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Treatment Outcomes of Periprosthetic Joint Infection in HIV-Positive Patients

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Abstract

Relevance. There is a limited number of publications reporting outcomes of primary large joint arthroplasty in patients with human immunodeficiency virus (HIV). The authors were unable to find papers on revision arthroplasty in patients with periprosthetic infection. ***Purpose of the study*** — to evaluate short term outcomes after revision arthroplasty in HIV-positive patients with periprosthetic infection of the hip and knee joint. ***Materials and Methods.*** 13 HIV-positive patients with periprosthetic infection of the hip (10 cases) and knee (3 cases) joint underwent treatment in the period from 2015 to 2019. Patients were examined by clinical, laboratory and roentgenological methods. Harris Hip Score and Knee Society Score were used for evaluation prior to and after the surgery. ***Results.*** Mean follow up period was 21.4±2.6 months. Successful two-stage treatment was performed in two (15.4%) out of 13 patients with periprosthetic infection. In 5 cases (38.5%) control over infection was achieved by resection arthroplasty, and in one case (7.7%) — by arthrodesis. Five patients (38.5%) refused from interchange of spacer to prosthesis. Mean Harris Hip score demonstrated insignificant increase postoperatively — from 45.3±2.2 to 52.2±4.15 (p = 0.2). ***Conclusion***. Despite following the international protocols for treatment of implant-associated infection the infection recurrence rate in HIV-positive patients in the asymptomatic phase remains very high. Efficiency of two-stage treatment using antibacterial spacers in the present group of patients amounted only to 15.4%.

Keywords: periprosthetic infection, revision arthroplasty, HIV-infection.

Total number of Russian population infected by human immunodeficiency virus (HIV) amounted to 1 040 040 people as of 30.06.2019 according to the monitoring of the Russian Agency for Health and Consumer Rights*.

HIV-patients have a higher risk for development of primary or secondary degenerative joint diseases [1]. HIV incidence in the overall population results in increased number of HIV-positive patients that require large joint arthroplasty. Many orthopaedic surgeons raise a question "Does the HIV affect the rate of periprosthetic infection?". The number of published studies dedicated to the present issue is small and opinions of the authors differ. Data of C.R. Lehmann et al, J. Parvizi et al and Q. Naziri et al report rate of complications, infection in particular, higher in such patients' group as compared

* http://aids-centr.perm.ru/images/4/hiv_in_Russia/hiv_in_rf_30.06.2019.pdf

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to control group [2, 3, 4]. In contrast to above the findings of N. Snir et al, V.A. Shilnikov et al and L.Yu. Voevodskaya et al demonstrate a relatively small share of septic complications after large joint replacement in HIV-positive patients [1, 5, 6]. However, the majority of publications analyze the outcomes of primary arthroplasty. We were unable to find separate papers with outcomes of revision arthroplasty in this group of patients. Nevertheless, revision procedure itself irrespective of the immunological status of the patient is the strongest risk factor for periprosthetic infection [7].

Purpose of the study — to evaluate short term outcomes of revision arthroplasty in HIV-positive patients with periprosthetic infection of the hip and knee joints.

Materials and Methods

Patients

After analyzing the electronic database, the authors found that 13 HIV-positive patients (13 joints) with periprosthetic infection of the hip and knee joints underwent treatment in their clinic in the period from 2015 to 2019.

Criteria of inclusion into the study was availability of infected implant at the moment of patient's admission to clinic and HIV-positive status. Patients with septic arthritis without an implant (prosthesis or spacer) were not included.

Study group consisted of 9 men (69%) and 4 women (31%) with mean age of 38.1±1.1 years (from 35 to 53 years). Mean BMI was 24.3±1.2 (from 18 to 40.7). 10 patients (77%) suffered infection after hip joint replacement and 3 patients (23%) — after knee joint replacement. Nine patients (69%) admitted historical intravenous narcotic drugs abuse. Viral hepatitis type C (69%) and type B (23%) as well as secondary mild anemia (38.5%) were most often diagnosed as concomitant diseases.

