CHRONIC INFECTIOUS LESIONS OF THE CERVICAL SPINE IN ADULTS: MONOCENTRIC COHORT ANALYSIS AND LITERATURE REVIEW

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Objective. To analyze the results of surgical treatment of chronic infectious cervical spondylitis and literature data.
Material and Methods. Design: retrospective monocentric cohort study for 2017–2020. The study included medical history and clinical and instrumental data of 25 patients who underwent 28 reconstructive surgeries on the suboccipital ($n_1 = 3$) and subaxial ($n_2 = 25$) spine. The average follow-up period was 1 year 2 months ± 4 months. Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS), version 22.0.
Results. The effect of the duration of the therapeutic pause ($p = 0.043$) and the T1 slope (T1S) ($p = 0.022$) on the intensity of vertebrogenic pain syndrome was established. When assessing the parameters of the sagittal balance a direct relationship between the age of patients and the value of cervical sagittal vertical axis (CSVA) ($p = 0.035$) was revealed, while CSVA ($p = 0.514$) and neck tilt angle (NTA) ($p = 0.617$) did not significantly affect the intensity of vertebral pain syndrome. The extent of vertebral destruction did not affect either the intensity of vertebral pain ($p = 0.872$) or the indices of the sagittal balance: CSVA ($p = 0.116$), T1S ($p = 0.154$), and NTA ($p = 0.562$). A significant predictor of postoperative complications is the level of comorbidity with an index of 7 or more ($p = 0.027$) according to the Charlson scale.
Conclusion. The leading predictors of complications of surgical treatment of cervical infectious spondylitis are the Charlson comorbidity index (7 points or more) and the variant of anterior reconstruction (the use of a blocked extraspinal plate). The factors influencing the intensity of vertebrogenic pain syndrome in this pathology are the duration of the therapeutic pause and the magnitude of T1S compensation. Anterior reconstruction of the cervical spine in the presence of infectious spondylitis provides a correction of the sagittal balance parameters, with the possibility of long-term maintaining the achieved values.
Key Words: spondylitis, cervical spine, cervical spine reconstruction, atlantooccipital fusion, sagittal balance.
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An infectious spondylitis is a heterogeneous group of diseases manifested by vertebral destruction, instability, abscesses formation and pain syndrome [1, 2]. Annually, the incidence of infectious spondylitis is evaluated in the range from 0.2 to 2.4 cases per 100 thousand population [3, 4]. Cervical spine lesions in the general structure of spondylitis are 5–20 %, accompanied by neurological symptoms in 35–50 % of cases, disorder of segmental stability and sagittal balance in 50–65 % [5–8].

The tactics of surgical treatment of cervical spondylitis is determined by the bone destruction prevalence and features of the clinical picture [9]. The best clinical results in suboccipital spondylitis (Oc–C2) are provided by atlantooccipital fusion in combination with trans-oral debridement and decompression [10–12]. In case of subaxial (C3–C7) lesions, an isolated anterior reconstruction – corpectomy and fusion is effective [13–15].

The literature data analysis proves the lack of integrated data regarding chronic infectious spondylitis of the cervical spine. The articles are mostly descriptions of individual cases or small series. This fact enables us to introduce our own experience.

The objective is to analyze the results of surgical treatment of chronic infectious cervical spondylitis and to perform a literature review.

The following questions are identified in the course of the study:

1) if the extent of bone destruction or sagittal balance malalignment of the cervical spine affect the acuteness of vertebrogenic pain syndrome; and

2) what factors are significant predictors of postoperative complications.

Material and Methods

Design: monocentric cohort study. The data was collected retrospectively in accordance with the following criteria:

– bacteriologically or histologically verified infectious spondylitis of the cervical spine;

– surgical treatment at the Research and Clinical Center of Spinal Pathology of Saint Petersburg Research Institute of Phthisiopulmonology, in the period from January 1, 2017 to December 31, 2020;

– the chronicity of the infectious process: the period from the onset of initial symptoms to the surgery is at least three months in the absence of the effect of complex conservative antibacterial therapy performed in tuberculosis lesions according to the recommended protocols [16]; in case of nonspecific – for at least 2 months;

– the patients should be over 18.

Exclusion criteria:

– discitis and spondylodiscitis corresponding to types A1–4 and B1–2 according to Pola et al. [17];

– surgeries in the volume of isolated debridement of cervical spinal epidural abscess (true primary epiduritis) or diagnostic biopsy (open/closed);

– the basal level of neurological disorders corresponding to types A and B according to Frankel, due to the inability to perform X-ray examination of patients in upright position;

– previously performed surgeries on the cervical spine.

