DIAGNOSIS AND TREATMENT OF PURULENT-SEPTIC COMPLICATIONS OF CATHETERIZATION OF THE SUBCLAVIAN VEIN
(literature review)

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Annotation:The problem of diagnostics and treatment of purulent-septic complications of subclavian vein catheterization has long attracted the attention of surgeons, anesthesiologists-resuscitators and specialists in surgical infections. The frequency of development of these complications, according to various authors, is very variable and fluctuates from 0.07% to 17.5%. According to the National Nosocomial Infection Surveillance, about 200 thousand cases of infection associated with the use of subclavian catheters are registered in the USA annually (NNIS System Report, 1998). In Russia and, in particular, in St. Petersburg, bacteremia is detected in 9.3% of patients with subclavian catheters.

Keywords:purulent-septic complications, diagnostics, catheterization of the subclavian vein.

Clinical picture, diagnostics and prevention of purulent-septic complications that developed after the introduction of the subclavian catheterblack grouse.

Microorganisms that cause catheter-associated infections most often enter the bloodstream from the skin at the site of catheter insertion. They migrate from the skin surface of the insertion sitecatheter along its outer surface, colonizing the distal end and thrombi located in the lumen of the vessel. Thus, a septic focus is formed. Its localization directly in the bloodstream determines the pathogenetic essence, clinical picture and prognosis of the disease.

The first sign of local manifestation of the inflammatory process in the catheterized vein, which subsequently leads to generalization of the infection, is the appearance of pain along the vein during infusion. Then complaints of pain in the neck area on the side of catheterization, swelling and cyanosis of the upper limb, and dilation of the subcutaneous veins of this area arise. Edema of the upper limb and neck on the side of catheterization develops [2]. Inflammatory edema may occur in the area where the catheter is located, hyperemia and purulent discharge may appear through the catheter wound when pressing on the area of insertion of the cavacatheter [2].

In the development of thrombosis of the internal jugular vein, in addition to swelling and pain in the neck, patients report pain when swallowing. The jugular vein is palpated as a dense, painful cord, often visible to the eye [4].

At the same time, colonization of the catheter (especially by representatives of the skin microflora) can often occur without clinically expressed symptoms, which is associated with the low virulence of such pathogens [5].

With the development of a primary lesion in the internal jugular vein due to the migration of a subclavian catheter there, together with the clinical picture of thrombosis of the subclavian vein, a picture of infiltration develops, and then deep phlegmon of the neck, which was described by V.F. Voyno-Yasenetsky in 1956 as the so-called “woody” phlegmon.

General clinical symptoms consist of signs of a systemic inflammatory response (SIRS): tachycardia (>90/min.), hyperventilation (RR>20/min.), blood leukocytosis (>12x109/l), fever (t>38°C) with further signs of sepsis as the complication progresses [6].

Clinically, angiogenic sepsis (catheter-associated sepsis) manifests itself with symptoms of sepsis of any other genesis, but at the same time has some features. A characteristic feature is the coincidence in time of periods of temperature rise with

intravenous administration of drugs [5].

M.I. Lytkin, N.N. Shikhverdiev (2017), based on their own observations (142 cases), identify the following criteria for a justifiedestablishing the diagnosis of angiogenic sepsis:

1. localization of the source of infection in the vascular bed

2. the presence of clinical and laboratory signs of sepsis: fever with chills and increased sweating, especially after intravenous and intra-arterial infusions, signs of intoxication, the presence of metastatic purulent foci, progressive deterioration of the condition, leukocytosis with a shift in the formula to the left, lymphopenia, anemia, hypoproteinemia, manifestation of insufficiency of certain organs or systems; discrepancy between local signs of infection and the general reaction of the bodynism, disappearance of clinical manifestations and normalization of laboratory parameters after removal of the catheter;

3. Presence of bacteremia.

If the blood culture data are negative, it should be borne in mind that bacteremia cannot be constant due to the bactericidal properties of the blood and the partially preserved ability of the body to limit the source of infection. A breakthrough of the infection into the bloodstream is usually accompanied by hyperthermia, and blood sampling for culture should be done precisely at the height of the fever (Lytkin M.I., Shpkhverdiev N.N., 2017; Schwartz N.S., Nguyen DC, 2009). V.A. Gologorsky and co-authors (2018) consider the identity of the microflora cultured from the catheter and blood in the presence of clinical signs of a generalized infectious process to be a prerequisite for diagnosing angiogenic sepsis.