Laboratory tests. All patients except one (virus markers first identified after the surgery) were followed up and treated in the center for prophylaxis and treatment of AIDS at their place of residence. Progression of HIV infection was evaluated by classification of V.I. Pokrovsky (2001) [8] and classification of Center for Disease Control and Prevention of the United States (CDC, 1993) [9], both presented in tables 1 and 2.

Table 1

Classification of HIV-infection proposed by V.I. Pokrovsky et al (2001)

	Stage	Progression types
1	Incubation	
2	Primary manifestation	А — asymptomatic seroconversion
		Б — acute infection without secondary diseases
		В — Acute infection with secondary diseases
3	Latent	
4	Secondary diseases	А — loss of body mass less than 10%, superficial fungal, viral and bacterial infection of skin and mucous membranes; Herpes Zoster, recurrent pharyngitis, sinusitis
		Б — progressive loss of body mass over 10%, unexplained diarrhea or fever over 1 month; pilous leukoplasia; pulmonary tuberculosis; recurrent or persisting visceral bacterial, viral, fungal, protozoal infection; disseminating Herpes Zoster; localized Kaposi sarcoma
		В — cachexia; generalized bacterial, viral, fungal, protozoal and parasitic diseases; pneumocystic pneumonia; candidiasis of esophagus, bronchi and lungs; atypical mycobacteriosis; extrapulmonary tuberculosis; disseminating Kaposi sarcoma; central nervous system lesions of varying etiology
5	Terminal	

Table 2

Classification of HIV-infection of the Center for Disease Control (1993)

Category	CD4+ lymphocyte count, cells in μl	Clinical category		
		A (asymptomatic)	B (symptomatic)	C (HIV-indicator condition)
1	≥500	A1	B1	C1
2	200-499	A2	B2	C2
3	<200	A3	B3	C3

Category A includes acute HIV infection, asymptomatic HIV infection and persisting generalized lymphadenopathy. Clinical B category includes bacillar angiomatosis, oropharyngeal and/or vaginal candidiasis, cervical dysplasia (carcinoma), constitutional symptoms, listeriosis, pilous leukoplasia, Herpes Zoster, idiopathic thrombocytopenic purpura, peripheral neuropathy, inflammatory diseases of pelvic organs. Clinical C category almost corresponds to the developed stage of AIDS by classification of V.I. Pokrovsky and is characterized by such AIDS-associated diseases as pneumocystic pneumonia, Kaposi sarcoma and toxoplasmosis.

Mean count of CD4 lymphocytes was 656±51/μl (from 218 to 1134), viral load was identified in 77% of patients (table 3). The mean hemoglobin blood content at admission to clinic was 119±3 g/l (from 98 to 143), ESR — 71.8±7.83 mm/h (from 20 to 120), and C-reactive protein — 49±6.6 mg/l (from 14.4 to 89).

Roentgenological examination. A series of anteroposterior, lateral and other x-rays of the joint was performed to evaluate positioning and stability of prosthesis or spacer. Teleroentgenograms of the lower limb was done to evaluate biomechanical axis in patients with knee joint pathology, these images were used to identify type of implant fixation, its stability, presence of bone defects and localization of fistulas and purulent leakages by introducing contrast through the fistula or wound.

Functional tests. Clinical outcomes after treatment of periprosthetic hip joint infection were evaluated by Harris Hip Score, and by Knee Society Score and Function Score [10] were used in patients with knee pathology.

History of previous surgeries. 6 out of 10 patients with hip pathology were admitted to the clinic with infected implant, other 4 patients with infected spacers. Two out of three patients with periprosthetic knee infection were admitted with infected spacer and one with infected prosthesis. Medical history of the majority of patients listed repeated surgeries on affected joint (from 1 to 7), mean number of previous surgeries was 3.9±0.5 (table 3). Debut disease in 8 (61.5%) patients was septic arthritis and in 5 (38.5%) patients the infection developed after joint arthroplasty.

All patients underwent PJI diagnosis according to recommendations of the International Consensus Meeting on Periprosthetic Joint Infection [11].

