache in aseptic thrombosis of cerebral veins and venous sinuses]. *Nevrologiya*. 2017;3(3):44-47. Russian.
- Tibekina LM, Shumakova TA, Nikolayeva AA, Shcherbuk UA. [Emergency diagnosis of cerebral venous thrombosis]. *Surgery herald named after I.I. Grekov*. 2016;(5):18-25. Russian. doi: <https://doi.org/10.24884/0042-4625-2016-175-5-18-25>
- Ramazanov GR, Korigova KhV, Petrikov SS. [Diagnostics and treatment of cerebral venous thrombosis]. *Journal named after N.V. Sklifosovsky Research Institute for Emergency Medicine*. 2021;10(1):122-34. Russian. doi: <https://doi.org/10.23934/2223-9022-2021-10-1-122-134>
- Ali S. Cavernous Sinus Thrombosis: Efficiently Recognizing and Treating a Life-Threatening Condition. *Cureus*. 2021 Aug 20;13(8):e17339. PMID: 34567880; PMCID: PMC8451531. doi: <https://doi.org/10.7759/cureus.17339>
- Ferro JM, Bousser M-G, Canhão P, et al. European Stroke Organization guideline for the diagnosis and treatment of cerebral venous thrombosis – Endorsed by the European Academy of Neurology. *European Stroke Journal*. 2017;2(3):195-221. doi: <https://doi.org/10.1177/2396987317719364>
- Geng B, Wu X, Malhotra A. Septic cavernous sinus thrombosis-Case series and review of the literature. *Clin Neurol Neurosurg*. 2020 Oct;197:106092. Epub 2020 Jul 16. PMID: 32693341. doi: <https://doi.org/10.1016/j.clineuro.2020.106092>
- Matthew TJH, Hussein A. Atypical Cavernous Sinus Thrombosis: A Diagnosis Challenge and Dilemma. *Cureus*. 2018 Dec 4;10(12):e3685. PMID: 30761237; PMCID: PMC6367117. doi: <https://doi.org/10.7759/cureus.3685>

9. Nazeer N, Ivaturi PB. Proptosis in Otorhinolaryngology: An Overview. *Int Arch Otorhinolaryngol.* 2021 Apr;25(2):e267-72. Epub 2020 Jun 30. PMID: 33968231; PMCID: PMC8096516. doi: <https://doi.org/10.1055/s-0040-1709986>

10. Sebaa B, Benkeroum D, Hadjadj C, Sahbatou R. Thrombophlébite du sinus caverneux d'origine infectieuse chez l'enfant: Revue de la littérature et de scription d'un cas. *Revue Médicale de l'HMRUO.* 2015;1(2):55-58.

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