B-ENT, 2018, **15**, 233-237

Recurrent neonatal suppurative submandibular sialadenitis: a case report

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Key-words. Sialadenitis, submandibular gland, infant, premature, soft tissue infections, suppuration.

Abstract. *Recurrent neonatal suppurative submandibular sialadenitis: a case report*. *Case report:* We describe a case of a premature infant born at 28 1/7 weeks of gestation who, 12 days after birth, developed a submandibular inflammatory mass with exudation of pus into the oral cavity. The growth of Staphylococcus aureus in the culture confirmed a diagnosis of submandibular sialadenitis. The symptoms rapidly improved under antibiotic therapy. The infection recurred on day 25, also with exudation of pus into the oral cavity. This time the culture showed the growth of Enterococcus faecalis. The symptoms resolved in response to antibiotic therapy.
Review of the literature: To date, 25 newborns with suppurative submandibular sialadenitis have been reported in the English language literature. To our knowledge, this is the first description of a recurrence.
Conclusion: Although neonatal suppurative submandibular sialadenitis is rare, this case report and literature review highlight the importance of prompt diagnosis and treatment.

Introduction

Neonatal suppurative submandibular sialadenitis is a rare condition in neonates that was first described in 1950.[1] It is defined by swelling in the submandibular area with the exudation of pus by the Wharton duct and the growth of a pathogen in the culture of pus, most commonly Staphylococcus aureus.[2] Prompt antibiotic treatment is essential, but there is no consensus regarding antibiotic type or treatment duration. Here we describe this case and discuss previous reports plus the etiology, diagnosis, and treatment of this condition.

Case report

A male neonate was delivered at 28 1/7 weeks of gestation by emergent caesarian section due to intractable labor. His initial clinical course was stable apart from respiratory distress syndrome that required surfactant and non-invasive respiratory support. When he was 12 days old, the infant developed a 4 cm × 2 cm inflammatory submandibular mass on the right side that was firm and tender to palpation. Pus was observed in the oral cavity (Figures 1 and 2). His hemoglobin level was 11.6 g/dl, the total white blood cell count was 25,100/mm3, and the C-reactive protein level was 48 mg/l. Blood cultures were negative. Empirical

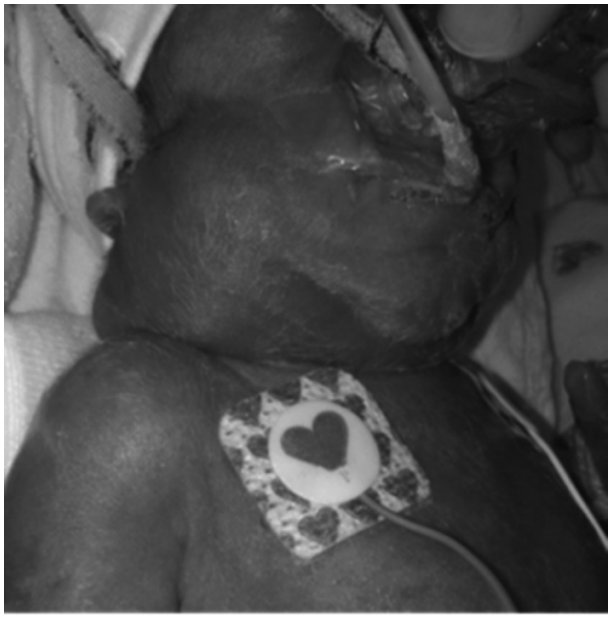

Figure 1
First episode day 1.

Funding: No funding was received.

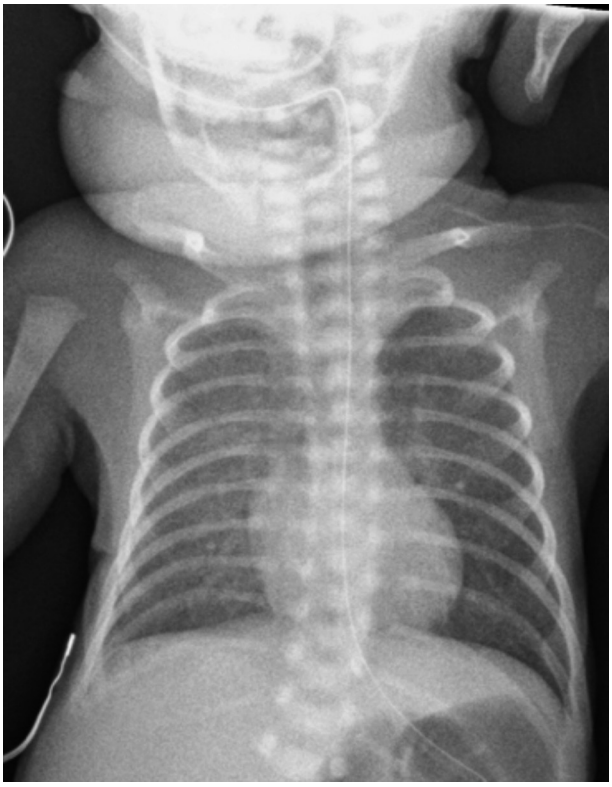

Figure 2
First episode day 1 — X-ray.