The neurological status was studied according to the Frankel scale before surgery and at the time of discharge.

The follow-up was performed in terms of 1 year 2 months ± 4 months (M ± m; Me – 1 year 3 months).

All patients underwent radiation screening before surgery:

1) Lateral X-ray image of the cervical spine, the parameters of sagittal balance were evaluated: CSVA, cervical sagittal vertical axis (with the allocation of reference indicators of sagittal imbalance >4 cm), T1S, T1 slope (>25°) and NTA, neck tilt angle (range from 13 to 25°) [18]; calculations were performed in the Surgimap v2.3.2.1, with preliminary data depersonalization (the calculation method is shown in Fig. 1);

2) CT study with determination of the bone destruction prevalence;

3) MRI with evaluation of intramedullary changes and the presence of epidural, para- and prevertebral abscesses.

The vertebrogenic pain syndrome severity was evaluated by VAS (from 1 to 10 points).

The analyzed values were recorded as the surgery duration (min) and blood loss (ml); a variant of anterior stabilization during 180° reconstruction: a titanium mesh cage filled with bone autograft or a titanium mesh cage filled with bone autograft in combination with an anterior plate, and the timing of development and the nature of complications.

The possible predictors of postoperative complications were the Charlson comorbidity index, the bone destruction extent, the variant of anterior spinal stabilization, the spondylitis etiology, the gender and age of patients, as well as the duration of the therapeutic pause.

The features of the patients are given in Table 1.

The methodology of search and processing of papers for literature review. The literature review was performed using eLibrary, MEDLINE/PubMed databases, and Google Scholar. The steps of selection and analysis of papers comply with PRISMA guidelines [18]. The retrospection depth is 2000–2020 inclusive. Key words: cervical spondylitis, atlantoaxial spondylitis, suboccipital spondylitis, spondylites, cervical spine. The papers were included in the review according to the following criteria: follow-up period at least 12 months, the data concerning etiological verification, the reconstruction nature of the surgery, the age of patients – 18 and older.

The publications devoted to the treatment of isolated epidural cervical abscesses were consciously excluded during the search.

A total of 23 papers were subjected to final analysis (Fig. 2); 13 of them focus on the surgery of infectious suboccipital spondylitis and 10 on subaxial lesions. The review findings are given in the "discussion" section.

Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS) software, version 22.0 (SPSS Inc., Chicago, IL, USA). The test of the investigated quantitative variables for the normality of the distribution was done according to the Kolmogorov–Smirnov and Shapiro – Wilk criteria. The two-sided significance level for all quantitative variables was $p < 0.05$, which indicates the abnormality of their distribution, and thus the results are presented in the form of M ± m and Me (min, max). In order to evaluate the significance of differences in the surgery duration and blood loss depending on the anterior stabilization variant, the Mann – Whitney U–test was applied. The significance of the influence of the parameters of sagittal balance, the bone destruction extent and the therapeutic pause duration on the pain severity of patients was evaluated using the Spearman correlation coefficient. The influence of qualitative parameters on the postoperative complications' development was tested according to the Pearson's chi-squared criterion (2). The differences were recognized as statistically significant with bilateral $p < 0.05$.

Results

The study cohort consisted of 25 patients aged 26–75 years (M ± m – 51 ± 13 years, Me – 49 years), who successively underwent 28 reparative surgeries in the suboccipital ($n_1 = 3$) and subaxial ($n_2 = 25$) cervical spine. The therapeutic pause duration ranged from 3 to 21 months (M ± m – 7 ± 5 months, Me – 5 months).

In the structure of co-morbidity, pulmonary tuberculosis (8 cases), HIV infection (7 cases), multiple foci of bone destruction (6 cases), persistent urological infection (4 cases), a history of sepsis (2 cases) were identified. The Charlson comorbidity index was M ± m – 3.6 ± 2.2 points (min – 1, max – 7; Me – 3 points).

A significant effect of the therapeutic pause duration on the pain intensity was established: the smaller it is, the more intense the pain syndrome ($r = -0.436$, $p = 0.043$).

There was a direct correlation between the age of patients and the CSVA value: the older the patients, the greater its deviation ($r = 0.528$, $p = 0.035$). We consider this to be explained

by the decrease in mobility and compensatory capabilities of the spinal motion segments with age, in particular, by less compensation of cervical lordosis due to an increase in T1S.

