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CASE REPORT

[^{99m}Tc]Tc-HMPAO-WBC SPECT/CT detection and treatment control of infection of the thoracic aortic prosthesis and paraprosthetic area caused by Morganella morganii after frozen elephant trunk surgery

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ABSTRACT

Vascular grafts and endografts infection (VGEI) are considered rare but the most difficult in cardiovascular surgery. Treatment requires complete replacement of the prosthesis. However, in situations where this is technically impossible, the patient is required to take long-term (sometimes-lifelong) antibiotic therapy. Diagnosis and monitoring of treatment success requires the use of clinical data, imaging techniques, and microbiologic tests. One method for specific imaging of septic inflammation is SPECT/CT with [^{99m}Tc]Tc-HMPAO-WBC. According to EANM and ESVS guidelines, [^{99m}Tc]Tc-HMPAO-WBC SPECT/CT results definitively confirm or reject the infection. However, the control of treatment efficacy is undiscussed. This report describes a case of severe infection of the prosthesis and paraprosthetic space by Morganella morganii one year after frozen elephant trunk (FET) surgery. We applied a multidisciplinary approach to patient management and monitoring of treatment success in particular using [^{99m}Tc]Tc-HMPAO-WBC SPECT/CT.

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INTRODUCTION

Frozen elephant trunk is a hybrid technique for surgical treatment of aortic pathologies and is the gold standard. The construction features of the prosthesis enable to prevent multistage surgical correction. This approach assists in recovery of the aortic lumen, reducing the risk of thrombosis and aortic remodeling [1]. Infection of the prosthesis is considered rare but requires a radical treatment with complete replacement of the prosthesis, or sanitation of the tissues surrounding the prosthesis with long-term, sometimes lifelong, antibiotic therapy [2]. In recent years, nuclear imaging modalities have been extensively used for the diagnosis of vascular grafts and endografts infection (VGEI). In 2016, diagnostic criteria for VGEI were proposed for the first time, where [^{99m}Tc]Tc-HMPAO-WBC SPECT/CT and positron emission computed tomography (PET/CT) with ^{18}F-fluorodeoxyglucose ([^{18}F]FDG) occupy a secondary position as methods to definitively confirm or reject the diagnosis [3, 4]. At the same time, the problems of monitoring the effectiveness of treatment with radionuclide imaging methods are almost never discussed.

CASE PRESENTATION

A 37-year-old man was admitted to the clinic with complaints of febrile episodes predominantly in the evenings and at nights, accompanied by weakness and sweating. From his past medical history, it is known that a year ago the patient had undergone Stanford type A aortic dissection with following surgical treatment: Frozen elephant trunk, prosthesis and reimplantation of bracheocephalic trunk, left common carotid artery, prosthesis of left subclavian artery during extracorporeal circulation, cardioplegia, unilateral antegrade cerebral perfusion, distal perfusion, circular arrest and 28C hypothermia. Dissection of the descending aorta was still present. He was discharged in satisfactory condition. After 6 months, a follow-up examination was performed with a recommendation of hospitalization for stent-graft elongation. In the next 3 months, the body temperature suddenly increased, accompanied by chills and weakness. He was hospitalized in the infectious disease clinic, where the patient was examined. The patient was started on antibiotics, but without proper effect. For this reason, he was admitted to a cardiac surgical hospital to determine treatment strategy (Figure 1).