antibiotic therapy was initiated according to our local protocol using cefotaxime (25 mg/kg/dose Q6H), oxacillin (charge dose, 50 mg/kg, then 25 mg/kg/dose Q6H), and amikacin (20 mg/kg, 1 dose/42 h). The swelling resolved rapidly. S. aureus was identified in the culture of pus and in maternal milk, and cefotaxime and amikacin were withdrawn based on the antibiogram. An ultrasound performed two days later showed no significant enlargement of the gland. Treatment with oxacillin was continued for 7 days.

On day 25, the infant was evaluated for recurrent apneic episodes. Clinical examination revealed painful palpation of the mandibular region without noticeable swelling and general signs of sepsis. The infant required immediate intubation, and yellowish and malodorous secretions appeared in the oral cavity during laryngoscopy. Investigation showed a hemoglobin level of 11.7 g/dl, a total white blood cell count of 19,900/mm3, and a C-reactive protein level of 80 mg/l. Blood cultures remained negative. Ampicillin and vancomycin-sensitive Enterococcus faecalis was found in the cultures of oral secretions, gastric liquid, and (on day 5 of the second infection) in maternal milk. S. aureus was not found in the cultures, making it unlikely that this was a local recurrence of the previous infection. Nevertheless, there was still a question of whether the oxacillin treatment duration was adequate.

Antibiotic therapy was initiated with vancomycin (10 mg/kg/dose Q8H) and cefotaxime (25 mg/kg/dose Q6H) with a good outcome. A specialized ear-nose-throat (ENT) examination did not find underlying salivary gland problems. The rapid resolution of this second episode made additional assessment unnecessary. Treatment was continued for 10 days. The rest of the infant's stay in the neonatal intensive care unit and the ENT follow-up when he was 3 years old were unremarkable.

Discussion

This description of two episodes of submandibular sialadenitis in the same patient prompted us to review previous reports of salivary gland infections in newborns. Submandibular sialadenitis has mainly been described as a complication of parotitis,[3,4] but here we focus on isolated submandibular sialadenitis. Some variables have been identified that have strong associations with suppurative submandibular sialadenitis (Table 1). Prematurity appears to be the most important risk factor,[3,4] which was confirmed in our literature review (73% of cases). The other identified risk factors are linked to prematurity: immunological immaturity, low birth weight (46% in infants <1500 g at birth), dehydration, and tube feeding (56%). Tube feeding is associated with an increased risk of dehydration and with salivary duct stasis as well as with an increased risk of oral lesions.[2,3,4] Investigation may find contaminated milk,[2] highlighting the need for careful handling and storage of maternal milk. Submandibular sialadenitis predominantly affects males (70%),[6] and the age at presentation ranges from 1 to 8 weeks, with a median of 12 days.

The diagnosis is clinical, and the definition of suppurative submandibular sialadenitis includes swelling in the submandibular area with exudation of pus via the Wharton duct and the growth of a pathogen in the culture of pus.[2] The infection is unilateral in 79% of cases and is right-sided in 74%. The total white blood cell count is >15,000/mm3 in 74% of patients. No link has been found with previous infections, with only 38% of cases concerned. The most frequent causal microorganism