Table 3

Data on the patients, laboratory findings and treatment outcomes

№	Gender	Age	Number of previous surgeries	PJI types by Tsukayama	HHS and KSS scores prior to surgery	AIDS stage by Pokrovsky (2001)	CDC classification	CD4/ µl	Viral load, qty/ml	HHS and KSS scores after revision	Follow up period, months	Outcome
1	m	35	5	Acute p/op infection	55.7	4A	A1	936	<50	47.5	9	Resection arthroplasty
2	m	53	5	PIC	KS — 29 FS — 35	3	B1	635	<75	KS — 61 FS — 45	25	Knee arthrodesis
3	m	45	4	PIC	39.6	4A	B2	218	100 000	34.5	5	Resection arthroplasty
4	m	38	2	PIC	43.15	4A	B2	302	<500	46.4	14	Resection arthroplasty
5	f	30	4	PIC	58.35	First identified	–	–	–	46.35	7	Spacer
6	m	37	6	PIC	60.55	3	A1	662	4000	56.75	27.5	Spacer
7	m	38	4	PIC	38	4A	B1	516	40	42.9	15.5	Resection arthroplasty
8	f	43	3	LCI	38	4Б	B1	849	4749	76.7	7	Endoprosthesis
9	m	37	3	PIC	40.7	3	A1	524	<150	74.2	15	Endoprosthesis
10	f	33	2	PIC	39	4a	A1	1134	<50	35.5	32	Spacer
11	m	34	5	LCI	KS — 32 FS — 30	4a	A2	459	3500	impossible to evaluate	24	Resection arthroplasty
12	m	40	7	LCI	FS — 32 FS — 44	3	A2	410	–	KS — 30 FS — 40	37	Spacer
13	f	33	2	LCI	39.2	4Б	B1	602	–	43.55	43	Spacer
Mean value		38.1±1	3.9±0.5		HSS — 45.3±2 KSS — 31±0.7			656±51		HSS — 52.2±4.1 KSS — 45.5	21.4±2.6	

P/op — postoperative; PIC — positive intraoperative culture; LCI — late chronic infection.

Surgical technique. After preoperative planning the infected joint was approached by: straight lateral Harding approach in patients with hip localization of infection, or a medial parapatellar approach in patients with knee joint infection. For arthrodesis the authors used horseshoe approach on anterior surface. All spacer or prosthesis components were removed using revision instruments, septic nidus was radically debrided. Preformed or block cemented space of corresponding size was then implanted. Bone cement with antibacterial agents (vancomycin and/or gentamicin, and/or cefazolin) was used in all cases. Material samples were collected during surgery for microbiological tests.

Course of etiotropic therapy was undertaken for at least 6 weeks postoperatively.

Postoperative follow up. Treatment outcomes were followed in all 13 patients from 5 to 43 months, with mean follow up of 21.4±2.6 months. All cases of repeated hospitalization, infectious complication, aseptic loosening, revisions on the joint as well as lethal outcomes were recorded. The authors evaluated range of motion, data of roentgenological examination and presence of PJI signs.

Statistical analysis

Statistical processing was done by Statistica 13 (Statsoft, USA) and Microsoft EXCEL 2010 software. Non-parametric statistical methods were used. Non-parametric Wilcoxon criterion was used to evaluate statistical significance of mean variances. Variances were considered statistically significant at $p \leq 0.05$.

Results

By the classification of D.T. Tsukayama the acute infection was observed in one case (7.7%), late chronic infection — in four cases (30.7%). In the majority of cases (61,5%) the infection was classified as positive intraoperative culture [12]. The interval between infection manifestation and admittance to clinic was over 4 weeks in all patients which was an absolute indication for removal of implants. Besides, instability of implants in 5 out of 6 cases was also a contraindication for debridement with preserving the components. After the clinical examination the authors identified fistulas in 12 patients (92.3%), edema and hyperemia in the area of postoperative scar — in one (7.7%) patient.

Classification of W.G. Paprosky [13] was used to systematize bone defects upon admission of patients with hip joint PJI. Acetabular defects of type 3 were observed in 5 cases (38.5%), 2B and 2C types — in two patients, respectively (15.4%). One patient (7.7%) has a 2A type defect. Femoral defects of type II were reported in 5 patients (38.5%), types IIIA and IIIB — in 3 (23%) and 2 (15.4%) cases, respectively. Among the three patients with knee joint infection two (15.4%) had a F3/T3 type defect by AORI classification [14], and one patient (7.7%) — F2B/T2B type.

