Editors' Choice

REVIEW ARTICLE

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Treatment strategy for upper cervical epidural abscess: a literature review

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ABSTRACT

We aimed to determine available evidences in the literature regarding surgical approaches and methods, timing of surgical interventions, duration of perioperative antibiotics, and duration of nonsurgical treatments (antibiotics administration) in patients with upper cervical (occiput–C2) epidural abscess (UCEA). We performed a literature review of the articles on surgical interventions and antibiotic therapy to treat UCEA, searching the PubMed database for relevant articles published in the English language (as of March 2020). In total, 53 patients with UCEA were identified. Permanent limb paralysis or death was observed in 1/15 (6.7%) patients who received the transoral approach and 2/15 (13.3%) patients who received the transcervical approach, 1/26 (3.8%) patients who underwent surgery before the onset of paralysis, and 2/4 (50.0%) patients who underwent surgery after the onset of paralysis. In 85%–89% of cases, antibiotic administration was continued for 6–12 weeks, which was determined by the confirmation of reduced inflammatory response and/or abscess disappearance on imaging. Differences in surgical approaches may not be associated with the incidence of permanent limb paralysis or death. Surgical interventions before limb paralysis onset are recommended in UCEA patients. In perioperative and nonoperative treatments, antibiotic administration for 6–12 weeks may be supported based on the confirmation of reduced inflammatory response and/or abscess disappearance on imaging. Further investigations are needed.

Keywords: upper cervical epidural abscess, surgery, antibiotics, paralysis, weakness

Abbreviations:
UCEA: upper cervical epidural abscess

INTRODUCTION

Upper cervical (occiput–C2) epidural abscess (UCEA) is a less common and more fatal

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condition than other spinal epidural abscesses.[1] This suggests that UCEA may be a unique disorder compared with lower cervical (C3–C7), thoracic, or lumbar epidural abscess, potentially due to the dynamic motion around the odontoid process, location around the laryngopharyngeal cavity, failure of the medulla oblongata and lower cranial nerves, and/or upper cervical spinal cord dominating the respiratory muscles.[1-23] The best treatment strategy for UCEA has not been fully elucidated because no standard treatment strategy exists for this disease.[2-23] Patients with a stable neurological status usually undergo nonsurgical (antibiotics administration) treatment for UCEA,[24-42] whereas those with progressive neurological deficits typically require surgical interventions.[2-23] Notably, UCEA-associated spinal cord compression is a severe complication that could result in fatal respiratory failure and/or limb paralysis[1]; therefore, in these cases, preventing UCEA-associated spinal cord compression during surgical treatment is vitally important. Nevertheless, the surgical approach used in the treatment of UCEA and the timing of surgical interventions are variable depending on the physician's choices and the patient's condition. The timing of surgical intervention varies from the onset of limb paralysis[5,6,16,19] to progressive limb weakness.[2,4,7-13]

The optimal surgical approaches for decompression and debridement of UCEA are categorized as the anterior approach and the posterior approach. The anterior approach, particularly performed transorally, is the most commonly performed approach, providing direct access for targeting the disease compared with other approaches[10-12]; however, surgeons must be able to perform an oral surgical procedure in a deep and narrow surgical field because the transoral approach proceeds from the oral cavity to the abscess. Conversely, the posterior approach is relatively familiar for spinal surgeon to perform with a wider operative field.[2-23]

In addition to decompression and debridement, surgical methods including odontoidectomy are subsequently and/or concurrently performed in UCEAs with destruction of the odontoid process.[6-12] Moreover, cases with instability of the upper cervical spine due to destruction and/or resection of the upper cervical vertebrae also receive instrumentation and fusion.[6-12] Instrumentation with transarticular screws and rods according to Magerl and/or fusion with iliac bone graft and sublaminar wiring according to Brooks or Gallie were performed in a single- or two-stage procedure.[3,5,10-12] Based on the initial presence of pus, two-stage instrumentation and fusion is performed from 10 days to 6 months later.[10-12] Single-stage instrumentation and fusion requires a lengthy operative time,[3,5] while two-stage instrumentation and fusion may involve a risk of neurological impairments due to spinal instability.[2,4,7,8,10-12] Their effectiveness in controlling infection was unclear.

The duration and route of perioperative antibiotics administration (oral versus intravenous) are also variable; some cases receive long-term antibiotic treatment for at least 3 months,[10-12,21,22] some receive short-term (4–6 weeks)[4,5,9,18,20] treatment, some receive intravenous antibiotics for 6 weeks,[20] and others switch to oral administration after 2 weeks of intravenous antibiotics, depending on the attending physician.[12,21] Moreover, the duration of antibiotic administration is determined by various reasons.[8,10,12,14,17,20-22,30,31,35,38]

The attending physician typically determines the surgical approach for UCEA, the timing of surgical interventions, and duration and route of antibiotics administration, because no comprehensive clinical trials have been performed to determine a standard treatment because of the extremely low incidence of UCEA. Therefore, our review aims to clarify the evidence regarding the surgical approach and method, timing of surgical intervention, timing of instrumentation and fusion, duration of antibiotic therapy, and duration of nonsurgical treatment (antibiotic administration) in the treatment of UCEA.

METHODS

Search strategy and criteria

We searched the PubMed database for relevant articles published in the English language (as of March 2020) on surgical interventions and antibiotics used in the treatment of UCEA to evaluate treatment choices, which were described as the association between treatment choices (surgical approach and method, timing of surgical intervention, timing of instrumentation and fusion, duration of antibiotic therapy, and duration of nonsurgical treatment) and clinical outcome in UCEA (permanent limb paralysis or death). We conducted a systematic review based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines. The key words "upper cervical epidural abscess," "C1 osteomyelitis," "C2 osteomyelitis," "C1 epidural abscess," and "C2 epidural abscess" were used in combination with the Boolean operators AND and OR. Fungal or tuberculous UCEA was excluded. Two reviewers (TK and HU) screened the extracted literature and performed data extraction, respectively, to ensure the consistency of the results.