Table 1

Author	Year of publication	n	Gender	Gestational age (weeks)	Birth weight (grams)	Previous infectious context	Age (days)	Side	Type of feeds	WBC (/mm3)	Blood culture	Pathogen	Antibiotic treatment Monotherapy	Bitherapy or tritherapy	Duration (days)	Incision/ drainage
Shulman	1950	1	M	T	NR	/	21	R	Breast	24600	NR	Staphylococcus Aureus	Antistaphylococcal	/	7	No
Wells	1975	2	M	32,5	1300	/	14	NR	Tube	13500	neg	Staphylococcus Aureus	Antistaphylococcal	/	7	Yes
		3	NR	35	1870	/	6	R	Tube	18500	neg	Staphylococcus Aureus	Antistaphylococcal	/	7	No
		4	F	31	1360	Maternal fever	6	NR	NR	NR	neg	Staphylococcus Aureus	Antistaphylococcal	/	7	No
Banks	1980	5	F	34	2350	PRM	21	R	Bottle	18000	neg	Staphylococcus Aureus	Antistaphylococcal	/	7	Yes
Ungkanont	1998	6	M	34	2290	/	8	R>L	Tube	14380	neg	Pseudomonas aeruginosa	3rd gen cephalo ←	Antistaph + aminoglycoside	21	No
Bafakeeh	1998	7	M	T	3100	/	7	R	Bottle	33500	neg	Staphylococcus Aureus	2nd gen cephalo	/	11	Yes
Subhani	1999	8	F	25	720	BC positive for SA	59	R/L	Tube	50000	neg	Staphylococcus Aureus	/	Vanco + clindamycin + 3rd gen cephalo	15	Yes
Bova	2000	9	F	T	3600	/	8	R	NR	20000	NR	Staphylococcus Aureus	/	Antistaphylococcal + clindamycin	3	Yes
Takahashi	2000	10	M	32	1815	/	7	R>L	Tube	14500	NR	MRSA	Vancomycin	/	NR	No
		11	M	32	1560	SMFI	12	L	NR	27000	NR	MRSA	Vancomycin	/	7	No
Salaria	2001	12	M	30	1300	/	10	R	Breast	NR	neg	Staphylococcus Aureus	3rd gen cephalo ←	3rd gen cephalo + aminoglycoside	14	Yes
Garavello	2002	13	F	30	1010	/	10	R	Tube	21000	neg	Staphylococcus Aureus	3rd gen cephalo →	3rd gen cephalo + vancomycin	8	No
De Haan	2003	14	M	27	1100	Maternal fever	29	L	Tube	6600	neg	Staphylococcus Aureus	Antistaphylococcal ←	3rd gen cephalo + vancomycin	10	No
Edwards	2003	15	NR	29	980	SMFI	18	L	NR	12400	neg	Staphylococcus Aureus	/	Vancomycin + aminoglycoside	NR	No
Singh	2004	16	M	35	830	/	40	R	Tube	14500	neg	Staphylococcus Aureus	Vancomycin	/	10	Yes
Weibel	2005	17	M	T	3910	/	10	L	Breast	20500	neg	Staphylococcus Aureus	/	Antistaphylococcal + aminoglycoside	10	No
		18	M	T	3840	/	13	R	Breast	23000	neg	Staphylococcus Aureus	/	Antistaphylococcal + aminoglycoside	16	Yes
Mc Adams	2005	19	F	26	900	PRM	32	L	Tube	27600	pos	MRSA	/	Vanco + aminoglycoside + clindamycin	21	Yes
Tapisiz	2009	20	F	36	2575	/	17	R	Breast	19000	neg	Staphylococcus Aureus	/	Antistaphylococcal + aminoglycoside	9	No
Uçkun	2010	21	M	T	3147	NR	14	NR	Breast	23000	neg	Staphylococcus Aureus	3rd gen cephalo	/	9	No
Tho	2011	22	M	29	1445	PRM	56	L	Tube	NR	neg	Staphylococcus Aureus	/	Antistaphylococcal + aminoglycoside	7	Yes
Pathak	2013	23	M	36	2500	/	12	R	Breast	34100	NR	Staphylococcus Aureus	/	Vancomycin + piperacillin/tazobactam	14	No
Pereira	2014	24	M	33	1350	Sepsis	11	R	Tube	17700	neg	SA/Klebsiella Pneumoniae	/	Vancomycin + aminoglycoside	15	No
Ryan	2015	25	M	T	NR	/	20	R/L	Bottle	NR	neg	Staphylococcus Aureus	/	3rd gen cephalo + flucloxacillin	7	No
Present case	2018	26	M	28	1200	/	12	R	Tube	25100	neg	Staphylococcus Aureus	/	Antistaph + aminogl + 3rd gen cephalo	7	No
						Previous episode	25	R/L	Tube	19900	neg	Entero faecalis	/	Vancomycin + 3rd gen cephalo	10	No
Total (%)		26	70% M	73% < 37W	46% < 1500g	38%	Median: 13	74% R	56% tube	74% > 15000	5% pos	92% Staph Aureus	40% → 48%	60% → 52%	Median: 9	37%

M : male, F : female, NR : not reported, T : term, PRM : premature rupture of membranes, BC : blood culture, SA : Staphylococcus Aureus, SMFI: suspicion of materno-fetal infection, R: right, L: left, WBC: white blood cells, MRSA: methicillin resistant Staphylococcus Aureus

by far is S. aureus (92%), and methicillin-resistant S. aureus (MRSA) has been reported in three cases.[4,5] Other pathogens have also been reported, including Pseudomonas aeruginosa[6] and Klebsiella pneumoniae.[7] This is the first reported case to involve E. faecalis. In most patients (95%), the blood cultures remain sterile. Submandibular gland abscess was described for the first time in 2000,[8] and 37% of the cases in the English literature needed incision and drainage (Table 1).