Microbiological tests of biomaterial from 13 patients demonstrated pathogenic microflora in 12 cases (92,3%). Gram positive Staphylococcus aureus sensitive to oxacillin was identified in all cases.

Infected implants were removed in all 7 patients (54%) admitted to the clinic with joint PJI (6 hips and 1 knee). Intraoperative exchange to hip spacer (two articulating and two block spacers) was performed in 4 patients. Later on a successful two stage treatment with implantation of a prothesis was done in one patient. Resection arthroplasty was done in two cases. Articulating spacer was implanted in one patient (7,7%) with knee infection after removal of prosthesis components.

Three out of six patients (46%) admitted with infected spacer underwent resection arthroplasty of the hip joint. One patient had a successful two stage treatment: spacer exchange and revision arthroplasty. Knee joint

arthrodesis was performed in one patient with recurrent purulent infection after spacer removal. One case was characterized by a complication of recurrent infection which required other revisions.

Thus, in two (15.4%) out of 13 HIV-positive patients with PJI two stage treatment was successful. After obtaining control over infection 5 (38,5%) patients refused from spacer exchange for prosthesis. In 5 cases (38,5%) resection arthroplasty was performed, and arthrodesis in one (7.7%) case. 5 out of 9 patients with previous history of narcotics abuse the authors reported recurrent periprosthetic infection.

Mean preoperative functional hip HHS score was 45.3±2.2 (min — 38 and max — 60.5). Mean postoperative score insignificantly varied from initial (p = 0.2) and was 52.2±4.15 (from 35.5 to 81.5 баллов). Outcome of successful two stage treatment in one patient (7.7%) was considered good, and in another two cases (15.4%) — satisfactory.

KSS score in patients with knee PJI at admission to clinic averaged 31±0.7, and by Functional Score — 36.3±2.9. Only one patient demonstrated improved scores after knee arthrodesis — 61 and 41 under KSS and Function Score respectively (table 3).

Revisions and complications. One patient of 34 y.o. experienced recurrent infection in 4 months after spacer exchange in the knee joint. Periprosthetic infection was complicated by spondilodiscitis, epidural abscess at Th9-Th10 level and spastic paraplegia with dysfunction of pelvic organs. Infection was controlled after sanation of epidural abscess and resection knee arthroplasty. Patient was discharged for outpatient treatment, however, the patient deceased 14 months postoperatively.

Discussion

Over 33 million people in the world are HIV-positive [15]. The risk of aseptic femoral head necrosis is higher in such patients as compared to the average in the population [4, 16, 17]. Osteonecrosis results in degenerative diseases which frequently required joint replacement [16]. This fact along with widespread nature of the disease leads to increased number of HIV-infected patients who need hip joint replacement. Outcomes of large joint arthroplasty in HIV-infected patients are actively discussed by orthopaedic society and one the most disputable is the complications rate, particularly periprosthetic infection.

J. Parvizi published the data on highly unfavorable outcomes of large joints arthroplasty (13 knees and 8 hips) in HIV-positive patients. Deep PJI was developed in 6 cases (21%) [3].

While examining the USA database — Nationwide Inpatient Sample (NIS) from 2000 to 2008 C. Lin et al analyzed more than 5.6 million addresses for hip and knee joint replacement. There were 8229 HIV patients (0.14%), 77% of these needed hip joint arthroplasty, and 33% — knee arthroplasty. Wound infection rate in HIV-positive group was 0.6% for hip arthroplasty and 0,4% — for knee arthroplasty. Infection rate in the overall group was 0.3% and 0,4% respectively [15]. It should be noted that NIS database recorded complications during hospitalization period, so this data can't be considered as mid- and long-term results. Q. Naziri et al identified 9275 HIV patients in the NIS database among those patients who underwent large joint arthroplasty from 1998 to 2010. Rate of wound infection within identified group was 0.7% while in the overall group — 0.2% [4].

D. Dimitriou et al made a systematic review of publications and observed that the risk of PJI in HIV-positive patients after large joint arthroplasty averaged 7.6% and in patients of control groups — 3.3% [18]. B.M. Capogna et al reported the PJI rate in the study group of 69 cases as 4.4% and in control group — 0.72%. Patients with infectious complications featured higher values of CD4-lymphocytes (>500) [19].