Demographic data and outcome parameters

Data were extracted on the research topic, first author, publication year, country, age, sex, clinical presentation, predisposing factors, organism, source of infection, empirical antibiotics, level of abscess, location of abscess, location of bone erosion, surgical methods, duration of perioperative antibiotics, and outcome. The location of abscess was classified into anterior and posterior spaces (Figure 1).[43] Limb weakness was defined as a condition in which patients had weak limb sensibility and/or reduced ability for limb movement, whereas limb paralysis was defined as a condition in which the patients were completely unable to move their limbs.[2-42]

Statistical analysis

Descriptive analyses were performed using the IBM Statistical Package for the Social Sciences, Version 19 (IBM Corp., Armonk, NY, USA).

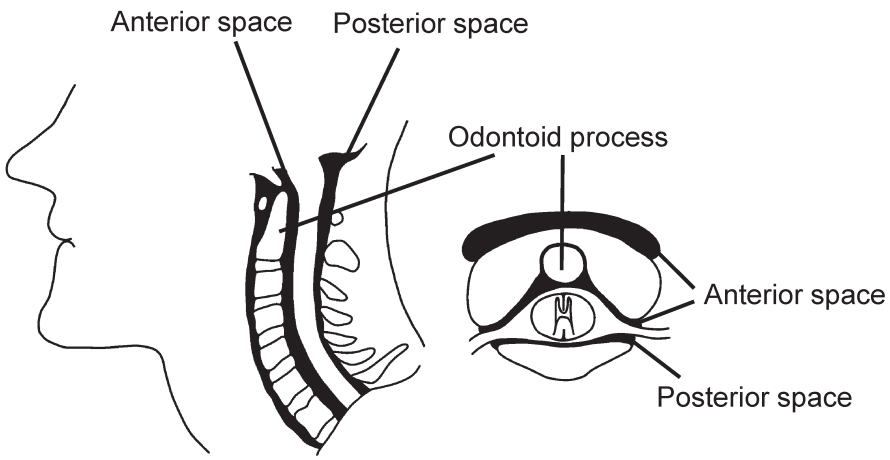

Fig. 1 Location of the upper cervical epidural abscess

RESULTS

Patient characteristics

Forty-one studies were eligible for this review (Figure 2),[2-42] and 53 cases of UCEA were identified. Among these, 35 (66.0%) patients were male and 18 (34.0%) were female, with an average age of 49.8 years. Regarding clinical presentations at admission, neck pain and/or stiffness was seen in 47 (88.6%) patients, limb weakness in 9 (17.0%), and limb paralysis in 9 (17.0%). Fever was reported in 24 (45.3%) patients, with 2 (3.8%) having dyspnea, dysphagia, or odynophagia due to the retroesophageal abscess directly compressing the trachea and esophagus. Sources of infection were intravenous drug abuse in six patients (11.3%), postoperative surgical site infection in four (7.5%), pneumonia in three (5.7%), otorhinolaryngologic disease in three (5.7%), skin lesions in two (3.8%), cat scratch in two (3.8%), and tooth extraction in two patients (3.8%). No specific pathogens were identified in 31 patients (58.5%). Pathogens isolated from cultures involving the blood (47.2%), pus obtained by transoral biopsy and surgery (20.8%), bone by transoral biopsy (3.8%), or soft tissue by transoral biopsy (3.8%), included *Staphylococcus aureus* in 28 patients (52.8%), *Streptococcus* spp in six (11.3%), no pathogen in 15 (28.3%), and others in four (7.5%). A summary of the patient and treatment characteristics is shown in Table 1 and review of the cases available to the authors is summarized in Table 2.

