Oro Facial Orofacial Space Infections in Medically Compromised Patients- A Systematic Review & Meta Analysis

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Abstract:

Introduction: This study reviews our understanding with Orofacial space infections requiring surgical intervention, including cervical necrotizing fasciitis in medically compromised patients. The purpose of the study was to recognize predisposing and aggravating factors of the disease and identify the possible factors that can lead to life-threatening complications and slow down the healing process

Materials and methods: We associate the results to previous data from 1985 to 2005 to discover possible changes and varying trends. The features of four lethal cases are defined. This retrospective analysis comprises patient data from 2005 to 2015 in tertiary referral hospital and in total, 277 patients were seen.

Results: Surgical drainage through a neck opening with/without intraoral incision was made in 215 (77.6%) patients; an intraoral incision was only done in 62 patients (22.4%). ICU care was needed in 66 (23.8%). Odontogenic etiology (44.8%) was the most usual origin. The most common comorbidity was a psychiatric disorder and/or dementia and occurred in 55 (19.9%)

subjects. Patients with underlying illnesses were more likely to be admitted to the ICU (p=0.020), required a longer ICU stay (p=0.004) and repeated surgery (p=0.009). Gas formation seemed to be predictive of a more severe course of infection. Early extraction of the odontogenic foci was connected to a lower length of stay (LOS) (p=0.039).

Conclusion: The yearly numbers have increased from 14 to 24 cases per year when linked to preceding data. OFSIs remain a cause of fatal complications; the mortality was 1.4% and overall complications ensued in 61 (22.0%) patients.

Key words: Facial space infections, medically compromised, review, Odontogenic.

Introduction

Orofacial space infections (OFSIs) are a group of severe bacterial infections in potential spaces and fascial planes of the neck. Abscesses, cellulitis and phlegmons can spread along these fascial planes from the skull base to the mediastinum and lead to serious and potentially lethal complications [1]. Few authors have stated that OFSIs are presently less frequent than in the past [2, 3]. However, the OFSIs remain a constant challenge because of the substantial morbidity and mortality rates [4–8]. From Finland there is evidence that OFSIs have become more prevalent in recent decades [9]. The most common etiology is odontogenic (35-42%) and pharyngotonsillar infections. Other reasons include salivary gland infections, penetrating or blunt trauma, a foreign body, iatrogenic factors such as prior surgery and dental procedures, neoplasm, lymphadenitis and infected cysts. Unidentified etiology varies in the literature and rests around 8-57% of cases [5, 10-12]. OFSIs need prompt and precise management. This comprises managing the oftencompromised airway, adequate antimicrobial therapy, surgical incision and drainage of the abscess, identifying and treating the possible cause (removal of the causal teeth or tonsils) and treatment of complications. Compromised airway, descending mediastinitis, thrombosis of the internal jugular vein, arterial erosion, pneumonia, meningitis and intra-cranial extensions are the potentially lethal complications, especially to immunocompromised patients or patients with comorbidities [7, 11]. The objective of the study is to identify the causes and predisposing factors of OFSIs and identify the possible factors that can lead to severe complications and slow down the healing process. We also validate the changing trends in morbidity, mortality and admissions for OFSIs in our tertiary referral hospital related to previously published data from 1985-2005.

Materials and methods

Present study is a retrospective analysis of clinical data collected from medical records between 1.1.2004 and 30.11.2015. Of the ~2500 patients identified 277 met the inclusion criteria, defined as OFSI requiring surgical treatment, including intraoral or extraoral openings, and admission to a specialized ward or ICU. We excluded peritonsillar abscesses without any complications and the OFSI patients, who were treated conservatively. A review is presented of patient demographics, associated systemic diseases, airway status, treatment, operations, reoperations, and duration of hospitalization, intensive care unit (ICU) days, bacterial cultures, hyperbaric oxygen therapy (HBO), complications, and the outcomes for OFSIs. SPSS ver 24 was used to analyze data by appropriate tools.

Results

Socio-Demographic: A total 277 patients operated for OFSIs were included in this study. Male were majority 64.6%, female =35.4%. Mean age was 42.3 (0.5-92). Significant poor dental status was seen between male and female as well as the odontogenic etiology taken from the patient records.