Currently, a point assessment of the severity of violation of thoseor other organs and systems in sepsis. Among the simplest and most common are the SOFA (Sepsis Oriented Failure Assessment) scale and the MODS (Multiple Organs Dysfunction Score). The SOFA scale was developed by JLVincent in 2006 and adopted by the European Society of Intensive Care Medicine (ESIM). The scale is very easy to use and is available to almost any hospital with a biochemical laboratory (Kostyuchenko A.L. et al., 2016). It is used to assess the severity of organ dysfunction, which allows one to objectively identify a group of patients with severe sepsis and describe developing disorders. To assess the severity of the condition at a specific point in time, the APACHE II (Acute Physiological and Chronic Health Estimation II) scale is most often used (Kostyuchenko A.L. et al., 2016; Beloborodov V.B., 2012; Gelfand B.R. et al., 2013).

Methods for diagnosing purulent-septic complications of subclavian vein catheterization primarily involve assessing clinical manifestations, carefully examining the catheterization site, upper limb, and neck on the side of catheterization. Measurement of central venous pressure is of great diagnostic importance for diagnosing vein thrombosis (Portnoy M.V., 2018; Stoyko Yu.M. et al., 2012; Sanders RJ, Haug S, 2018; Ena J. et al., 2018).

A modern method for diagnosing subclavian vein obstructions is ultrasound. The advantage of ultrasound diagnostics is its ease of use, non-invasiveness, and the possibility of repeated use to assess the dynamics of the process [7,8,9].

The leading method for diagnosing venous thrombosis today is duplex angioscanning [10,11], which allows combining the ability to view (morphology information) with the definition of Doppler analysis (hemodynamic information). In the studies of GM Baxter et al. (2015), color Doppler ultrasound in the diagnosis of subclavian vein thrombosis had a sensitivity and specificity of 100% compared to the results of phlebography. Other authors note that ultrasound methods of examination can often give false results in the diagnosis of subclavian vein obstruction [12,6]. MB Grinev et al. (2010) indicate the great diagnostic value of ultrasound methods of examination in the diagnosis of infiltrates, abscesses and phlegmons in the area ofsubclavian catheter.

When conducting an ultrasound examination of catheterized veins with developed thrombosis, the acute stage of the process is characterized by a homogeneous, hypo- or anechoic thrombus structure, while the subacute stage and the stage of post-thrombotic disease are characterized by a heterogeneous structure with the presence of areas of both low and high echogenicity in the structure [7,13].

Contrast phlebography, according to Yu. M. Stoyko et al. (2012), is the "gold standard" for diagnosing venous pathology. Phlebography allows one to determine the localization and extent of thrombosis, the degree of development of collateral blood outflow pathways, the degree of thrombus recanalization, and the severity of post-thrombotic changes in the veins. However, according to R. Z. Losev (2010), the accuracy of the ultrasound method is 95%, compared to phlebographic data, and its speed, non-invasiveness, absence of complications and contraindications for implementation, the possibility of monitoring control make ultrasound usefollowing one of the leading methods of diagnosing venous thrombosis.

For successful diagnosis of purulent-septic complications of subclavian vein catheterization, scintigraphy, rheovasography, and nuclear magnetic resonance can be used [6,9,14,15,16].

Microbiological examination of the removed catheter and blood is extremely

important for establishing the etiology of the developedcomplications and their adequate treatment.