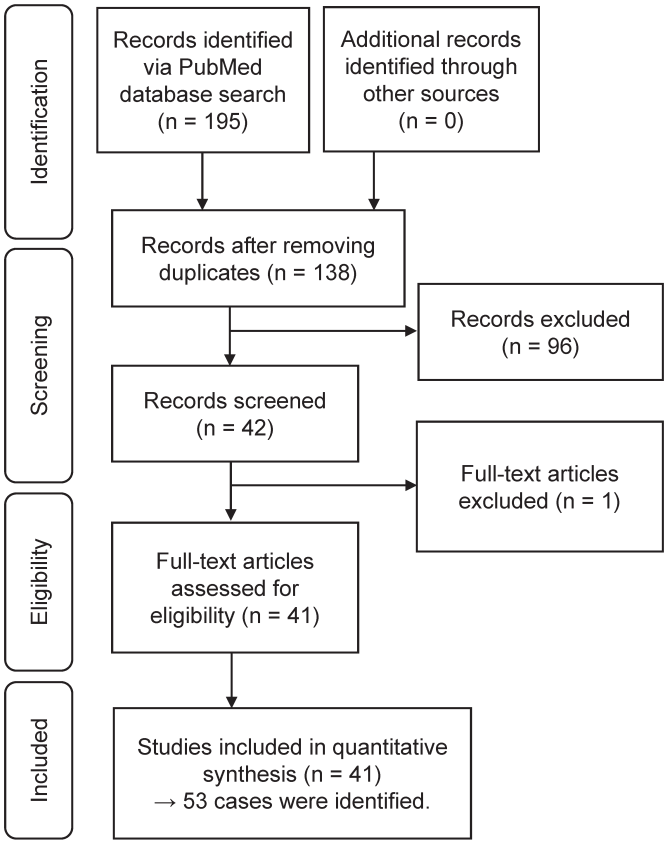

Fig. 2 Flow chart of the paper selection

Table 1 Characteristics of the 53 patients with upper cervical epidural abscess

Variable	Value
Age (years), mean ± SD [range]	49.8 ± 22.8 [0 to 88]
Female, n (%)	18 (34.0)
Clinical presentation at admission, n (%)	
Neck pain or Neck stiffness	47 (88.6)
Limb weaknesses	9 (17.0)
Limb paralysis	9 (17.0)
Respiratory failure	1 (1.9)
Fever	24 (45.3)
Dysphagia or odynophagia	2 (3.8)
Predisposing factor, n (%)	
Diabetes mellitus	9 (16.9)
Hypertension	4 (7.5)
Chronic renal failure	2 (3.8)
Parkinson`s disease	2 (3.8)
Source of infection, n (%)	
Intravenous drug abuser	6 (11.3)
Post-surgery	4 (7.5)
Pneumonia	3 (5.7)
Otorhinolaryngologic disease	3 (5.7)
Skin problem	2 (3.8)
Cat scratch	2 (3.8)
Tooth extraction	2 (3.8)
No specific pathogens	31 (58.5)
Culture, n (%)	
Blood	25 (47.2)
Pus (Transoral biopsy and/or operative culture)	11 (20.8)
Bone (Transoral biopsy)	2 (3.8)
Soft tissue (Transoral biopsy)	2 (3.8)
Non-identified	13 (24.5)
Organism, n (%)	
Staphylococcus aureus	28 (52.8)
Streptococcus spp.	6 (11.3)
Non-identified	15 (28.3)
Others	4 (7.5)
Level, n (%)	
C1	2 (3.8)
C1–C2	29 (54.7)
C2	7 (13.2)
C1–C3	3 (5.7)
C2–C3	3 (5.7)
Others	9 (16.9)

Location of abscess, n (%)	
Anterior space	16 (30.2)
Posterior space	5 (9.4)
Anterior space and Posterior space	19 (35.8)
None	5 (9.4)
Unavailable data	8 (15.1)
Bone erosion, n (%)	
Odontoid process	25 (47.2)
Cervical vertebrae	11 (20.8)
Outcome, n (%)	
Full recovery	33 (62.3)
Neck pain or Neck stiffness	10 (18.9)
Permanent limb weakness	3 (5.7)
Permanent limb paralysis	2 (3.8)
Death	5 (9.4)

Table 2 Patients with upper cervical pyogenic epidural abscess

Author	Age (year)	Gender	Clinical presentation	Culture	Organism	Bone erosion	Location of abscess	Timing of surgical intervention	Initial surgical procedure	Additional surgical procedure	Duration of antibiotics	Outcome
Anton et al., 1999[2]	75	Female	Neck pain, Limb paralysis	Pus	*Streptococcus* spp	None	Anterior space and posterior space	Before limb paralysis	Transcervical anterior approach (decompression and debridement)	Second-stage transcervical posterior approach (instrumentation and fusion)	Non-available	Limb weakness
Curry et al., 2007[3]	37	Female	None	Operative culture	None identified	C3 vertebrae	Anterior space	Before limb paralysis	Transcervical anterior approach (decompression and debridement)	Single-stage transcervical posterior approach (instrumentation and fusion)	8 weeks	Full recovery
Suchomel et al., 2003[4]	50	Male	Neck pain/ stiffness, Limb weakness, Fever	Pus	*Staphylococcus aureus*	Odontoid process, Anterior arch of C1	Anterior space	Before limb paralysis	Transoral anterior approach (decompression and debridement)	Second-stage transcervical posterior approach (instrumentation and fusion)	6 weeks	Full recovery
	51	Female	Neck pain/ stiffness, Fever	Operative culture	*Staphylococcus aureus*	Odontoid process	Anterior space	Before limb paralysis	Transoral anterior approach (decompression and debridement)	Second-stage transcervical posterior approach (instrumentation and fusion)	6 weeks	Full recovery

	52	Male	Neck pain/ stiffness	Operative culture	*Staphylococcus aureus*	Odontoid process, C1-C2 vertebrae	Anterior space and posterior space	Before limb paralysis	Transoral anterior approach (decompression and debridement)	Second-stage transcervical posterior approach (instrumentation and fusion)	6 weeks	Full recovery
Aranibar et al., 2015[5]	70	Female	Neck pain, Limb weakness	Pus	Methicillin-resistant *Staphylococcus aureus*	C1–C2 vertebrae	Anterior space	After limb paralysis	Transcervical anterior approach (decompression and debridement)	Single-stage transcervical posterior approach (instrumentation and fusion)	6 weeks	Limb weakness
Burns et al., 2015[6]	69	Female	Limb paralysis, Fever, Odynophagia	Blood	*Streptococcus* spp	Odontoid process	Anterior space and posterior space	After limb paralysis	Transoral anterior approach (decompression and debridement)	Single-stage transcervical posterior approach (instrumentation and fusion)	Non-available	Full recovery
	55	Male	Neck pain	Non-identified	None identified	Odontoid process, C1–C2 vertebrae	Posterior space	Before limb paralysis	Transoral anterior approach (decompression and debridement)	Single-stage transcervical posterior approach (instrumentation and fusion)	Non-available	Neck stiffness
Keogh et al., 1992[7]	41	Male	Neck pain, Fever	Blood	*Staphylococcus aureus*	Odontoid process	Anterior space and posterior space	Before limb paralysis	Transoral anterior approach (decompression and debridement)	Single-stage transcervical posterior approach (instrumentation and fusion)	Non-available	Full recovery
Hardias et al., 2003[8]	65	Male	Neck pain, Limb weakness	Blood	*Staphylococcus aureus, Proteus mirabilis*	Odontoid process, C1 vertebrae	Posterior space	Before limb paralysis	Transcervical anterior approach (decompression and debridement)	Second-stage transcervical posterior approach (instrumentation and fusion)	8 weeks	Limb paralysis
Fukutake et al., 1998[9]	74	Male	Neck pain, Limb weakness, Fever	Blood	*Streptococcus* spp	Odontoid process	None	Before limb paralysis	Transcervical posterior approach (decompression and debridement)	None	6 weeks	Full recovery
Reid et al., 2007[10]	58	Male	Neck pain	Blood	Methicillin-sensitive *Staphylococcus aureus*	Odontoid process, left atlanto-occipital joint, atlanto-axial joint	Anterior space	Before limb paralysis	Transoral anterior approach (decompression and debridement)	Single-stage transcervical posterior approach (instrumentation and fusion)	24 weeks	Full recovery