Comorbidities: Nearly half the subjects had 114 several comorbidities. Comparable comorbidities were seen between genders. Psychiatric disorders and/or dementia was found in 55 (19.9%). 31 (11.2%) were diabetic patients on medication of which 17 (6.1%) patients had insulin treatment. 23 (8.3%) were classified as immunocompromised including patients receiving medications for autoimmune diseases or other known immunodeficiency. Alcohol abuse was mentioned in the patient history of 29 (10.5%) patients. Heart and vascular diseases were reported in 20 (7.2%) of patients. These included coronary artery disease or previous myocardial infraction, congestive heart failure, previous stroke or transient ischemic attack (TIA); however, solitary hypertension was excluded. 11 (4.0%) had malignancy in their patient history. Eight (2.9%) had clinically important liver disease, including hepatitis and cirrhosis. Six (2.2%) patients had a history of intravenous substance abuse. Poor dental status was noted in 101 (36%) of all patients based on status findings and/or dental imaging but was as high as 50.1% (n=28) in the psychiatric/dementia group. The difference was significant (p=0.013). Odontogenic etiology in the psychiatric/dementia group was increased (54.5%), however, it was statistically not significant (p=0.091). As expected in the whole odontogenic subgroup poor dental status was noted in 73 (59%) cases (p=0.000). Table-1 Etiology: An odontogenic source was the most common reason for OFSI accounting for 124 (44.8%) of the cases. 20(16.1% of the odontogenic) patients had dental surgery afore admission to the hospital. The second common etiology was of a pharyngeal or tonsillar origin 104 (37.5%). The other sources were lymphadenitis in 12 (4.3%) and sialadenitis, neoplasm, infected cyst accounting for four cases (1.4%) each. 2 (0.7%) penetrating trauma to the cervical region, an otogenic infection (0.4%), a foreign body (0.4%)and a post-operative infection (0.4%) were identified. The source of the infection was not determined in 20 (7.2%) cases.

Diagnosis and treatment: Diagnosis of OFSI was based upon a thorough otorhinolaryngological examination typically together with fiberoptic nasopharyngoscopy and imaging. In cases of odontogenic foci, an oral and maxillofacial surgeon was consulted. Orthopantomography (OPG) was carried out on 147 (53.1%) patients. The most common imaging technique was a contrastenhanced computer tomography (CECT) of the neck, which was directed on 174 patients (62.8%). The initial CECT comprised the mediastinum when a descending infection was alleged. Magnetic resonance imaging was obtained from 37 (13.4%) patients and five patients underwent both imaging examinations. Ultrasonography was used on 11 (4.0%) patients. 37 (13.4%) patients were treated only with an OPG and seven patients (2.5%) were treated using no imaging examinations; in these cases, diagnosis of OFSI was made by a clinical examination and a surgical exploration. Airway management is crucial when treating Orofacial space infections. 36 patients (13.0%) needed a tracheostomy. A wide spectrum of intravenous empirical antimicrobial therapy was given to all patients and it was later stated according to microbiological findings and drug sensitivity tests. Cervical incision and surgical drainage with/ without intraoral incision and removal of necrotic tissue were made in 215 (77.6%) patients and an intraoral incision in 62 (22.4%). Tonsillectomy was done in 63 cases (22.7%). Dental extraction was made in 93 (33.6%) cases at the referral hospital and overall to 113 (40.8%) of the patients and to 100