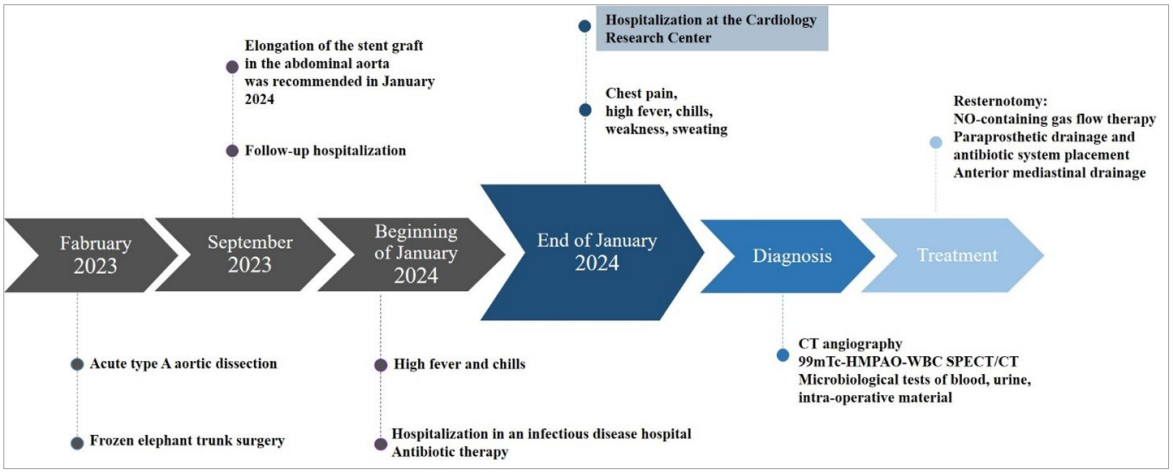

Figure 1. Patient history timeline

On admission, the general blood analysis revealed leukocytosis (20*109/liter) with a severe shift of the leukocytic formula to the left, high erythrocyte rate sedimentation (93 mm/hour) and high level of C-reactive protein (204 mg/liter). The patient underwent CT-pan aortography (CTA). According to the results a fluid mass (density 28 HU) surrounded by a capsule at the level of the aortic arch and proximal third of the main arch vessels were visualized. The capsule wall was irregularly thickened and had an irregular inner contour. At the level of the sternum handle (manubrium), the retrosternal fatty tissue was fibrously modified and was no clearly encapsulated (Figure 2). Due to equivocal CTA results, a [^{99m}Tc]Tc-HMPAO-WBC SPECT/CT was performed.

Preparation and quality control of white blood cells (WBC) labelled with [^{99m}Tc]Tc-HMPAO was performed in accordance with EANM Guidelines [5]. The first whole body scan was acquired at 30 minutes after an intravenous infusion of 300MBq of [^{99m}Tc]Tc-HMPAO-WBC using SPECT/CT scanner GE NM/CT 850 (GE Healthcare, Milwaukee, WI, USA) equipped with high resolution, high sensitivity, low

energy collimators (LEHRS), using a 20% energy window at 140 keV was used. Delayed SPECT/CT images were obtained at 3 hours post-injection and late SPECT/CT images – at 20 hours [6]. Hybrid SPECT/CT images were reconstructed on the dedicated workstation (Xeleris 4.0; GE Healthcare, Haifa, Israel) into axial, sagittal, and coronal planes, using Volumetrics MI (GE Healthcare, Haifa, Israel) software. The reconstructed fused SPECT/CT images were viewed in multiplane projections.

No areas of septic embolization were visualized on the whole-body images. After 3 hours [^{99m}Tc]Tc-HMPAO labelled leukocytes injection, low-intensity foci of accumulation in the paraprosthetic tissue behind the sternal manubrium were visualized on the SPECT-CT images (foci/background coefficient 1.39). After 20 hours post-injection the intensity of [^{99m}Tc]Tc-HMPAO labelled leukocytes uptake increased 1.5 times (focal/background coefficient 2.12) (Figure 2B). Besides, new moderate intensity areas of pathological accumulation of [^{99m}Tc]Tc-HMPAO labelled leukocytes were imaging, anatomically matching the wall of the distal part of the prosthesis along its lower contour, as well as the proximal part of the prosthesis as a homogeneous circular accumulation (focal/background coefficient - 2.09) (Figure 2A).