Weidau-Pazos et al., 1999[11]	74	Female	Neck pain/ stiffness	Non-identified	Non-identified	Odontoid process	Anterior and posterior space	Before limb paralysis	Transoral anterior approach (decompression and debridement)	Second-stage transcervical posterior approach (instrumentation and fusion)	Non-available	Full recovery
	63	Male	Neck pain/ stiffness	Blood	*Staphylococcus aureus*	None	Anterior space and posterior space	Before limb paralysis	Transoral anterior approach (decompression and debridement)	None	14 weeks	Full recovery
Zigler et al., 1987[12]	62	Female	Neck pain, Limb paralysis	Axis	*Staphylococcus aureus*	Odontoid process, C1–C2 vertebrae, atlanto-axial joints, atlanto-occipital joints	None	Before limb paralysis	Transcervical posterior approach (instrumentation and fusion)	Second-stage transcervical posterior approach (instrumentation and fusion)	12 weeks	Full recovery
	72	Male	Neck pain/ stiffness	Blood	Methicillin-sensitive *Staphylococcus aureus*	Odontoid process, Occipito-cervical joints	None	Before limb paralysis	Transcervical posterior approach (instrumentation and fusion)	Second-stage transcervical posterior approach (instrumentation and fusion)	Non-available	Full recovery
	56	Female	Neck pain/ stiffness, Limb weakness	Blood	*Pasteurella multocida*	C2 vertebrae	None	Before limb paralysis	Transcervical posterior approach (instrumentation and fusion)	None	Non-available	Full recovery
	66	Male	Neck pain, Fever	Blood	Methicillin-sensitive *Staphylococcus aureus*	Odontoid process	Anterior space	Before limb paralysis	Transcervical anterior approach (decompression and debridement)	None	32 weeks	Full recovery
	67	Female	Neck pain, Fever	Operative culture	Methicillin-sensitive *Staphylococcus aureus*	Odontoid process	Anterior space and posterior space	Before limb paralysis	Transoral anterior approach (decompression and debridement)	None	6 weeks	Full recovery
Deshmukh et al., 2010[13]	59	Female	Neck pain, Limb paralysis, Fever	Blood	Methicillin-sensitive *Staphylococcus aureus*	None	Posterior space	Before limb paralysis	Transcervical posterior approach (decompression and debridement)	None	8 weeks	Full recovery

Ruskin et al., 1992[14]	57	Male	Neck pain, Fever, Sore throat	Pus	*Staphylococcus aureus*	None	Anterior space	Before limb paralysis	Transoral anterior approach (decompression and debridement)	None	12 weeks	Full recovery
Kubo et al., 2002[15]	52	Male	Neck pain, Fever	Pus	*Staphylococcus aureus*	Odontoid process	Anterior space	Before limb paralysis	Transoral anterior approach (decompression and debridement)	None	12 weeks	Neck stiffness
Al-Hourani et al., 2015[16]	66	Male	Neck pain, Limb paralysis	Blood	*Streptococcus* spp	None	Anterior space and posterior space	After limb paralysis	Transcervical posterior and transoral anterior approach (decompression and debridement)	None	Non-available	Death
Paul et al., 2005[17]	54	Male	Neck pain	Bone	*Pseudomonas aeruginosa*	Odontoid process, C2–C4 vertebrae	Anterior space	Before limb paralysis	Transcervical anterior approach (decompression and debridement)	None	12 weeks	Neck pain
Papp et al., 2003[18]	0	Male	Fever, Tachycardia, Hypotonia	Soft tissues	*Staphylococcus aureus*	C1–C2 vertebrae	Anterior space	Before limb paralysis	Transcervical posterior approach (decompression and debridement)	None	6 weeks	Neck stiffness
Kurimoto et al., 1998[19]	72	Female	Neck pain, Neck stiffness, Limb weakness	Non-identified	Non-identified	Odontoid process	Posterior space	After limb paralysis	Transoral anterior approach (decompression and debridement)	Single-stage transcervical posterior approach (instrumentation and fusion)	Non-available	Limb paralysis
Bartels et al., 1990[20]	49	Male	Neck stiffness	Blood	*Staphylococcus aureus*	None	Anterior space	Before limb paralysis	Transcervical anterior approach (decompression and debridement)	None	6 weeks	Full recovery
Mirouse et al., 2015[21]	14	Male	Neck pain/ stiffness, Fever	Operative culture	*Bartonella henselae*	C2 vertebrae	Anterior space	Before limb paralysis	Transcervical posterior approach (decompression and debridement)	None	10 weeks	Full recovery