patients (80.6%) (p< 0.000) in the odontogenic subgroup. It is notable that the length of stay was significantly reduced from a median of 7 days to 5 days (p = 0.039) when extraction was made simultaneously (same day) with the incision and drainage compared to those with delayed extraction (range 1—9 days). However, the differences in complications (p = 0.153), the need for ICU (p = 0.105) or ICU stay days (p = 0.223) were not distinguished between early and late extraction. 47 patients (17.0%) had revision surgery through neck opening(s) and seven (2.5%) patients also needed mediastinal canalization or thoracotomy. In the subgroup analysis, the odontogenic group was more likely to need repeated surgery (p = 0.022) as well as the patients with comorbidity (p=0.009). The mean overall LOS (n-260) in our tertiary referral center was 8.5 days, median 6.00 days (range 2-114 days, SD 10.1). The data of 17 (6.1%) patients were missing because of their transfer to another hospital. 1-36 days, SD 7.4). Patients with underlying illnesses were more likely to be admitted to the ICU (p = 0.020) and had a longer ICU stay, their median days being 2 vs. 7 (p= 0.004). Diabetic patients had an overall longer hospital stay with a median of eight days (range 2-48 days, SD 13.0) and a stay of over 6 days (all patients' median) occurred more frequently. There was a significant difference between diabetic and non-diabetic patients (p = 0.040). Similarly, ICU treatment was needed more frequently for diabetic patients (n = 16; 51.6%; p < 0.000). HBO therapy was mainly used once a day (except twice for two patients) as an adjuvant therapy for 42 (15.2%) patients during the intensive care period with a median of 6 days (range 1-15 days). HBO treatment was begun immediately (at least within 24 h) after initial surgery in 23 (54.89c; range 0-12 days) of the cases.

Complications: Complications occurred in 61 (22.09) patients and are specified in Table 2. 18 (6.5 â) patients developed necrotizing fasciitis (NF) which is a rapidly progressing fulminant complication. NF was defined as a severe soft tissue infection (need for ICU treatment) with intense pain being mentioned or gas between the fascial layers; in all cases clinically confirmed necrotic tissue was found during surgery. Descending mediastinitis was diagnosed in 12 (4.3%) patients and 7 patients needed operations involving mediastinum. Two patients needed repeated thoracic surgery in addition to neck revisions to control the infection. However, all except one of the patients who arrived in an exceedingly advanced stage, suffering from mediastinitis, survived and were discharged from the hospital. HBO treatment was used in nine mediastinitis patients (75.0%). Of all the OFSI patients, 18 (6.5%) had multiple complications, nevertheless most of the patients 216 (78.0%) recovered without aggravating factors. The mortality rate was 1.4%. Comorbidities were associated with increased mortality (p = 0.015). In these cases, infection was primarily advanced and involved multiple spaces. Three of the cases were categorized as NF. Two were of odontogenic origin and two pharyngotonsillar. The complication rate among diabetic patients was slightly augmented being 32.3% when compared to nondiabetics (20.7%) but it was statistically insignificant (p=0.144). Patients with a (former) malignancy had complications more frequently (n = 8; 72.7%; p < 0.000). All patients having comorbidities seemed not to have associations with complications (p = 0.131). However, taking merely the somatic underlying illnesses into account (excl. psychiatric and dementia subgroup), there was a significant connection to complications (p = 0.048). Gas formation was noted in 41 (14.8%) patients in the radiological investigations. It was associated with higher a complication rate 46.3% (p other viridans group streptococci 25 (13.0%) were the most frequent findings. Streptococcus anginosus, constellatus and intermedius are part of the anginosus group streptocci (formerly known as the Streptococcus milleri group) and were involved altogether in 35.8% (n = 69) of the cases. Staphylococcus aureus was found in 22 (11.4%) of the cases. Comparison

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to previously published data from our institute In 2008, Aitasalo published a review of 293 patients of OFSIs in Turku University Hospital between 1985 and 2005 [13]. To conduct a relevant evaluation, we excluded the years 2004–2005 from our current data. In total, 293 patients were analyzed in the former study.

Comparison and characteristics are presented in Table 4. A 168 (57%) of the patients were male and 125 (43%) female. Age distribution was 4–91 years, mean 38.5 years. Patients were significantly older in the present study (mean 43.3 years; p<0.000). Bacterial samples from surgery were available for 226 (8 1.69) patients. 33 (14.69) of the 226 had negative cultures and 193 (85.4â) had positive culture results for one or several bacteria. The most frequent bacterial organisms are presented in Table 3. Polymicrobial growth was present in 59.69 (n — 115) of the positive cultures. Most common pathogens to involve were Streptococcus species n — 123 (63.7 fi). Prevotella species were found in 70 (36.39%) of the positive cultures but interestingly only in one (0.5 9) case was it the only pathogen identified. Streptococcus an ginosus (n = 31) and an unspecified anginosus group streptococci (n- 7) accounted together for 19.7 â of the bacteria, the Fusobacterium species 29 (15.0 %), Streptococcus constellatus 21 (10.99) and the other viridans group streptococci 25 (13.0â) were the most frequent findings. Streptococcus anginosus, constellatus and intermedius are part of the anginosu s group streptocci (formerly known as the Streptococcus milleri group) and were involved altogether in 35.8 % (n-69) of the cases. Staphylococcus aureus was found in 22 (11.4%) of the cases.