For its part, the Charlson comorbidity index appeared to be a significant development predictor of postoperative complications (2 = 7.194, p = 0.027), the largest number of which was observed in patients with an index of 7 points.

The evaluation of initial parameters in sagittal balance showed a statistically significant influence of the T1 slope angle (T1S) on the severity of vertebrogenic pain syndrome (r = 0.567, p = 0.022), while CSVA (r = 0.176, p = 0.514) and NTA (r = -0.135, p = 0.617) had no significant relationship with this indicator.

The extent of vertebral destruction did not affect either the intensity of vertebral pain (r = -0.036, p = 0.872) or the indices of the sagittal balance: CSVA (r = -0.409, p = 0.116), T1S (r = -0.373, p = 0.154), and NTA (r = -0.157, p = 0.562).

The results of an intergroup comparison of the surgery duration and surgical blood loss in patients underwent corpectomy with anterior spinal fusion using a titanium mesh cage filled with bone autograft (ACCF) and corpectomy with anterior spinal fusion using a titanium mesh cage filled with bone autograft and anterior plate (ACCF + AP) are given in Table 2.

In the cohort, 7 postoperative complications were observed with their predominance in the AACF + AP group. Nevertheless, a significant effect of the reconstruction variant has not been proven (2 = 3.689, p = 0.297). In the early postoperative period, three patients had a pain syndrome with a severity of 5 to 6 VAS points in the autograft sampling area (rib autograft fragment), the relief of which was ensured by a course of NSAIDs followed by physiotherapeutic treatment.

We have observed the preservation of an epidural abscess in a particular case 3 months after the surgery: hemilaminectomy of C4–C5, rehabilitation and posterior instrumental fixation were performed.

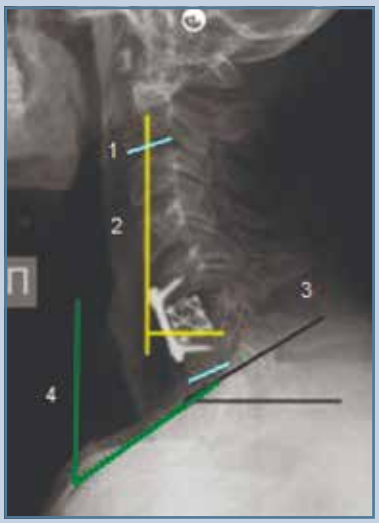

Fig. 1
The calculation method for sagittal balance parameters: *1* – cervical lordosis of C2–C7; *2* – CSVA; *3* – T1S; *4* – NTA

The spinal reconstruction area instability was revealed in three cases, manifested by a recurrence of vertebrogenic pain syndrome; in a particular case – against the background of a deep infection of the surgical site. The above-mentioned complications had a duration of 8.0 ± 7.2 months (Me – 6 months). The surgical explorations were performed in the volume of the anterior refusion using a titanium mesh cage filled with bone autograft (n_1 = 2) and the debridement of the anterior column in combination with the posterior instrumental fixation (n_2 = 1).

During the analysis of the sagittal balance, a significant change was observed. First of all, it was found in the parameters of T1S and NTA. Meanwhile, there was no significant association of these changes with the spondylitis etiology (Table 3).

The surgical findings of suboccipital and subaxial chronic spondylitis are given in Fig. 3, 4.

Discussion

The treatment of infectious lesions of the cervical spine consists of three main principles: the need for etiological verification, debridement of the inflammatory tissue, and correction of orthopedic complications. Meanwhile, cervical spondylitis is early complicated