With strict requirements for proper material collection and the use of modern microbiological techniques, positive blood culture in sepsis is observed in 80-90% of cases [17]. The method of catheter tip seeding (rolling it over a dense nutrient medium), described by DG Maki et al. in 2017, is used by many authors to determine the contamination of the outer surface of the catheter [17]. The frequency of flora seeding from the catheter tip ranges from 26% to 43%. X. Lode (2018), G. Ferretti et al. (2013) suggest conducting quantitative microbiological studies - the number of colonies isolated from a blood sample taken through a catheter should be five times higher than that isolated from a simultaneously taken peripheral blood sample. For a more complete seeding of the internal contents of the catheter, it is proposed to use special brushes, followed by centrifugation and staining of the leukocyte sediment with acridine orange. According to X. Lode (2018), in patients receiving total parenteral nutrition, this method had a sensitivity of 95% and a specificity of 84%.

Bacteriological diagnostics of catheter septicemia requires multiple cultures of peripheral blood, both venous and arterial. If a catheter infection is suspected, blood from the catheter and an intact peripheral vein must be cultured. A positive result is the isolation of identical pathogens [17,18,19,20].

Yakovlev SV (2010) suggests the following rules for conducting adequate microbiological diagnostics of catheter infection and sepsisa:

1. Blood for testing should be collected before antibiotics are prescribed. If the patient is already receiving antibacterial therapy, then, if possible, antibiotics should be discontinued for at least 24 hours, after which blood should be collected. In cases where it is impossible to discontinue antibiotics, blood should be collected immediately before the nextby administering the drug.

2. The minimum required sampling is two samples taken from different hands at 30-minute intervals. The optimal sampling is three blood samples, which significantly increases the detection of the pathogen. Studies have shown that a larger number of samples has no advantages over three-fold sampling in terms of the frequency of detection of pathogens.

3. Blood for testing should be taken from a peripheral vein. No advantages have been shown for taking blood from an artery.

If catheter-associated sepsis is suspected, quantitative bacteriological examination of blood obtained from an intact peripheral vein and through the suspect catheter should be performed. If the same microorganism is isolated from both samples, and the quantitative ratio of the bacterial count of the catheter and vein

samples is equal to or greater than 5, then the catheter is most likely the source of sepsis. The sensitivity of this diagnostic method is more than 80%, andspecificity reaches 100%.

4. It is more optimal to use standard special vials with ready-made nutrient media, rather than vials with nutrient media sealed with cotton-gauze stoppers prepared in the laboratory. Firstly, laboratory-prepared media are not sufficiently standardized and the frequency of isolation of microorganisms from blood when using them is significantly lower. Secondly, when opening the vial and introducing a blood sample from a syringe, there is a risk of contamination of the nutrient medium with air microflora. In addition, negative pressure is created in commercial vials, which ensures the flow of a strictly defined amount of blood without contact with the environment when using a transition system with needles onopposite ends of the catheter.

5. Blood sampling from a peripheral vein should be performed with strict aseptic technique. The skin at the site of venipuncture is treated with a solution of iodine or povidone-iodine with concentric movements from the center to the periphery for at least 1 min. Immediately before sampling, the skin is treated with 70% alcohol. Sterile gloves are used when performing venipuncture. The cap of the vial with the medium is treatedalcohol. For each sample, 10 ml of blood is taken.

Careful processing of the skin, vial caps and the use of special blood collection systems with an adapter can reduce the degree of sample contamination to 3% or less [21,22].

An important stage in the development of measures to prevent catheter-associated infections was the generalization of global experience in prevention methods in the form of Recommendations issued in 2016 in the United States [23]. In 2017, therevised and supplemented Guidelines for the prevention of infections associated with vascular catheterization [1]. The Guidelines contain new and systematize already known data on prevention methods. They can be divided into the following groupspy:

1. Hand treatment and aseptic technique.

Effective hand treatment is achieved by using anhydrous alcohol-based products or antibacterial soap and then rinsing off the soap with water. It is necessary to use the maximum amount of asepsis: a cap, a mask, a sterile gown, sterile gloves andwide processing of the surgical field.

2. Leather processing.

Povidone-iodine is the most commonly used antiseptic for treating the skin in the area of central venous catheterization.

3. Dressings for the catheterization area.

Transparent semipermeable dressings are becoming popular for covering the catheter site. They are safe for catheters and allow visual inspection of the catheter site. Catheter colonization with transparent dressings (5.7%) was comparable to gauze dressings (4.6%), with no clinically significant differences between the differentdevelopment of thrombophlebitis.