Comorbidity	No. patients (= 227)	%
Psychiatric diagnosis or dementia	55	19.9
Diabetes	31	11.2
Alcohol< 1 abuse	29	10.5
immunocompromised	23	8.3
Heart and vascular disease	20	7.2
Malignancy (previous)	11	4.0
Liver disease	8	2.9
I.v. substance abuse	6	2.2
One or several comorbidity	114	41.2
Healthy	163	58.8

Table 1: Comorbidities of patients with deep neck infections

 Table 2: Complications of deep neck space infections

Complication $(n = 277)$	No. patients	%
Necrotizing fasciitis	18	6.5
Pneumonia	16	5.8
Sepsis (blood culture positive)	13	4.7
Mediastinitis	12	4.3

Neural damage	12	4.3
Internal jugular vein thrombosis	6	2.2
Total airway obstruction	4	1.4
Death	4	1.4
Orocutaneus fistula	3	1.1
Disseminated intravascular coagulation	2	0.7
latrogenic tracheal stenosis	2	0.7
Delirium	1	0.4
Pulmonary embolism	1	0.4

Table 3: Ten most common results in positive bacterial cultures

Bacterial cultures	No. cases	%
Prevotella species	70	36.3
Streptococcus anginosus and unspecified anginosus	38	19.7
Fusobacterium species	29	15.0
Viridans group streptococci'	25	13.0
Staph5lococcus aureus	22	11.4
Streptococcus constellatus	21	10.9
Streptococcus pyogenes	15	7.9
Streptococcus betuhaemol yiicus non A	14	7.3
Streplococcus iiiierinedius	10	5.2
Profiionihoc'terium oc ne.s'	8	4.1
Unspecified polymicrobial growth	29	15.0

Table 4: Characteristics of deep neck infections in two time periods

	1985–2005	%	2006–2015	%	p value
Patients (n)	293		239		
Male	168	57.3	152	63.6	0.142
Female	125	42.7	87	36.4	0.142
Patients/year/mean	14	24 (15-32)			
Age distribution(mean)	38.5				0.000
Age distribution(range)	4.0-91				
ICU treatment	61	20.8	58	24.3	0.342
HBO treatment	36	12.3	41	17.2	0.112
Complications	42	14.3	55	23.0	0.009
Comorbidity	51	17.4	103	43.1	0.000
Mortality	0	0.0	4	17	0.040

Etiology					
Odontogenic	64	21.8	101	42 3	0.000
Prev. dental surgery	32	10.9	16	6.7	0.091
Pharyngotonsillar	69	23.5	92	38.5	0.000
Unknown	54	18.4	16	6.7	0.000
Space infected					
Parapharyngeal	114	39	46	19.2	0.000
Submandibular	82	28	72	30.1	0.588
Retropharyngeal	32	_	-	1 2.6	0.560
Multilocular	_	-	_	15.5	