However, there are publications demonstrating no differences in post-arthroplasty complications rate in HIV-positive and HIV-negative patients. C.-S. Zhao et al report on 100% implants survival in 28 patients with HIV infection during 1.5 years after the surgery [20].

A group of orthopaedic surgeons from Germany published outcomes of arthroplasty of 55 large joints in patients with HIV infection. PJI rate was 12.7%. Five out of seven patients with infection admitted historical intravenous narcotics injections [21].

Trauma surgeons from California University performed 41 large joints replacement and observed infection in HIV-positive patients in 14% of cases; in patients with historical narcotics abuse — in 25%, and in combination of those factors — in 40% [3]. In this respect the study of K. Weiser et al seems of interest, this research is based on analysis of 27 arthroplasty cases in patients with previous history of intravenous narcotics use. Rate of deep periprosthetic infection within 5 years after surgery was 30% [22].

Almost all researchers define the level of CD4-lymphocytes and viral load as the common and available markers of human immune system. So, C.A. Lin et al reported on two cases of infection in the studied cohort of 22 patients, where the level of CD4-lymphocytes was 1147/ml and 563/ml evidencing good control over viral infection [23].

No correlation between CD4-lymphocyte count and possible infection development was either observed in the studies of other authors [1, 2, 19, 21]. The publication of N. Snir et al reports that the majority of patients who avoided infection featured a very low level of viral load — less than 50 copies/ml [1].

Upon reviewing 21 clinical publications D. Dimitriou et al concluded that increased viral load is a more sensitive predictor of infectious complications in contrast to decreased count of CD4-lymphocytes [18]. G.N. Guild J. and Pretell-Mazzini claim the contrary, that risk of infectious complications is higher in patients with uncontrolled viral load and CD4-lymphocyte count less than 400/ml [24, 25].

According to the proceedings of the Second International consensus meeting on musculoskeletal infection (2018) it's needed to optimize the level of CD4-lymphocytes and viral load [26]. The level of abovementioned laboratory markers in patients of the studied group can prove the controlled progression of viral disease (table 3). However, the literature data and own results can evidence that these serological criteria are not reliable predictors for risk of PJI. Varying data in the literature demonstrates that combinations of serological tests improve diagnostic accuracy, however, further research is needed to specify their sensitivity and specificity.

The results of the present study demonstrate only 15.3% efficiency rate of two stage treatment in HIV-positive patients with PJI. Meanwhile the authors did not find any publications in world literature dedicated to revision arthroplasty in such patients. At the same time revision is in itself a serious risk factor and repeated revisions increase even greater the probability of PJI [7]. It should be noted that the average number of procedures performed in patients of the study group was 3.9±0.4 which, undoubtedly, increased risk of recurrent infection and affected the treatment tactics.

Study limitations. Short follow up doesn't allow to conclude on the long-term outcomes. Small number of cases in the present study is also a limitation, the analysis of a bigger sample would allow to verify the consistency of our opinions. However, the present pathology is rare which is confirmed by absence of similar publications in the literature. The authors plan to perform analysis of late outcomes in next papers.

Two stage revision arthroplasty using antibacterial spacer is the most common option for treatment of periprosthetic infection. Despite compliance to international protocols for treatment of implant-associated infection the recurrence rate in HIV-positive patients in asymptomatic stage remains rather high. The efficiency rate of two stage treatment in the present study was only 15,4%. Based on the above we should consider the reasonability of performing revision arthroplasty in HIV-positive patients with PJI.

Ethics of publication

The study was approved by ethics committee of Ilizarov Scientific Center for restorative traumatology and orthopaedics and conducted in accordance to the ethical standards under Declaration of Helsinki (1975, revision of 2008).

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Authors' contribution

A.S. Tryapichnikov — study design development, review of literature, collection and analysis of obtained data, preparing text of publication, statistical processing of obtained data, correction and final editing

A.M. Ermakov — study design development, collection and analysis of the data, preparing text of publication, correction and final editing

N.M. Klyushin — coordination of study participants, editing of publication text

Yu.V. Ababkov — collection and analysis of the data

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