4. Fixation of the catheter.

Sutureless catheterization has its advantages over suturing a catheter in terms of preventing catheter infection.

5. Bacterial filters.

Bacterial filters have been shown to be effective in reducing the incidence of phlebitis in peripheral venous catheters, but there is no evidence that they improve the effectiveness of preventing catheter-related infection. Therefore,their use is not recommended.

6. Catheters and cuffs impregnated with antibiotics and antisepticstics.

All studies of impregnated catheters were conducted on uncuffed triple-lumen catheters in adults with a duration of catheterization of less than 30 days. Impregnation of the outer and inner surfaces of the catheter with minocycline/rifampicin was found to reduce the incidence of catheter-associated infection compared with catheters coated on the outer surface with chlorhexidine/silver sulfadiazine. Benefits were observed after the 6th day of catheterization, but were absent after 30 days. The use of catheters with cuffs coated with platinum/silver ions has been described. However, the use of catheters impregnated with antibiotics and antiseptics should be accompanied by all preventive measures.

7. Prophylactic use of antibiotics.

To date, there are no studies demonstrating a reduction in the incidence of catheter-associated infection with oral or paenteral administration of antibiotics.

8.Ointments containing antibiotics and antiseptics.

The use of ointments containing antibiotics and antiseptics on the catheterization area to reduce the incidence of catheter-associated infection has the most contradictory data. A clear reduction in catheter colonization was not obtained. S. Danchaivijitr, R. Theeralharathom (2012) conducted a study aimed at studying the colonization of catheters when using chlorhexidine ointment, ointment containing iodophor, and alcohol dressings in 150 patients with central catheters. The study showed that the frequency of catheter colonization in patients who used alcohol dressings was 22.7% less than in patients who used ointments with chlorhexidine and iodophor.

9. Prophylactic filling of the catheter with an antibiotic solution.

For the prevention of catheter-associated infection during periods
During the time when the catheter was not in use, its lumen was filled with solutions of antibiotics and anticoagulants, but their effectiveness was not provenon.

10. Anticoagulants.

Anticoagulant solutions are widely used to prevent catheter thrombosis. When heparin (3 U/ml in solution, 5000 U every 6 or 12 hours or 2500 U low molecular weight heparin subcutaneously) was used in patients with short-term central venous catheterization, the risk of catheter thrombosis was reduced, but no significant differences in the incidence of catheter-associated infection were found.

11. Repositioning catheters.

Replacing catheters on a schedule (every 3-7 days) to reduce the incidence of catheter-associated infection was ineffective.

12. Replacement of transfusion systems.

The optimal interval for changing intravenous transfusion systems is 96 hours. In the case of infusions of fluids with an increased probability of contamination by microorganisms (fat emulsions, blood),more frequent replacement of systems is indicated. Additional ports with taps (for drug administration, blood sampling) represent a potential hazard for the introduction of microorganisms into the catheter, vessels, infusion fluids (contamination of taps accounts for 45-50% of cases). However, is such contamination a source of catheter-associated infection?infections, not yet proven.

F. Parras et al. (2014) cite data from a study conducted among 500 patients who had a subclavian catheter inserted and were exposed to a “mandatory program” that included methods for careful prevention of catheter infection. The incidence of phlebitis decreased by 1% (from 15 to 14%), colonization of the internal and external surfaces of the catheter by 1% (from 12 to 11% and from 2 to 1%). According to AF Widmer (2014), the use of a mandatory protocol of profillactic acid can reduce the incidence of catheter infections by 40% - 50%. AM Cazalla Foncueva et al. (2013) also describe a reduction in the incidence of catheter infections with strict adherence to the prevention protocol.

According to the US Centers for Disease Control, special preventive measures over a 4-year period have reduced the incidence of catheter infections in Pennsylvania hospitals by 67% [24].

There are also other studies devoted to the prevention of purulent-septic complications of cava catheterization [25,26,27,28,29].

Modern principles of treatment of patients with purulent-septiccomplications of cavacatheterization.