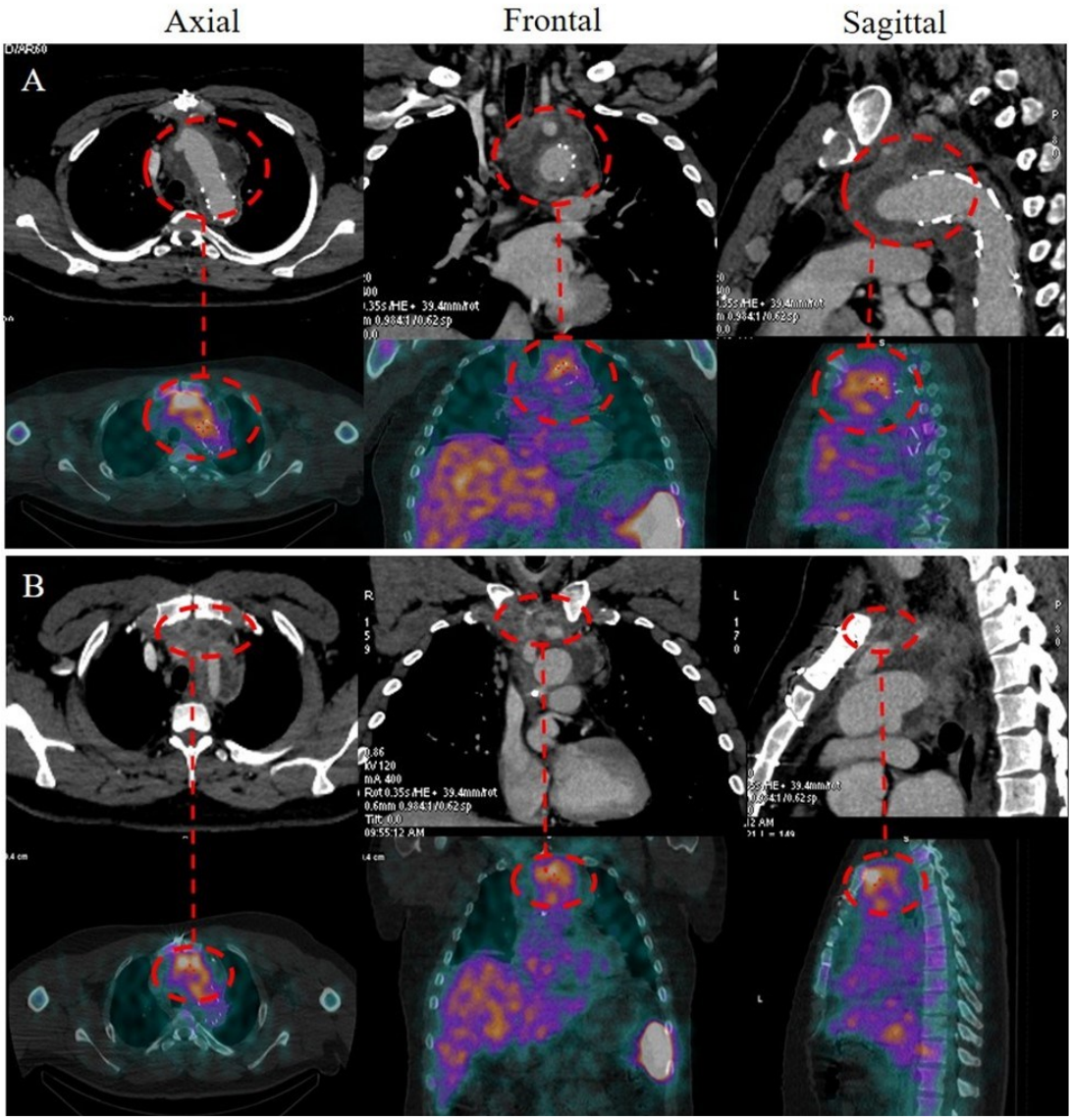

Figure 2. CT-angiography and [^{99m}Tc]Tc-HMPAO-WBC SPECT/CT images (20 hours post-injection) performed on the first day of hospitalization (axial, frontal and sagittal views). A: Area of fluid mass surrounded by a capsule at the level of the aortic, proximal third of the main arch vessels and its corresponding area of [^{99m}Tc]Tc-HMPAO-WBC uptake (highlighted red dotted line), B: Area of fluid masses retrosternal behind the manubrium and its corresponding area of [^{99m}Tc]Tc-HMPAO-WBC uptake (highlighted red dotted line)

Thus, based on the results of CT angiography, [^{99m}Tc]Tc-HMPAO labelled leukocytes SPECT/CT, and laboratory data (1 major criterion and 2 minor MAGIC criteria), the patient was diagnosed with paraprosthetic space infection and osteomyelitis of the sternum.