Young et al., 1999[22]	58	Male	Neck pain, Fever	Blood	*Staphylococcus aureus*	Odontoid process	Anterior space	Before limb paralysis	Transoral anterior approach (decompression and debridement)	None	12 weeks	Neck stiffness
LaFave et al., 2019[23]	45	Male	Limb weakness, Respiratory failure, Fever, Low back pain	Blood	Methicillin-resistant *Staphylococcus aureus*	None	Posterior space	Before limb paralysis	Transcervical posterior approach (decompression and debridement)	None	Non-available	Limb weakness
Frank et al., 1944[24]	43	Male	Neck pain/ stiffness, Fever	Non-identified	Non-identified	Non-available	Non-available	None	None	None	Non-available	Death
Limbird et al., 1988[25]	61	Male	Neck pain, Limb paralysis	Blood	*Escherichia coli*	Non-available	Non-available	None	None	None	Non-available	Death
	51	Male	Neck pain/ stiffness, Limb weakness, Fever	Blood	*Staphylococcus aureus*	Non-available	Non-available	None	None	None	Non-available	Neck stiffness
Ahlbäck et al., 1970[26]	44	Female	Neck pain/ stiffness, Difficulty pronouncing	Non-identified	Non-identified	Odontoid process, right atlanto-axial joint	Anterior space	None	None	None	12 weeks	Neck stiffness
	43	Male	Neck pain/ stiffness	Non-identified	Non-identified	Odontoid process	Anterior space and posterior space	None	None	None	Non-available	Neck stiffness
Lam et al., 1996[27]	58	Male	Neck pain, Fever	Blood	*Staphylococcus aureus*	None	None	None	None	None	Non-available	Full recovery
Ueda et al., 2009[28]	37	Male	Neck pain, Fever	Blood	*Streptococcus* spp	Odontoid process	Anterior space and posterior space	None	None	None	Non-available	Full recovery
Leach et al., 1967[29]	49	Female	Neck pain/ stiffness, Fever	Blood	*Staphylococcus aureus*	Non-available	Non-available	None	None	None	Non-available	Full recovery
Tomazewski et al., 2011[30]	0	Female	Jaundice	Non-identified	Non-identified	Odontoid process	Anterior space and posterior space	None	None	None	8 weeks	Full recovery
	0	Male	Jaundice	Pus	*Staphylococcus aureus, Klebsiella pneumoniae*	Odontoid process	Anterior space and posterior space	None	None	None	6 weeks	Full recovery
Venger et al., 1986[31]	29	Male	Neck pain/ stiffness, Fever	Blood	*Staphylococcus aureus*	Odontoid process, C2 vertebrae	Anterior space and posterior space	None	None	None	6 weeks	Full recovery
Sasaki et al., 2006[32]	76	Female	Neck pain/ stiffness	Blood	Non-identified	None	Anterior space and posterior space	None	None	None	Non-available	Full recovery
Rimalovski et al., 1968[33]	48	Female	Neck pain/ stiffness, Limb paralysis	Blood	*Staphylococcus aureus*	None	Anterior space	None	None	None	Non-available	Death

Odelberg et al., 1932[34]	16	Female	Neck pain/ stiffness, Fever	Non-identified	Non-identified	Non-available	Non-available	None	None	None	Non-available	Neck stiffness
Noguchi et al., 2000[35]	68	Male	Neck pain/ stiffness	Soft tissues	*Streptococcus* spp	None	Anterior space and posterior space	None	None	None	24 weeks	Full recovery
Dimaala et al., 2006[36]	1	Male	Neck stiffness, Weight loss, Anorexia	Non-identified	Non-identified	Odontoid process	Non-available	None	None	None	Non-available	Full recovery
Azizi et al., 1995[37]	65	Male	Neck pain/ stiffness	Non-identified	Non-identified	None	Anterior space	None	None	None	12 weeks	Full recovery
Lubotzky et al., 2017[38]	0	Male	Neck stiffness	Non-identified	Non-identified	None	Anterior space and posterior space	None	None	None	6 weeks	Full recovery
	0	Male	Neck stiffness, Fever, Mouth ulcers	Non-identified	Non-identified	None	Anterior space and posterior space	None	None	None	6 weeks	Full recovery
Lee et al., 2012[39]	47	Female	Neck pain/ stiffness, Fever	Non-identified	Non-identified	None	Non-available	None	None	None	12 weeks	Full recovery
Kobayashi et al., 2019[40]	88	Male	Neck pain/ stiffness, Limb paralysis, Fever	Blood	Methicillin-sensitive *Staphylococcus aureus*	None	Anterior space and posterior space	None	None	None	Non-available	Death
Yüceer et al., 2001[41]	72	Male	Neck pain, Limb paralysis	Blood	*Staphylococcus aureus*	None	Anterior space and posterior space	None	None	None	Non-available	Full recovery
Vemireddi et al., 1978[42]	58	Male	Neck stiffness, Limb weakness	Blood	*Staphylococcus aureus*	Non-available	Non-available	None	None	None	Non-available	Neck stiffness

Characteristics of patients with limb weakness

There were 18 (34.0%) patients who had limb weakness and/or paralysis at admission.[2,4-6,8,9,12,13,16,19,23,25,33,40-42] Of these, 10 were male and 8 were female, with an average age of 63.4 years. We found 13/18 (72.2%) patients with limb weakness and/or paralysis to have bacteremia.

Surgical approach and method for UCEA

Of 53 patients,[2-42] 30 received surgical interventions (Table 3).[2-23] Regarding initial surgical procedures, three (5.7%) patients with C1–C2 invasion without abscess received stabilization of the upper cervical spine using posterior instrumentation and fusion. Conversely, 15 (28.3%), 7 (13.2%), and 5 (9.4%) patients with UCEA underwent decompression (C1 and/or C2 laminectomy) and debridement using a transoral anterior approach, transcervical anterior approach, and transcervical posterior approach, respectively. Permanent limb paralysis or death was observed in 1/15 (6.7%) patients who received the transoral approach and in 2/15 (13.3%) patients who received the transcervical approach for UCEA treatment (Table 2). The choice of approach stratified by erosion of the odontoid process and location of the abscess is illustrated in Figure 3. In addition, 15 (28.3%) with odontoid process invasion underwent removal with odontoidectomy and stabilization of the upper cervical spine was performed using posterior instrumentation according to Magerl and/or fusion according to Brooks or Gallie.[4-15] Based on previous studies,[3,5,6,10,13,23]

the complications of each surgical approach are summarized in Table 4. There was no incidence of severe wound infection, aspiration pneumonia, and respiratory failure regardless of surgical approach.