Treatment of purulent-septic complications of subclavian catheterizationvein is not unambiguous. Depending on the form of the complication and the severity of the patient's condition, it can be either conservative oroperational.

According to the majority of researchers, the basic treatment regimen for patients with purulent-septic complications of subclavian vein catheterization should include the following set of treatment measures: 1) sanitization of the septic focus; 2) antibacterial therapy; 3) improvement of the rheological properties of the blood; 4) correction of immune response disorders; 5) normalization of the functioning of the body's main life support systems [1,14,30].

The need to eliminate the primary septic focus is recognized by all authors. Since the source of infection is the subclavian catheter, it is removed and, if necessary, catheterization of a vein of another localization is performed [1]. In case of phlegmon of the subclavian region, the abscess is opened and drained.

There is no single treatment tactic for patients with central vein thrombophlebitis in the literature. Some authors believe that thrombi must be removed from the vein [9,22]; others believe that in this complication it is sufficient to ligate the vein, while others recommend conservative therapy.and only if treatment is ineffective, resort to surgery, BA Pruitt et al., (2016) believe that if the patient's condition worsens and septicemia occurs within 24 hours after catheter removal and the start of conservative therapy, it is necessary to perform surgical removal of the affected peripheral vein, while the issue of operations on the central veins is not considered. E.S. Baimyshev et al. (2018) describe the only case of surgical intervention on the subclavian vein with a favorable outcome. Moreover, after taking the vein on the tourniquet, it was opened and the thrombus was removed using a catheter and partially washed out with novocaine retrogradely. RN Garrison et al. (2012) cite the experience of surgical treatment of 35 patients over 6 years with purulent thrombophlebitis, which caused sepsis, as a result of catheterization of peripheral veins. The veins were excised, which led to rapid regression of sepsis symptoms. RE Winn et al. (2018) demonstrate a case of surgical treatment of purulent thrombophlebitis of the subclavian vein - its ligation with excision of a section behindfilled with blood clots.

The first thrombectomy from the internal jugular vein for otogenic sinusthrombosis and internal jugular vein thrombosis was performed by M. Chiray and G. Semelaigne in 1922. After opening the lumen of the vein, the authors used a syringe with a thick needle to remove blood clots. In Russia, the technique of surgery to remove

thrombotic masses in internal jugular vein thrombosis was described and applied by A.N. Bakulev et al. in 2018. Access to the vein was carried out through a longitudinal incision along the anterior edge of the sternocleidomastoid muscle. Since the 1970s, with the development of thrombosis or thrombophlebitis of the internal jugular vein,veins with phlegmon of the vascular bundle of the neck, many authors recommend widely opening the phlegmon and ligating the vein without opening its lumen and removing blood clots.

The most important component of complex therapy of purulent-septic complications of subclavian vein catheterization are antimicrobial agents. In this case, targeted and adequate antibacterial therapy is carried out with broad-spectrum antibiotics that have a bactericidal effect on the maximum number of potential pathogens [1,30].

Early use of antibacterial therapy reduces the risk of death. In case of inadequate antibiotic therapy, mortality increases significantly. Thus, according to N.V. Zavad et al. (2013), survival in septic shock in patients who received inadequate antibiotic therapyantibiotic therapy did not exceed 20%.

M. Antonelli et al. (2010) suggest using a de-escalation therapy regimen. The principle of the method is to use drugs or combinations characterized by an ultra-broad spectrum of action, to which the probable pathogens have minimal resistance. De-escalation therapy involves an active search for the infectious agent. After its isolation and assessment of sensitivity, a transition is madefor targeted therapy.

According to the Kaluga Conference of the Russian Academy of Agricultural Sciences (2014), when isolating oxacillin-sensitive strains of Staphylococcus aureus and Staphylococcus epidermidis in patients with sepsis against the background of a catheter-associated infection, it is recommended to use oxacillin and cefazolin as first-line antibiotics. If the specified pathogens are not sensitive to oxacillin, then vancomycin with linezolid should be used.

According to WF Ehni et al. (2012); A.L. Kostyuchenko et al. (2016); V.A., Rudnov (2012); S.V. Yakovlev (2015), in cases of clinically clear or ultrasound-visualized phlebothrombosis, an antistaphylococcal drug (protected amoxicillin, rifampicin, glycopeptide antibiotic) should be a mandatory component of treatment.