On the 5th day of hospitalization, the patient underwent a resternotomy with revision of the mediastinum and paraprosthetic area. During revision of the anterior mediastinum, there was an exit of tissue detritus. The paraprosthetic haematoma contained fibrin. All samples were taken for microbiological examination. There were also signs of osteomalacia of the sternal manubrium. The paraprosthetic space was irrigated several times with betadine solution and NO-containing airflow for 4 minutes [7]. Drainage into the paraprosthetic area and an antibiotic infusion system (Ceftazidim 1.0 g x 3 times a day, 6 days) were placed through supraclavicular incisions. In addition, drains were placed subxiphoidally into the anterior mediastinum.

Under the supervision of a clinical pharmacologist, the patient was started antibiotic therapy, which was adjusted throughout the entire period of hospitalization, taking into account the clinical picture and the results of laboratory and instrumental tests. The dynamics of leukocyte, CRP levels and antibiotic therapy are shown in Figure 3.

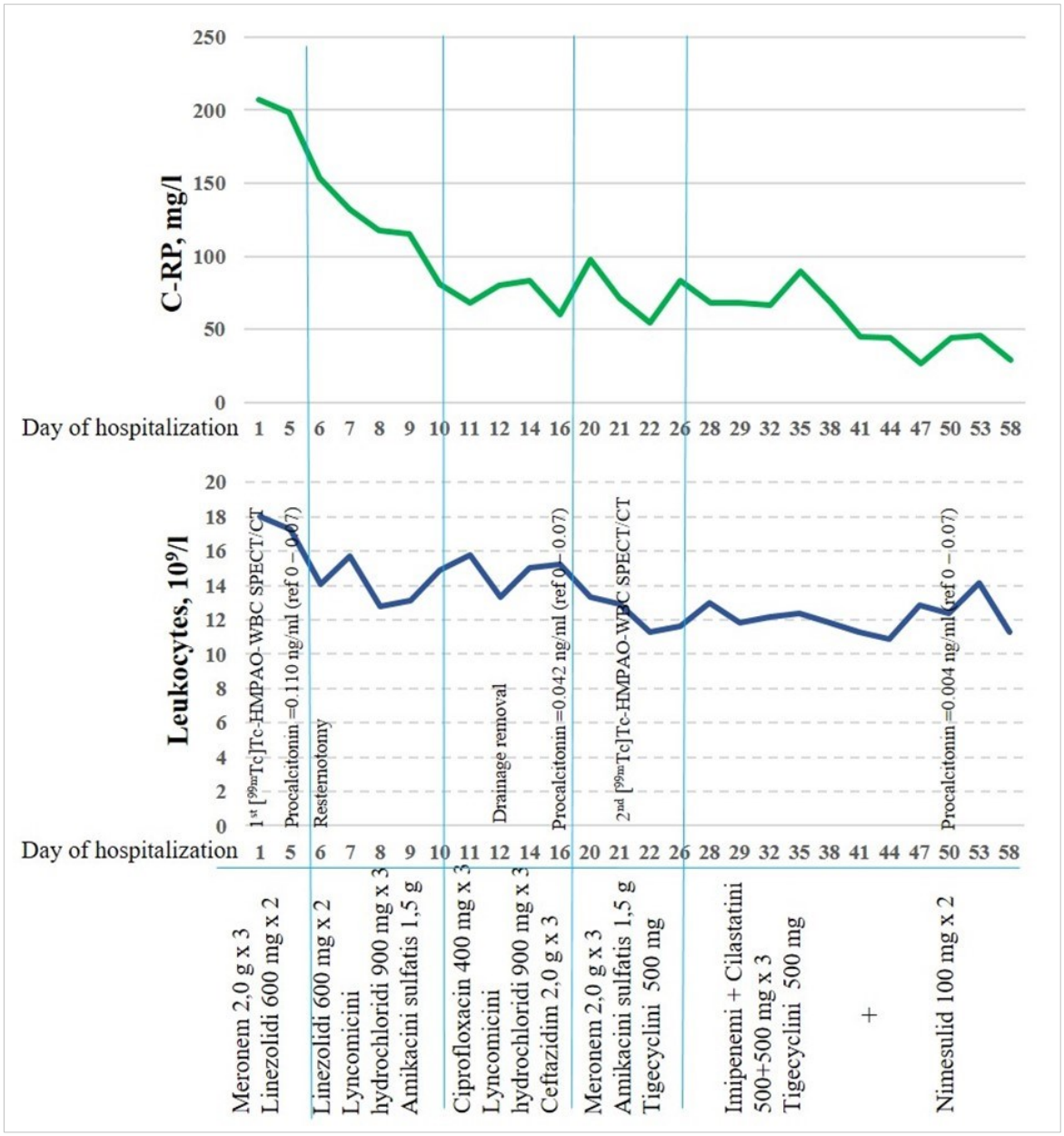

Figure 3. Dynamics of leukocyte level, CRP, antibiotic therapy and main checkpoints of examinations

During the first week of hospitalization, the patient underwent multiple blood sampling at the peak of fever for microbiological examination, which identified Morganella morganii. At the same time, no growth of bacterial flora was detected in the intraoperative material, as well as in the drainage effusion. Only by the 11th day of hospitalization, the results of M. morganii sensitivity to antibiotics - ceftazidime, cefotaxime, cefepime, ciprofloxacin, amikacini and meropenem - were confirmed. This made it possible to select the optimal combination of antimicrobial agents. Microbiological examination of blood on the 40th day of hospitalization showed the absence of pathogenic microflora growth.

After 3 weeks from the beginning of treatment CT-angiography and [^{99m}Tc]Tc-HMPAO-WBC SPECT/CT were performed again. The CTA scans showed positive dynamics as a reduce in the infiltration volume. SPECT/CT showed a significant reduction of the area of the previously identified foci in the paraprosthetic tissue behind the sternum handle, [^{99m}Tc]Tc-HMPAO-WBC accumulation in the proximal part of the prosthesis was already multifocal, but the foci/background ratio remains at the same level (2.07 and 2.1, respectively) (Figure 4).