Table 3 Treatment strategy of 53 patients with upper cervical pyogenic epidural abscess

Valuable	Value
Treatment choice, n (%)	
Surgical treatment (Antibiotics + Surgery)	30 (56.6)
Nonsurgical treatment (Antibiotics)	23 (43.4)
Initial surgical procedures, n (%)	
Transcervical posterior approach (instrumentation and fusion)	3 (5.7)
Transoral anterior approach (decompression and debridement)	15 (28.3)
Transcervical anterior approach (decompression and debridement)	7 (13.2)
Transcervical posterior approach (decompression and debridement)	5 (9.4)
Unavailable data	23 (43.4)
Additional surgical procedures, n (%)	
Transcervical posterior approach (instrumentation and fusion)	15 (28.3)
Unavailable data	38 (71.7)
Timing of surgical intervention, n (%)	
Before the onset of paralysis	26 (49.1)
After the onset of paralysis	4 (7.5)
Unavailable data	23 (43.4)
Surgical stage of additional surgery, n (%)	
Single–stage	7 (13.2)
Second–stage	8 (15.1)
Unavailable data	38 (71.7)
Procedure of additional surgery, n (%)	
Magerl	5 (9.4)
Magerl and Brooks or Gallie	10 (18.9)
Unavailable data	38 (71.7)
Indications of surgical intervention, n (%)	
Progressive neurological symptoms due to spinal compression	9 (17.0)
Abscess in the retropharyngeal space	8 (15.1)
Cervical instability due to bone erosion	13 (24.5)
Ineffective conservative treatments	5 (9.4)
Unavailable data	23 (43.4)
Antibiotics, n (%)	
Empirical monotherapy	3 (5.7)
Empirical combination therapy	11 (20.8)
Monotherapy based on susceptibility	10 (18.9)
Combination therapy based on susceptibility	5 (9.4)
Unavailable data	24 (45.3)

Change of antibiotics, n (%)	
Presence	13 (24.5)
Absence	16 (30.2)
Unavailable data	24 (45.3)
Duration of antibiotics in surgical treatment cases, n (%)	
6 weeks	8 (15.1)
8 weeks	3 (5.7)
10 weeks	1 (1.9)
12 weeks	5 (9.4)
>13 weeks	3 (5.7)
Unavailable data	33 (62.3)
Duration of antibiotics in nonsurgical treatment cases, n (%)	
6 weeks	4 (7.5)
8 weeks	1 (1.9)
12 weeks	3 (5.7)
>13 weeks	1 (1.9)
Unavailable data	44 (83.0)
Reasons of antibiotic discontinuation, n (%)	
Image inspections (disappearance of the abscess)	5 (9.4)
Blood test (normalization of inflammatory response)	6 (11.3)
Both image inspections and blood test	2 (3.8)
Unavailable data	40 (75.5)

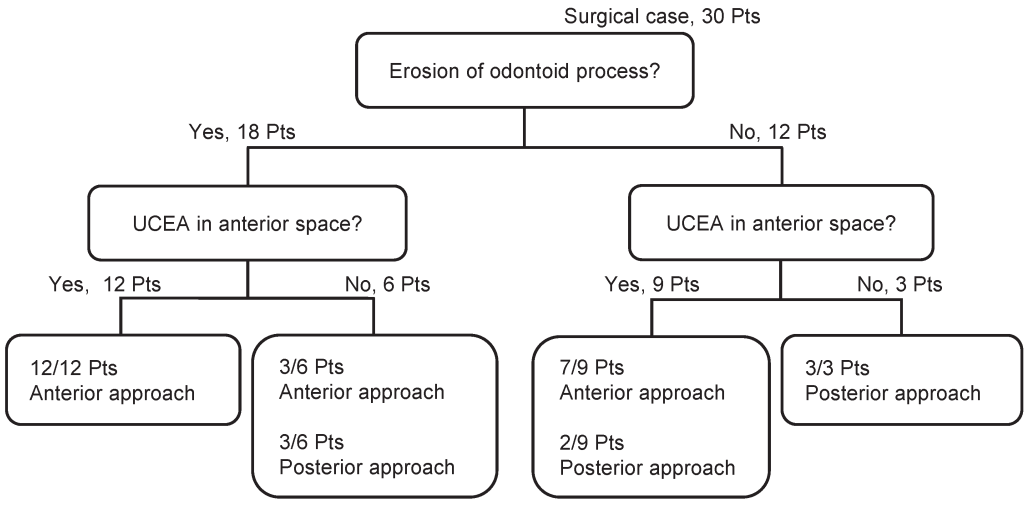

Fig. 3 Initial surgery approach
UCEA: upper cervical epidural abscess
Pts: patients

Table 4 Complications of each approach

Surgical approach	Complications
Transoral anterior approach	• Liquorrhea • Superficial mucosal infection • Laryngopharyngeal edema • Limited jaw mobility • Malocclusion • Dysgeusia • Dysphagia • Eversion of bone graft
Transcervical anterior approach	• Cervical spine injury due to cervical extension • Esophageal • Tracheal injury • Jugular arteriovenous injury • Vertebral artery injury • Recurrent laryngeal nerve injury (right > left) • Dysphagia • Horner syndrome
Transcervical posterior approach	• Vertebral artery injury due to implants • Cervical spine injury due to implants • Venous sinus injury • Dysphagia due to cervical kyphosis • Respiratory failure due to cervical kyphosis • Liquorrhea • Skin disorders on the occipital external protuberance • Limited cervical range of motion due to occipitocervical fusion

Timing of surgical intervention

Of the 53 patients,[2-42] 23 received nonsurgical treatment and 30 received surgical interventions (Table 3). Of the 23 patients who received nonsurgical treatment, 6 presented limb weakness and/or paralysis at admission, and 3/6 (50.0%) patients experienced permanent limb paralysis or death (Table 2). Conversely, 17 did not present limb weakness and paralysis at admission, and no patient experienced permanent limb paralysis or death (Table 2). Of the 30 patients who received surgical interventions, permanent limb paralysis or death was noted in 1/26 (3.8%) patients who underwent surgery before the onset of paralysis and in 2/4 (50.0%) patients who underwent surgery after the onset of paralysis (Table 2). The timing of the surgical intervention was determined by different conditions: (1) progressive limb paralysis and/or respiratory failure due to cervical spinal compression[6-8,10,16,19,22,23]; (2) UCEA in the retropharyngeal space and its associated inflammation spreading through the laryngopharynx[3,6,13-15,17,18,20]; (3) cervical instability due to bone erosion[4-6,9,11,12,17]; and (4) ineffective conservative treatments.[3,6,10,11,21] Focusing on the neurological symptoms, surgical interventions before the onset of limb paralysis in patients with UCEA may be helpful in preventing permanent paralysis or death.