Discussion

We found OFSIs to be an increasing burden on the health care system. In this article, we presented an analysis of 277 OFSI patients requiring surgical treatment. OFSIs can be mostly well managed in adults with intravenous antimicrobial therapy often combined with the timely incision and drainage [1, 6, and 11]. A widespread progression can be prevented with an efficient treatment which also includes airway control. Due to the complex anatomy of the neck, surgical treatment tends to be challenging. Additionally, in present study, severe and lethal complications did occur and associated systemic disorders were shown to aggravate the disease. The male predominance of OFSI patients has been documented in many studies but the underlying cause remains unclear [5, 7, 8, 11, 14]. The distribution of 64.6% males in this study was in concordance with these previous findings. The males in the study population were associated with both poor dental status and odontogenic etiology which in part could explain the increased morbidity. The median hospitalization (LOS) was 6 days (mean 8.5). A comparable LOS, a median of 7 days was reported by Tapiovaara et al. 2017, in surgically treated OFSIs [12]. A mean LOS of 9.5 days was reported by Parhiscar et al. 2001, 13 days by Huang et al. 2004, and 13.1 days by Ridder et al. 2005 [3, 5, 14]. Early extraction combined with incision and drainage accompanied by antibiotics can be considered as the mainstay of treatment when managing odontogenic infections [15, 16]. The presented results show that the overall hospital stay was significantly reduced when extraction was made immediately (same day) as the incision and drainage, compared to those with delayed extraction. Comparable results were reported recently by Heim et al. 2019, concluding that immediate removal of the focus tooth is the best approach to achieve the lowest LOS [17]. According to this study, a psychiatric disorder or dementia (19.9%) can be observed as a significant comorbidity in patients suffering from OFSIs. In 2009, Daramola et al. reported a 10.4% rate for psychiatric illnesses [18]. In this subgroup, the majority of infections (54.5%) were odontogenic. This might be due to poor commitment to dental hygiene. Kisely et al. 2016 demonstrated an association between poor oral health and psychiatric morbidity in a meta-analysis of 334,503 patients [19]. Similarly, dementia has been strongly linked to oral health problems [20]. Diabetes is a well described risk factor for OFSIs [5, 11, 18]. In the present study, we confirmed that the median overall LOS (6 days) was more often exceeded by diabetic patients and significantly more ICU treatment was needed. These diabetic patients were more likely to need repeated surgery, although the complication rate was not substantially different. Furthermore, all somatic comorbidities (excluding psychiatric and dementia) had an association with complications and the need for repeated surgery. Gas formation has traditionally been a sign of fulminant and rapidly progressive infections such as

necrotizing fasciitis, which is present in 56.39% of the cases of cervical NF in recent metaanalysis [21, 22]. Additionally, with odontogenic infections, crepitus was described as a sign of severity by Alotaibi et al. 2015 [23]. In our study, 15 (83.3%) of the NF cases presented gas formation as well as 10.2% (n=26) of the OFSIs others than NF. We confirmed that gas formation was linked to a more severe course with a higher complication rate, increased mortality, longer hospitalization and both increased ICU treatment and a longer ICU stay; this was also true for OFSIs not diagnosed as NF. Lin et al. 2014 stated that gas formation detected on CT scans of OFSIs was a sign of anaerobic pathogens and a higher complication rate [24]. As of the retrospective nature of our study, it is likely that some cases of true NFs were miscategorized using a strict criteria of necrosis during surgery and although that might increase the difference, it is unlikely to alter all the results representing a more severe course. OFSIs continue to cause significant morbidity and mortality. We found 22% suffering complications and 1.4% mortality. Numerous other authors have reported comparable statistics, such as 18% had complications and a mortality rate 0.3% by Boscolo-Rizzo 2012, 16.2% and 1.6% by Huang 2004, 27.5% and 2.6% by Ridder 2005 [5, 11, 14]. Nevertheless, the differences in complications reported are present and should be noted. In this study, it is likely that excluding conservatively treated OFSIs and including necrotizing fasciitis, we have created a bias towards analyzing infections with a more severe course. The advantage of HBO treatment as an adjuvant in cervical necrotizing infections is unsolved [25-29]. Descending mediastinitis can still be deliberated a highly life-threatening condition having a reported mortality rate varying from 0 to 40%, being overall 17.5% in the latest systematic review of 84 patients by Prado-Calleros 2016 [5, 22, 30-33]. In the present series 11 out of 12 mediastinitis patients lived, resulting in an 8.3% mortality rate. HBO therapy was utilized in nine cases (75%) and was started immediately (at least within 24 h) after surgery in most cases (n=7/9). Shaw et al. 2014 settled that HBO treatment can be beneficial especially for those patients who were very ill with necrotizing soft tissue infections [29]. HBO treatment could be beneficial with the most severe cases of OFSIs, such as mediastinitis, when seeing our results of mediastinitis survival, although a need for a larger and case-controlled series is evident. We established Streptococcus species in 63.7% of the cases and these have been widely reported in earlier studies [5, 7, 8, 11, 14]. The Streptococcus anginosus group (35.8%) has been shown to be a vital pathogen in the head and neck area causing locally extensive infections and a metastatic spread of infection [34]. Anaerobic Prevotella 870 European Archives of Oto-Rhino-Laryngology (2020) 277:863-872 1 3 species were involved in one third (36.3%) of all cases. In 1994, Shinzato et al. showed in a mouse model that the Streptococcus anginosus (former milleri) group in synergy with Prevotella intermedia produced a more severe pneumonia and increased mortality [35]. This synergy is possibly present in the pathogenesis of OFSIs and should be further inspected. Possible changes in the antibiotic susceptibility could contribute to more severe course of infection, though the specific analysis on sensitivities was lacking. In odontogenic infections, sensitivity rate for penicillin is reported high (87.1–100%) for these viridans streptococcal species [36, 37]. But, bacteria presenting low susceptibility to one or more of the standard antibiotic therapy regimes, have been shown to cause spreading infections and increased need and longer stay for inpatient treatment [36-38]. According to the present evaluation the incidence of OFSIs is not decreasing. The annual numbers have risen from 14 to 24 cases per year. Odontogenic etiology was the predominant cause of these infections in this study and we demonstrated a clear increase compared to previous decades. Seppänen et al. 2010 found alike upwards trend in Helsinki, Finland, Thomas et al. 2008 in UK national data, and Bottin 2003 in Italy [9, 10, 39]. Patients were considerably