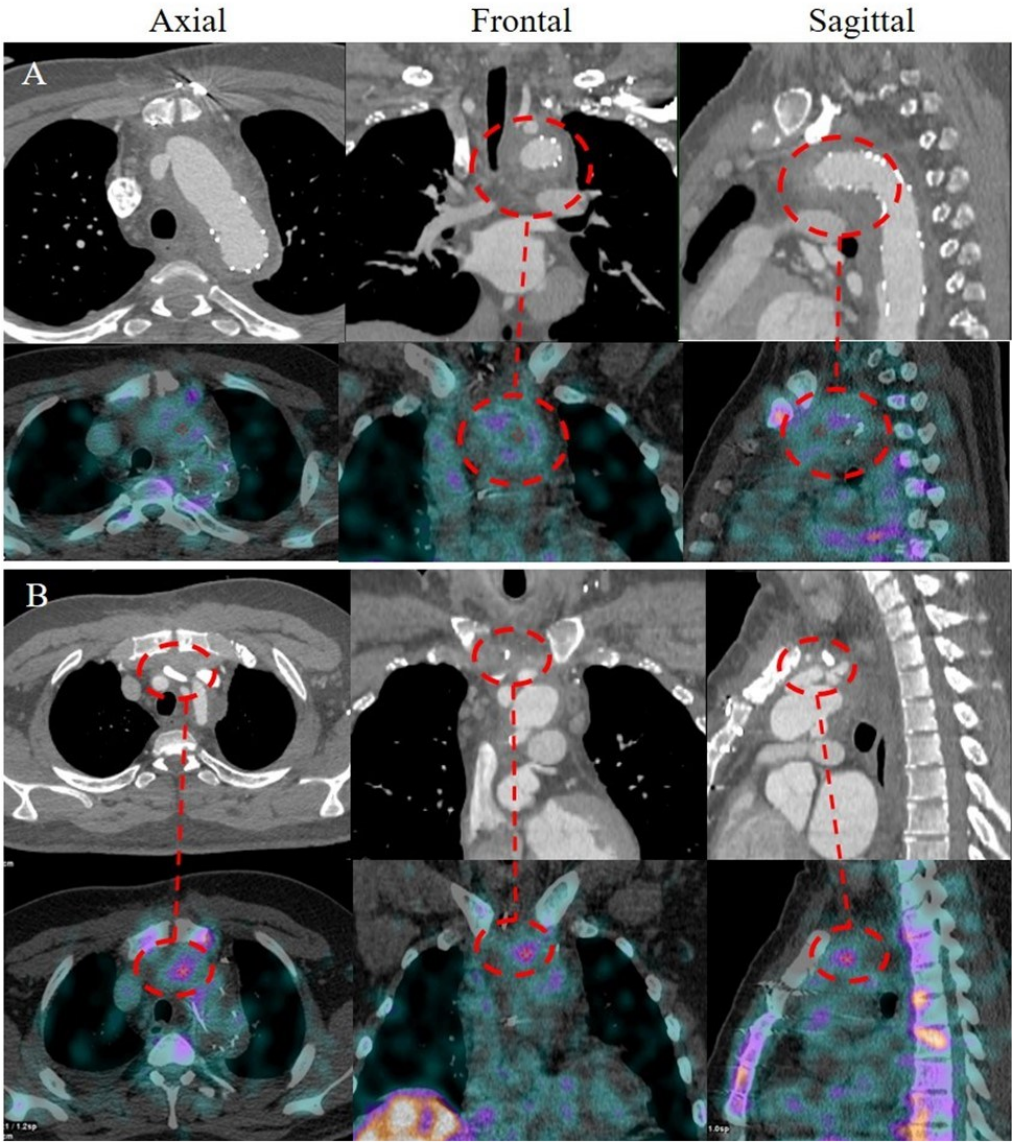

Figure 4. CT- angiography and [^{99m}Tc]Tc-HMPAO-WBC SPECT/CT SPECT/CT images (20 hours post-injection) performed on the first day of hospitalization (axial, frontal and sagittal views). A: Area of fluid mass surrounded by a capsule at the level of the aortic, proximal third of the main arch vessels and its corresponding multifocal of [^{99m}Tc]Tc-HMPAO-WBC uptake (highlighted red dotted line), B: Area of fluid masses retrosternal behind the manubrium and its corresponding area of [^{99m}Tc]Tc-HMPAO-WBC uptake (highlighted red dotted line)

Despite conservative therapy, there were still signs of inflammation in the blood, as well as an increase in the body temperature to subfebrile values (37.2-37.4°C) in the evening. For these reasons, anti-inflammatory therapy (nimesulide 100 mg x 2 times a day) was added to the treatment, and the temperature reached normal values.

After 58 days of treatment, the patient was discharged from the clinic for outpatient follow-up. Taking into account that the infiltration around the prosthesis (according to the control CT scan) persisted, the possibility of infection of the previously implanted aortic prosthesis, the removal of which is technically impossible, could not be excluded. It was recommended to continue antibiotic therapy, the duration of which will be determined clinically and by controlling the blood indices, acute-phase C-reactive protein and blood microbiology studies.

DISCUSSION

Infectious complications of aortic vascular grafts and endografts are among the most challenging cases in cardiovascular surgery for both surgeons and patients. According to different estimates, the incidence of deep sternal wound infection is 1.5 to 4% [8], while the incidence of thoracic aortic graft infection, including FET, can reach 6%. Mortality rates, based on the clinical presentation, can be as high as 75% [9]. VGEI is commonly categorized as early (less than 4 months) and late (more than 4 months). Early complications are usually the result of surgical wound contamination, while late complications are due to hematogenous dissemination of infection because of venous catheter related infections, urinary tract or oral infections [2, 10]. Morganella morganii, detected during microbiological examination in patient's blood, belongs to the family Enterobacteriaceae and is a gram-negative opportunistic bacillus of the human intestinal microflora, with extensive drug resistance and can cause severe infections in patients with weakened immune system [11]. Several types of infections have been described, including endocarditis, osteomyelitis, pericarditis, etc. [12].