Difference in outcome between single- and second-stage instrumentation and fusion

Of 53 patients,[2-42] 15 underwent additional instrumentation and fusion (Table 3).[2-8,10-12,19] Pedicle screws and rods were placed away from the site of infection or osteomyelitis after complete

debridement of the abscess.[2-23] Permanent limb paralysis or death was noted in 1/7 (14.3%) patients who underwent single-stage instrumentation and fusion at the time of surgical debridement for spinal infection and in 1/8 (12.5%) patients who underwent second-stage instrumentation and fusion after decompression and debridement (Table 2). No patient had to undergo implant removal due to infection after instrumentation and fusion.

Duration of antibiotics

Of 53 patients,[2-42] 20 who received surgical treatments with detailed information were evaluated (Table 3).[3-5,8-18,20-22] We found that 8/20 (40.0%), 3/20 (15.0%), 1/20 (5.0%), 5/20 (25.0%), and 3/20 (15.0%) patients received antibiotics (oral and/or intravenous) for 6, 8, 10, 12, and >13 weeks, respectively. Of 53 patients,[2-42] nine who did not undergo surgical treatments with detailed information were evaluated (Table 3).[25,29,20,34,36-38] We found that 4/9 (44.4%), 1/9 (11.1%), 3/9 (33.3%), and 1/9 (11.1%) patients received antibiotics (oral and/or intravenous) for 6, 8, 12, and >13 weeks, respectively. The disappearance of the abscess on image inspections[14,20-22,30,35] and normalization of inflammatory response in the blood test[8,10,12,17,21,30,31,38] were indications for discontinuation of antibiotic administration.

DISCUSSION

Our literature review recommends surgical interventions before the onset of limb paralysis in patients with UCEA to prevent permanent paralysis or death.[2-23] Conversely, UCEA patients with neck pain and/or stiffness without progressive limb weakness can be sufficiently treated with antibiotics only.[24-42] In perioperative and nonoperative treatments, antibiotic administration (including oral and intravenous) for 6–12 weeks may be generally supported based on the confirmation of reduced inflammatory response[8,10,12,17,21,30,31,38] and/or abscess disappearance on imaging.[14,20-22,30,35]

The most commonly performed surgical approaches and methods for UCEA included transoral decompression and debridement.[10-12,14,15] Subsequently, odontoidectomy was performed to remove the odontoid process, and the upper cervical spine was stabilized with instrumentation and fusion.[2-12] The transoral approach to UCEA is an oral surgical procedure utilizing fluoroscopic- or microscopic-assisted guidance due to the narrow operative field[4-7,10-15]; this approach is indicated in patients with UCEA localized to C1–C2, which is the most commonly involved site.[1-42] In patients with UCEA involving the lower cervical spine (C3–C7), the transcervical approach was chosen because of the wide operative field, whereas the transoral mandibular tongue-splitting approach may be used in patients with UCEA involving lower cervical abscesses with neck stiffness, trachectomy with intubation, and dermatopathy of neck because cervical rotation and hyperextension could not be performed in these patients and the approach may be useful to reach the UCEA directory via the oral cavity.[2-22,44] Our literature review suggests that differences in surgical approaches may not be associated with the incidence of permanent limb paralysis or death, while the choice of surgical approach and methods may be dependent not only on the surgeon's skills but also on the location of UCEA and bone erosion.[2-23]

Multiple surgeries could be an option in the treatment of recurrent UCEA after CT-guided pus drainage[4,5,8,11,15] or cervical instability after debridement and decompression.[2-8,10-12,19] Posterior instrumentation and fusion play an important role in preventing neurologic injury in patients with spinal instability and spinal cord compression.[2-23] Methods of instrumentation and fusion include single- and two-stage instrumentation and fusion (performed from 10 days to 6 months after decompression and debridement). In the present study, no association was seen between the timing of instrumentation and fusion and the incidence of permanent limb paralysis or death.

Thus, the physician may determine whether to perform single- or two-stage instrumentation and fusion according to the condition of the spine and/or spinal infection site.[7,8,44]

In this literature review on UCEA, antibiotic administration (oral and/or intravenous) was discontinued after confirmation of reduced inflammatory response[8,10,12,17,21,30,31,38] and/or abscess disappearance on imaging,[14,20-22,30,35] leading to variation in the duration of antibiotic administration (6–32 weeks). Nevertheless, antibiotics were administered for 6–12 weeks in most cases (85%–89%).[3-5,8,12-15,17,18,20-22,26,30,31,37-39] *S. aureus* and *Streptococcus* species were identified as the main pathogens of UCEA.[1-42] Moreover, there were some studies on UCEA caused by methicillin-resistant *S. aureus*.[5,23] Therefore, we recommend empirical antibiotic therapy targeting these gram-positive species.

The characteristics of UCEA are quite different than those of spinal epidural abscess; the most common risk factors for spinal epidural abscess were found to be diabetes and intravenous drug use,[45,46] whereas our findings demonstrated that those for UCEA with progressive neurological deficits were ageing and bacteremia. Furthermore, the main sources of infection are hematogenous spread and direct inoculation (e.g., recent spinal procedure) in spinal epidural abscess[45] and hematogenous spread and contiguous spread (e.g., otorhinolaryngologic disease and tooth extraction) in UCEA. Therefore, the early diagnosis of UCEA could be made, based on the appearance of neck pain and/or stiffness with the presence of otorhinolaryngologic or oral diseases or bacteremia.