older in the present study which could be a result of the ageing population in general. Age has been shown to be a risk factor for OFSIs [7, 40]. Additionally, considering the aging population, more patients are having full dentition until the last years of life. Fu et al. 2018 stated that admissions to ICU for OFSIs were rising [41]. We found increasing tendency between two cohorts (20.8–24.3%) but the difference did not reach statistical significance. Seppänen et al. 2010 stated odontogenic maxillofacial infections had become more severe over a 10-year period and patients with underlying diseases had increased in their latest cohort [9]. Comorbidities were significantly increased in our recent data. The results could be due to dissimilarities in noted comorbidities but nevertheless patients were significantly older and potentially more morbid. Furthermore, the complication rate was significantly greater in the present series. One reason for the higher percentage might be the wider scale of complications noted from the patient data. Mortality was increased from 0 to 1.7% because of four lethal cases occurring during the latest decade. Increasing incidence and intermittent probability might partially explain that rise, but finding the causes of growing mortality should trigger further studies. All these trends highlight the growing complexity of OFSIs and should emphasize further development of efficient management and treatment protocols. The most common etiologies were odontogenic and pharyngotonsillar in the present and relative cohorts although the proportion had significantly increased in the recent group. This finding is in concordance with earlier reports [5, 7, 10]. The unknown etiologies were reduced in the latest data and this might be due to the strict diagnostics or a more detailed data collection. An OPG was obtained (53.1%) to identify dental foci, which is more frequent compared to previous reports from Staferi 2014 (36.5%) and Bottin 2003 (43%) [10, 42]. In the odontogenic subgroup an OPG was available in 79.7% of the cases. In the remaining 20.3%, dental imaging was possibly obtained from nonelectric versions in earlier visits by or information from CT scans was used. As earlier stated by several writers parapharyngeal, submandibular and retropharyngeal spaces were those most commonly involved in both groups [5, 7, 10]. Although multilocular involvement was not mentioned in the previous data which can have affected the exact proportions. The limits of the present study are acknowledged and mostly due to the retrospective nature of the analysis. The lack of comparable detailed data from previous decades weakened the analysis in this respect.

Conclusion

In our study an increasing trend was noted for the OFSIs. Oral health problems, and furthermore, odontogenic infections are a growing challenge. Early dental intervention is advocated to prevent complication. OFSIs continue to cause fatal complications and provoking comorbidities need to be accounted. Gas formation is predictive of worse prognosis that needs hospital admission. HBO therapy as an adjuvant might be helpful in most severe cases such as descending mediastinitis. Timely recognition and speedy management are vital to prevent sequelae.

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