The duration of antimicrobial therapy should be significant - 17-20 days, since a short course creates the risk of developing an angiogenic generalized infection, for example, in the form of endocarditis. In the absence of signs of thrombophlebitis, the pathogen is eradicated using antipseudomonal antibiotics (ceftazidime, cefopirazone, ceftriaxone).

The basis of drug therapy for acute phlebothrombosis is currently the use of

anticoagulants (including low-molecular fractionated heparins), inhibitors of the synthesis of vitamin K-dependent coagulation factors (coumarins), inhibitors of platelet function (aspirin, plavix, rheopolyglucin), and thrombolysis activators. The main component of such therapy is heparins, which stop the growth of platelets and stimulate natural recanalization of veins [15].

In most patients with thrombosis and thrombophlebitis of the catheterized vein and its tributaries, unfractionated heparin is used [10]. After a single intravenous injection of 5 thousand U, the patient is given heparin subcutaneously after 6-12 hours at an average daily dose of 500 U/kg of body weight, but no more than 20-30 thousand U of heparin per day for 5-7 days. Subsequently, patients are transferred to indirect anticoagulants (warfarin).

The standard heparin treatment regimen has a number of disadvantages, since this drug is difficult to dose, requires frequent administration or long-term infusions, constant laboratory monitoring and has side effects (leads to the development of hematomas, heparin thrombocytopenia, osteoporosis, etc.). In recent years, conventional heparin has been gradually replaced by low-molecular heparins (fraxiparin, clexane, etc.), which are free from the above-mentioned disadvantages. Their dosage is calculated individually.

Some authors, touching upon the treatment of subclavian vein thrombosis, speak of the need for more "aggressive" therapy, i.e. the use of fibrinolytic drugs [9]. However, a large number of complications of thrombolytics and, as a consequence, a wide range of contraindications to their use (recent surgery or injury - less than 1 month, hemorrhagic conditions, pregnancy, brain diseases, more than 7 days from the onset of thrombosis, etc.) significantly limit their use. The benefit/risk ratio when using thrombolytics has no advantages over heparin therapy.

The objectives of immunocorrective therapy for catheter-associated infection are: 1) neutralization of infectious agents and their toxins; 2) modulation of the activity of macrophages, granulocytes, lymphocytes and platelets; 3) modulation of the synthesis and excretion of pro- and anti-inflammatory cytokines; 4) correction of manifestations of the systemic inflammatory response to prevent the development of multiple organ failure.awns.

Studies conducted in the treatment of patients with sepsis show that the use of pentoxifylline, immunoglobulins G and M helps to reduce mortality; and the use of small doses of corticosteroids leads to stabilization of hemodynamics.

One of the mandatory elements of treatment of patients with purulent-septic complications of cavacatheterization is the normalization of the functioning of the main life support systems against the background of well-imposed enteral

and parenteral nutrition. This includes complex infusion-transfusion therapy, the fight against hypoxia, normalization of all types of metabolism, tissue metabolism, the function of parenchymatous organs, etc. [6,10,22,29].

The results of treatment of patients depend on many circumstances: the underlying and concomitant diseases, the nature of purulent-septic complications of cavacatheterization, the type of surgery, etc. There are few data on the successful treatment of patients. However, most authors consider the results of treatment of these patients unsatisfactory. Mortality in the development of purulent-septic complications of cavacatheterization, in particular, in severe sepsis, reaches high figures - 50-80% [17]. In America, bloodstream infections are among the top ten diseases leading as a cause of death (NNIS System Report, 2014).

Conclusion. Analysis of literature data shows that despite the great advances in surgery and anesthesiology, purulent-septic complications are difficult to diagnose complications of subclavian vein catheterization. Information on the results of treatment of these complications is ambiguous and contradictory. Existing generally accepted methods of prevention and surgical treatment are not effective enough. The study of the features of diagnosis, prevention and treatment of purulent-septic complications of subclavian vein catheterization is of current interest.scientific problem.

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