The early and effective diagnosis of infection and its prevalence is crucial for determining patient management and usually requires the use of clinical data, imaging techniques and microbiological tests [6]. Until 2016, there was no evidence-based consensus on the diagnosis and treatment of VGEI. The Management of Aortic Graft Infection Collaboration (MAGIC) presented major and minor criteria for the diagnosis of VGEI that included clinical, surgical, radiological and laboratory findings. According to the MAGIC criteria, VGEI can be suspected in the presence of one major or two minor criteria from three different categories. VGEI is diagnosed if there is at least one major criterion and any other criterion from another category [3, 4].

According to EANM [6] and ESVS [4] guidelines, CT angiography is the first line method in method in the diagnosis of VGEI. However, according to the meta-analysis by Reinders Folmer et al. [13], the use of isolated CTA is not sufficient to establish the diagnosis, as the sensitivity of CTA in the diagnosis of VGEI is only 67% and specificity is 63%. CTA does not always differentiate between septic and aseptic inflammation, which is crucial for treatment. Nuclear medicine imaging techniques have shown high diagnostic accuracy, thus being complementary tools to morphological imaging. Both [^{99m}Tc]Tc-HMPAO-WBC SPECT/CT and PET/CT with [^{18}F]FDG are currently used to visualize infections. In a recent large prospective study by Sollini et al. [14] demonstrated high specificity of SPECT/CT and sensitivity of PET/CT in the diagnosis of prosthesis infection after Bentall surgery. However, the positive prognostic value of PET/CT was low due to the lack of standardized criteria for image interpretation.

One of the main advantages of [^{99m}Tc]Tc-HMPAO-WBC SPECT/CT over PET/CT is the ability to differentiate septic from sterile inflammation, which is crucial in the early or very early post-surgery period. There is also no strong evidence that prior antibiotic therapy influences the results of SPECT/CT [6], however, PET/CT is recommended to be performed before antibiotic therapy, which may decrease the metabolic activity in the focus of infection. This fact determines the possibility of using [^{99m}Tc]Tc-HMPAO-WBC SPECT/CT in follow-up of the activity of the inflammatory process. In this presentation, the second study was performed on 21 days of antibiotic therapy. During this period, there was a decrease in the level of leukocytes in blood and acute-phase C-reactive protein (Figure 3). We observed a decrease in the size of [^{99m}Tc]Tc-HMPAO-WBC accumulation and a modification of shape of the lesion from diffuse to multifocal with unchanged uptake intensity. The clinical significance of the accumulation pattern is not shown in the literature. However, in the study of Grambow-Velilla et al. [15] it was shown that in patients with prosthetic valve endocarditis the area of accumulation decreased in size starting from 3 weeks of antibiotic therapy, but the intensity (in some patients) could stay at the baseline level up to 6 weeks. These results were interpreted for the need to prolong conservative treatment. It should

be noted that the therapy according to the sensitivity of M. Morganii was administered 10 days before the study. Thus, we believe that the prescribed treatment was effective, which is also confirmed by the level of procalcitonin on the 16th and 50th day of hospitalization. Assessment the dynamics of the severity of the inflammation by PET/CT with [^{18}F]FDG after revision of the mediastinal cavity and sanitation (as in this case) would have been difficult due to changes in metabolic activity resulting from the healing process and aseptic inflammation.

CONCLUSION

This case presents a multidisciplinary approach for the management of a patient with infection of the prosthesis and paraprosthetic area in a technically impossible situation for total prosthesis replacement. The case emphasizes the importance of using [^{99m}Tc]Tc-HMPAO-WBC SPECT/CT for the diagnosis of aortic prosthesis infection and monitoring the effectiveness of antibiotic therapy. However, there's limited information about how to follow up during treatment, which raises questions about interpreting the results of repeated [^{99m}Tc]Tc-HMPAO-WBC SPECT/CT scans and requires further investigation.

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