The treatment strategy for UCEA is also different from that for spinal epidural abscess[45,46] at four points. First, surgical procedures for UCEA are related to the oral cavity, occipital bone, odontoid process, and/or atlantoaxial vertebrae. These require advanced surgeon skills. Second, the postoperative course (e.g., ventilator) is complicated particularly in the transoral approach, which is the most commonly performed surgical approach for UCEA.[2-23] Third, the treatment duration for UCEA in most cases (85–89%) is slightly longer than that generally recommended for spinal epidural abscesses and vertebral osteomyelitis (4–8 weeks).[45] This may result in difficulty of treatments for UCEA.[2-23] Lastly, UCEA can lead to more fatal neurological conditions (e.g., permanent limb paralysis and death) than spinal epidural abscess. Therefore, the evidence on the treatment strategy for UCEA independent of spinal epidural abscess is required.

This is a literature review based on other authors publishing UCEA. Therefore, the study is not homogenous and has many limitations. We did not include fungal or tuberculous UCEAs in our study because neither of these infections was identified in the blood culture results of any patient. In cases of infants, symptoms were not sufficient to describe neck pain, limb weakness, dysphagia, and odynophagia in detail. Details of limb weakness and paralysis are unclear because no standard evaluation of symptoms, such as Frankel scale, is used. To the compare surgical procedures, complications and outcomes as well as operative time, hemorrhage volume, and length of hospitalization should be investigated. The sample size was small because UCEA is a relatively rare condition,[1] thus leading to difficulty of investigation by age. Furthermore, medical advances from 1932 to 2019 (e.g., surgical technique and implants, imaging modalities and their interpretations, and conservative treatments including various classes of antibiotics) may influence these results. However, this is the first study to investigate detailed treatment strategies for UCEAs. Due to the nature of literature review, there may be publication bias; cases which are systematically different from results of published cases could be unpublished.[47] However, there is no evidence regarding treatment choice for UCEA, and the case reports were lack of ability to generalize.[47] Our study was not able to elucidate the prognostic factors of treatments for UCEA, as it reviewed the case reports between 1944 and 2019 and the frequency of permanent limb paralysis or death was low (i.e., seven cases[8,16,19,24,25,33,40]). Therefore, further investigations toward this issue are required. As a supplementary information, in 30 cases who

received surgical interventions, we found that patients with permanent limb paralysis or death were older (with, 67.7 ± 3.8 years; without, 54.5 ± 17.2 years; Mann–Whitney's U test, p = 0.005) and received more delayed surgery after the onset of limb paralysis (with, 2/3; without, 2/27; Fisher's exact test, p = 0.039) than those without permanent limb paralysis or death. In contrast, in 23 cases who received nonoperative treatments, there was no significant difference in patient characteristics (e.g., age, sex, comorbidities, bacteremia, and bone erosion) between patients with permanent limb paralysis or death (n = 4) and without permanent limb paralysis or death (n = 19). Further investigations are required.

CONCLUSION

Differences in surgical approaches may not be associated with the incidence of permanent limb paralysis or death. Early surgical intervention before the onset of paralysis seems to be recommended in patients with progressive limb weakness because of UCEA, whereas nonsurgical treatment (antibiotics) may be sufficient in UCEA patients with only neck pain and/or stiffness before appearance of limb weakness. In perioperative and nonoperative treatments, antibiotic administration (including oral and intravenous) for 6–12 weeks may be generally supported based on the confirmation of reduced inflammatory response and/or abscess disappearance on imaging. However, a standard treatment strategy has not been determined for UCEA; therefore, further investigation is necessary.

IRB APPROVAL

A systematic review is not a research that must be approved by the IRB.

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CONFLICT OF INTEREST

The authors declare that there are no conflicts of interest.

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Appendix: Supplementary data

Supplementary data 1 Comparison of patients' demographics, surgical approach, timing of surgical intervention, and additional instrumentation and fusion in surgical cases stratified by neurological outcomes

	With permanent limb paralysis or death (n = 3)	Without permanent limb paralysis or death (n = 27)	p value
Patients' demographics			
Age (years)*	67.7 ± 3.8 (65 to 72)	54.5 ± 17.2 (0 to 75)	0.005
Sex (male:female)	2:1	17:10	1.000
Predisposing factors, n (%)	3 (100)	9 (33.3)	0.054
Bacteremia, n (%)	2 (66.7)	12 (44.4)	0.586
Bone erosion, n (%)	2 (66.7)	21 (77.8)	0.564
Surgical approach			
Transoral, n (%)	1 (33.3)	14 (51.9)	
Transcervical, n (%)	2 (66.7)	13 (48.1)	1.000
Timing of surgical intervention			
Before the onset of paralysis, n (%)	1 (33.3)	25 (92.6)	
After the onset of paralysis, n (%)	2 (66.7)	2 (7.4)	0.039
Additional instrumentation and fusion			
Done, n (%)	2 (66.7)	13 (48.1)	
None, n (%)	1 (33.3)	14 (51.9)	1.000

Predisposing factors included diabetes mellitus, hypertension, chronic renal failure, and Parkinson's disease. Bone erosion included erosion of odontoid process and cervical vertebrae.
The Fisher's exact test was used to compare qualitative data, and Mann–Whitney's U test was used to compare the quantitative data between the two groups.
*Values are expressed as the mean ± standard deviation (range).

Supplementary data 2 Comparison of patients' demographics in nonsurgical cases stratified by the neurological outcomes

	With permanent limb paralysis or death (n = 4)	Without permanent limb paralysis or death (n = 19)	p value
Patients' demographics			
Age (years)*	60.0 ± 20.1 (43 to 88)	37.6 ± 27.0 (0 to 76)	0.107
Sex (male:female)	3:1	13:6	1.000
Predisposing factors, n (%)	3 (75.0)	6 (31.6)	0.260
Bacteremia, n (%)	3 (75.0)	8 (42.1)	0.317
Bone erosion, n (%)	0 (0)	7 (36.8)	0.273

Predisposing factors included diabetes mellitus, hypertension, chronic renal failure, and Parkinson's disease. Bone erosion included erosion of odontoid process and cervical vertebrae.
The Fisher's exact test was used to compare qualitative data, and Mann–Whitney's U test was used to compare the quantitative data between the two groups.
*Values are expressed as the mean ± standard deviation (range).