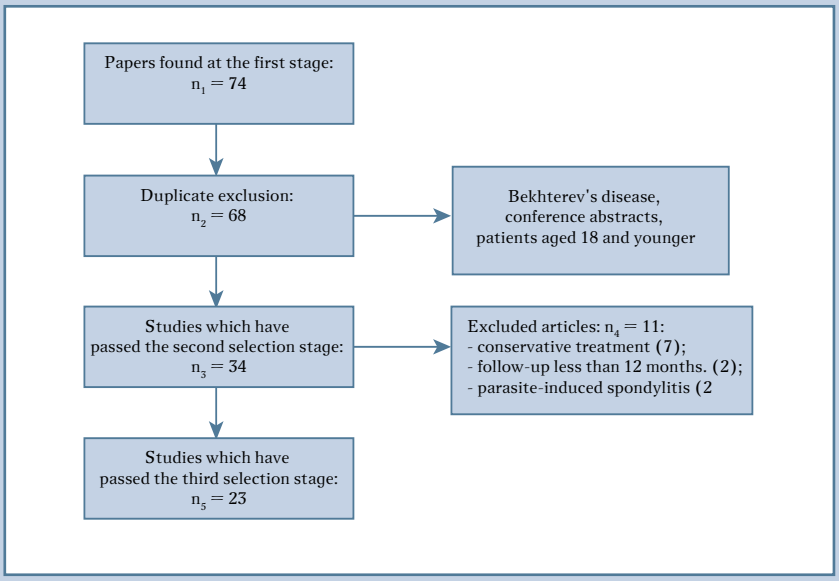

Fig. 2
Paper selection scheme

Table 1
Characteristics of patients included in the study

Patient	Gender / age, years	Charlson comorbidity Index	Level	Therapeutic pause, mon.	Cobb angle of kyphosis, deg	CSVA, cm/ T1S, deg./NTA, deg.	VAS, points	Frankel		Reconstruction option	Surgery duration, min/blood loss, ml	Complication/follow-up period, mon.
								before	after			
1	f / 33	7	C1–C2	5	56	2.5 /48.5/38.3	8	C	E	360°	235/170	donor site pain/1
2	m / 61	3	C3–C4	6	–	5.4/27.7/35.5	5	R	E	ACCF	95/50	–
3	m / 47	7	C3–C6	6	34	6.3/23.4/47.8	7	C	D	ACCF + AP	110/100	an epidural abscess persistence/3
4	f / 75	4	C4–C7	4	28	6.5/8.3/39.5	7	R	E	ACCF + AP	115/100	–
5	m/ 52	3	C5–C6	13	31	3.3/28.9/61.3	4	R	E	ACCF + AP	100/100	–
6	f / 66	3	C5–C6	7	–	4.7/26.3/57.4	3	D	E	ACCF + AP	100/50	–
7	m / 39	1	C5–C7	18	33	2.5/ 9.0/35.8	4	D	E	ACCF + AP	135/50	anterior column instability/16
8	m / 65	3	C6–T1	24	–	3.6/16.6/58.6	3	E	E	ACCF	95/50	–
9	m / 26	1	C7–T1	7	–	4.1/20.3/41.2	5	D	E	PI + AD	115/70	–
10	f /45	7	C7–T1	4	23	5.1/18.2/39.7	7	D	E	ACCF	105/60	–
11	f / 44	2	C1–C2	12	–	4.5/40.2/39.6	8	D	E	360°	245/350	–
12	m / 48	2	C1–C2	4	–	5.3/60.3/36.9	8	D	E	360°	245/200	donor site pain/1
13	m / 67	3	C3–C4	5	21	6.3/27.1/47.8	6	E	E	ACCF	75/50	–
14	m / 73	4	C3–C5	4	28	3.1/38.5/50.8	7	E	E	ACCF + AP	160/50	surgical site infections, anterior column instability/1
15	m / 37	1	C4–C5	6	24	2.4/26.6/49.2	7	R	E	ACCF	70/50	–
16	f / 35	7	C5–C6	5	11	4.8/19.9/44.6	7	R	E	ACCF	70/55	anterior column instability/1
17	f / 44	7	C5–C6	5	–	3.5/36.4/42.7	6		E	ACCF + AP	140/100	–
18	f / 47	7	C5–C6	3	–	4.2/23.5/46.3	8	E	E	ACCF	105/50	–
19	m / 50	3	C5–C6	7	25	3.3/20.6/49.1	7	E	E	ACCF + AP	115/250	–
20	f / 36	5	C5–C6	8	13	4.2/12.3/41.2	4	E	E	ACCF	90/50	–
21	f / 63	3	C5–C7	3	40	9.7/18.8/50.9	6	D	E	ACCF + AP	125/100	–
22	m / 39	7	C6–C7	10	37	1.7/6.3/44.4	4	D	E	ACCF + AP	120/150	donor site pain/1
23	m / 49	1	C7–T1	4	19	2.6/4.9/57.1	6	D	E	ACCF	145/50	–
24	f / 56	2	C7–T1	4	39	3.7/38.2/42.7	5	D	E	ACCF + AP	110/100	–
25	f / 67	3	C7–T1	3	15	3.2/7.6/48.3	3	D	E	ACCF	90/100	–