Although the condition is usually easy to recognize, the differential diagnoses include parotitis, submandibular lymphadenitis, cellulitis, and subcutaneous fat necrosis as well as (less often) congenital conditions such as lymphangiomas, dermoid cysts, or even tumors, although these are rarely associated with inflammation.[7,9] The possible workup includes ultrasound and, if needed, computed tomography (CT) and specialized ENT examination. Ultrasound is the most useful non-invasive tool. Ultrasound may show enlargement of the gland with hypervascularization and edema, the presence of sialolithiasis, and it may differentiate between lymphadenitis and congenital malformation.[9] Ultrasound should be repeated if there is no improvement after 24 to 48 hours of antibiotics to exclude abscess formation.[7]

Contrast-enhanced CT should be considered in more complex situations as a complementary tool for abscess evaluation or to monitor a situation that is difficult to manage with antibiotic therapy with or without incision and drainage. Contrast-enhanced CT can also identify duct stricture, anatomic deformity of the oral cavity, congenital cyst, calculi, or congenital sialectasis.[10] However, in order to avoid radiation exposure, it is rarely performed in the neonatal period for conditions that are easily treatable with adequate antibiotic therapy. Magnetic resonance imaging (MRI) may further refine the diagnosis, but its use is limited by cost and availability. Consultation with an ENT specialist may be appropriate when an anatomical anomaly is suspected based on imaging modalities in order to optimize management of this condition.

When considering salivary gland infections, submandibular sialadenitis is less frequent than parotitis. Notably, submandibular sialadenitis shows mixed serous and mucous secretion with bacteriostatic properties and contains IgA and lysozyme. Stasis of secretions may predispose to infection, while a longer duct with ascending course may predispose to stone formation.[4] Table 2 shows the main differences between these infections.[11,12] Notably, prematurity is less prevalent in parotitis case reports (25%–38% versus 73%), the blood culture is positive in 35% of cases of parotitis compared to in 5% of cases of submandibular sialadenitis, and S. aureus is frequently found in parotitis but is found less often than in submandibular sialadenitis (56%–69% versus 92%).

Table 2

	Parotitis [11,12]	Submandibular sialadenitis
Prematurity	25-32%	73%
Male Gender	77-87%	70%
Age (weeks)	2-4	1-8
Tube feeding	NR	56%
Positive Blood culture	35%	5%
Staphylococcus Aureus	61-69%	92%
Incision or drainage	6-23%	37%

Antibiotic therapy is the cornerstone of treatment, but antibiotic type and adequate duration have yet to be determined. Given the strong preponderance of S. aureus, the combination of an antistaphylococcal and an aminoglycoside seems to be the most suitable empiric therapy. Caution must be taken concerning MRSA[4,5] in the context of vancomycin or clindamycin use. On the other hand, suppurative sialadenitis and parotid abscesses have been reported that were positive for Branhamella catarrhalis, Streptococci, Escherichia coli, and K. pneumoniae, so adequate antibiotic therapy should cover both gram-positive and gram-negative strains.[13] Various combinations of antibiotics have been described in the literature (Table 1). First-line treatment is typically either an antistaphylococcal, a third-generation cephalosporin, or vancomycin. Aminoglycosides or clindamycin are generally chosen for use in combination therapy. The total duration of treatment is generally 3 to 21 days (median, 9 days), and there is no consensus regarding anti-infectious management. In the case described here, it remains unclear whether the second episode was due to the rapid withdrawal of cefotaxime and amikacin based on the S. aureus antibiogram. Few other reports narrowed the spectrum so quickly to synthetic antistaphylococcal penicillin monotherapy. However, targeted treatment remains

the standard of care to mitigate the continuing emergence of multidrug-resistant bacteria.

Gentle massage of the swelling may be performed initially to obtain a bacterial specimen, but this should be avoided subsequently to prevent septicemia.[10] On the other hand, incision and drainage may be necessary when an abscess has formed or if no improvement is noted within 48–72 h of starting antibiotic therapy[10] (37%). Adequate hydration is mandatory. Indeed, it has been suggested that stasis of secretion predisposes to infection. The high proportion of premature infants that have a correlated risk of dehydration supports this hypothesis. Moreover, stasis also predisposes to the formation of stones.

The prognosis of submandibular sialadenitis is usually good, and no local or general complications have been reported in the last 60 years. This is, to our knowledge, the first description of a recurrence after antibiotic therapy. The patient rapidly improved, the outcome was good, and there was no underlying anatomical anomaly.

Conclusion

This is the 26th report in the English literature of the rare condition of isolated suppurative submandibular sialadenitis. We reviewed the characteristics of this condition and confirmed the main risk factors, namely prematurity and tube feeding. Our case highlights the need for treatment guidelines. To our knowledge, this is the first description of a second episode in the same patient and the first report to implicate E. faecalis.

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