Patients 1–10 – tuberculous spondylitis; 11–25 – chronic nonspecific spondylitis; R – isolated radicular pain syndrome from the destruction level, without motor deficiency; 360° – posterior instrumental fixation + transoral resection and decompression; ACCF – corpectomy + anterior spinal fusion using a titanium mesh cage filled with bone autograft; ACCF + AP – corpectomy + anterior fusion using a titanium mesh cage filled with bone autograft + anterior plate, PI + AD - posterior instrumentation + anterior debridement.

by secondary myelopathy with a high level of neurological disorders with a certain complexity of invasive diagnostic manipulations, including closed trephine biopsy, and early reconstructive surgeries [19–21]. The main part of the papers focuses on the surgical treatment of this pathology, including surgical approaches, options for plastic replacement of a resection defect of the anterior column and modes of antibacterial chemotherapy [22–24]. Recently, it has been moving towards evaluation of the life quality of patients, the possibility of minimizing surgical aggression and analyzing the long-term results of surgeries from the view of local and global sagittal balance [24–27].

A particular attention is drawn to the consensus on surgical techniques in relation to infectious suboccipital spondylitis [26, 28]. Two major clinical series published by Chaudhary et al. and Qureshi et al., show the high efficiency of atlantooccipital fusion in combination with transoral debridement and decompression. In case of absence of neurological deficit and predominant lesion of the C2 odontoid process, the spinal fusion according to Harms or Magerl is recommended [28]. In our cohort, three reconstructions of the atlantoaxial section were performed in the scope of atlantooccipital fusion and transoral debridement and decompression of the spinal cord (Table 1) due to the different severity of neurological complications.

The tactics of treatment for subaxial spondylitis remains controversial. Sung-Kyu et al. [23] recommend complementing the anterior spinal fusion with anterior plate. Nevertheless, the main reason for this is the correction of the sagittal balance parameters, mainly during polysegmental reconstructions. The surgical outcomes for monosegmental lesions remain comparable.

We argue that the application of an anterior plate is not only a crucial criterion for a favorable outcome, but also increases the risks of postoperative complications. It may be associated with an increase in the surgery duration and the blood loss volume (risk factors of surgical site infections).

The results obtained by analyzing the local sagittal balance in this category of patients were vacant for researchers. This fact enables us to consider the obtained data as the basis for subsequent research.

Conclusions

The incidence of anterior column instability associated with isolated anterior fusion performed for infectious

Table 2

Intergroup comparative analysis of surgical indicators

Surgery option	Surgery duration, min (M ± m; Me)	Blood loss, ml (M±m; Me)	Significance level, p
ACCF	93 ± 24; 92	56 ± 17; 50	0.007*
ACCF + AP	120 ± 18; 115	104 ± 56; 100	0.020**

The significance of the differences was analyzed using the Mann – Whitney U criterion; * significance for the surgery duration;

** significance for blood loss; ACCF – corpectomy + anterior spinal fusion using a titanium mesh cage filled with bone autograft;

ACCF + AP – corpectomy + anterior spinal fusion using a titanium mesh cage filled with bone autograft + anterior plate.

Table 3

Sagittal balance parameters

Sagittal balance parameters	Before surgery	After surgery	p
Tuberculous spondylitis			
CSVA	3.9 ± 1.6	3.4 ± 1.3	0.746
T1S	23.1 ± 15.2	16.3 ± 9.2	0.034
NTA	41.9 ± 9.7	24.8 ± 7.6	0.024
Chronic nonspecific spondylitis			
CSVA	4.2 ± 2.2	3.7 ± 1.9	0.683
T1S	27.4 ± 17.1	19.3 ± 11.4	0.031
NTA	46.5 ± 6.1	27.2 ± 3.4	0.018
Average value			
CSVA	4.1 ± 1.9	3.5 ± 1.4	0.657
T1S	26.1 ± 16.1	17.8 ± 10.3	0.038
NTA	44.8 ± 7.6	25.9 ± 5.2	0.016

* The significance of the differences was analyzed using the Mann – Whitney U criterion.

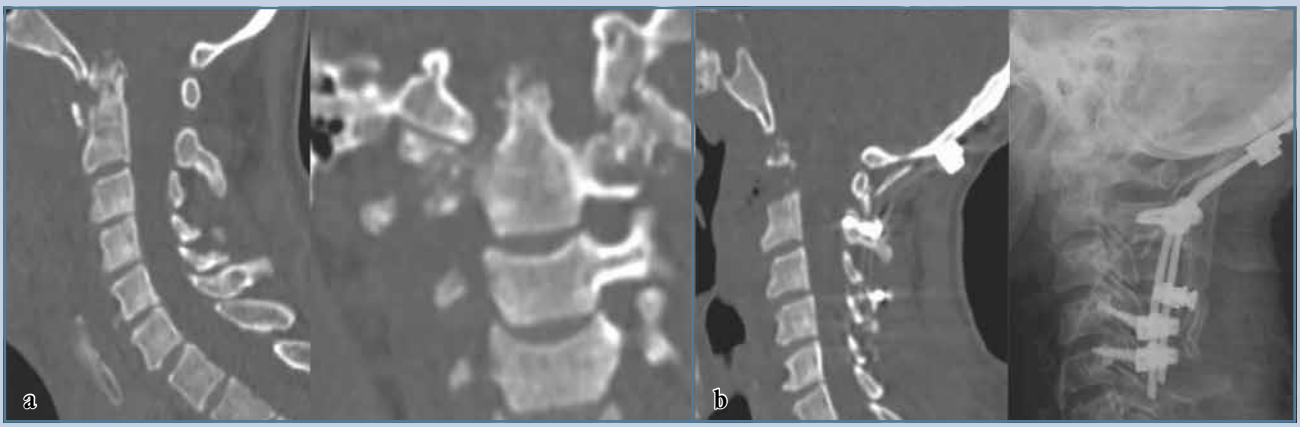

Fig. 3
Pre- and postoperative imaging studies of a patient with C1–C2 spondylitis (patient 12, Table 1): **a** – sagittal and frontal sections of SCT scan; **b** – sagittal section of the SCT scan and X-ray 6 months after surgery

cervical spine spondylitis does not overstep 10 %, including in the long-term period – 3.5 %.

The most common cause of complications in the early postoperative period is surgical site infections, and in the late one is the pseudoarthrosis formation.

The main predictors for surgical treatment complications of cervical infectious spondylitis are the Charlson comorbidity index (7 points or more) and the anterior reconstruction option (the use of an anterior plate).

The factors affecting the vertebrogenic pain syndrome intensity in this pathology are the therapeutic pause duration and the amount of T1S compensation.

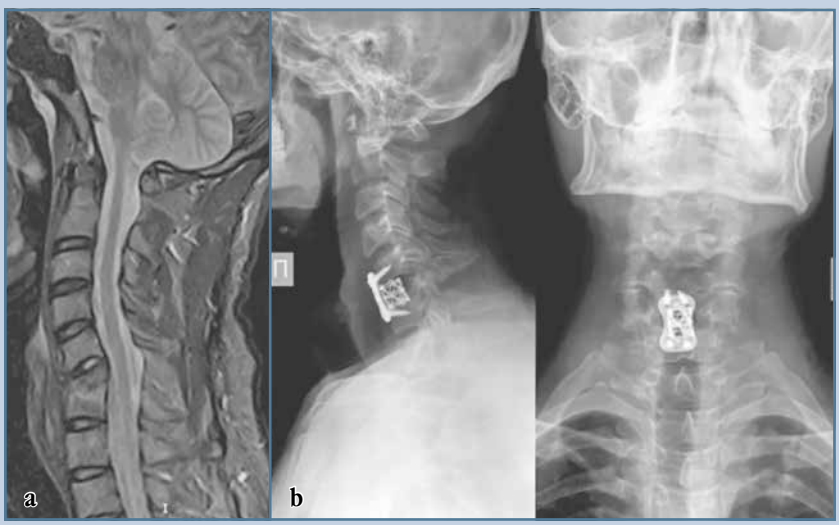

Fig. 4
Pre- and postoperative imaging studies of a patient with C6–C7 spondylitis (patient 22, Table 1): **a** – sagittal section of MRI; **b** – sagittal and frontal X-rays 8 months after surgery

The anterior reconstructions of the cervical spine in the conditions of infectious spondylitis provide a correction of the sagittal balance parameters, with the long-term possibility of preserving the achieved indicators.

Limitations of the results' reliability. The study is monocentric, with a predominant analysis of cases over the past 3 years. The retrospection depth is due to the inability to systematize data for an earlier period. From 2010 to 2017, the Research and Clinical Center of Spinal Pathology of Saint Petersburg Research Institute of Phthisiopulmonology performed more than 90 cervical spine reconstructions in infectious spondylitis in adults. Nevertheless, the scope of clinical and radiological examination is limited by the minimum set of parameters possible for an integral analysis.

The study had no sponsors. The authors declare that they have no conflict of interest.

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