

## ABSTRACT

**Background:** Seasonal influenza infection is associated with secondary bacterial complications involving the upper and lower respiratory tract. However, the association of influenza infection with secondary severe or complicated head and neck infections is not appreciated.

**Methods:** We performed a retrospective review of pediatric patients hospitalized at Texas Children's Hospital with bacterial head or neck infections following influenza infection from October 2017 – March 2018. We queried the infectious diseases consult database using the search terms: orbital cellulitis, mastoiditis, retropharyngeal abscess, peritonsillar abscess, deep neck abscess, subdural empyema, Lemierre's syndrome, and Pott's puffy tumor. Based upon medical records review and ICD-10 codes, patients were included in this study if they had a head or neck infection and reported a positive rapid influenza diagnostic test within 30 days preceding hospital admission.

**Results:** We identified 44 patients with head or neck infections, of which 6 patients met inclusion criteria (Table). The male to female ratio was 5:1 and the median age was 11.6 years (range 1.7-13.9 years). Most patients were diagnosed with influenza during a period of high influenza activity and the median time from influenza diagnosis to hospital admission was 4.5 days (range 1-6 days). One patient had received seasonal influenza vaccination. Patients had a wide range of infections, including: orbital cellulitis (3), retropharyngeal abscess (2), and 1 of each of the following: Lemierre's syndrome, peritonsillar abscess, Pott's puffy tumor, and subdural empyema; 4 also had sinusitis. A causative pathogen was established in four cases: methicillin-resistant *Staphylococcus aureus*, *Streptococcus anginosus* group, *S. pyogenes*, and *S. intermedius*. The median duration of hospitalization was 22 days (range 5-35 days) and treatment duration ranged from 3.5 – 6 weeks. All patients completed antibiotic treatment successfully and had favorable outcomes.

**Conclusion:** We suggest that complicated bacterial head and neck infections may represent an under recognized co-infection or secondary complication of infection with influenza virus, further stressing the importance of prevention and treatment of influenza infection.

## OBJECTIVE

To describe the epidemiology, clinical manifestations, and outcomes of patients presenting with complicated head and neck infections following infection with influenza virus.

## INTRODUCTION

- Influenza and bacterial co-infections or secondary infections are important causes of morbidity and mortality among children.
- In the United States from 2010-2016, 675 influenza-related pediatric deaths were reported (Shang et al. *Pediatrics* 2018;141(4):e20172918) and an estimated annual 1,000,000 to 3,600,000 influenza-associated outpatient medical visits and 5,000 to 19,000 hospitalizations for children 5 to 17 years old were reported. (Rolfes et al. *Influenza Other Respir Viruses* 2018;12(1):132-7)
- Common bacterial complications following infection with influenza A and B viruses in children involve the upper and lower respiratory tracts, especially acute otitis media and pneumonia. (Peltola et al. *Clin Infect Dis* 2003;36(3):299-305)
- The predominant bacterial pathogens causing influenza-related complications include *Streptococcus pneumoniae*, *Staphylococcus aureus*, and *Streptococcus pyogenes*. (Chertow et al. *JAMA* 2013;309(3):275-282)
- We suggest that influenza virus infection may also predispose children to serious or complicated secondary bacterial infections of the head and neck region.

## METHODS

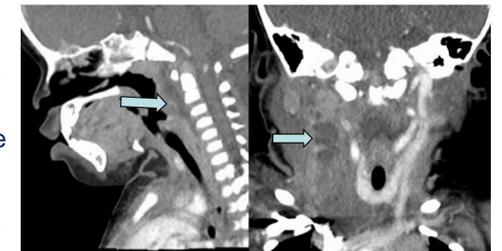
- We performed a retrospective review of pediatric patients hospitalized at Texas Children's Hospital (TCH) with bacterial head or neck infections following influenza infection between October 1, 2017 – March 30, 2018.
- The consultation database of the pediatric infectious diseases (ID) service at TCH was queried for patients using the search terms: sinusitis, orbital cellulitis, mastoiditis, retropharyngeal abscess, peritonsillar abscess, deep neck abscess, subdural empyema, Lemierre's syndrome, and Pott's puffy tumor.
- Based upon medical records review and *International Classification of Diseases, 10<sup>th</sup> revision* (ICD-10) codes, patients were included in this study if they had a head or neck infection and reported a diagnosis of influenza (e.g. a positive rapid influenza diagnostic test) in the 30 days preceding hospital admission.
- Demographic and clinical information was obtained from the electronic medical records system. Age, gender, clinical presentation, immunization history, microbiologic data, and treatment agents and duration were recorded when available for each patient.
- This study was approved by the Baylor College of Medicine Institutional Review Board.

## RESULTS

- Forty-four patients were identified with bacterial head or neck infections, of which 6 patients met inclusion criteria and their clinical characteristics are described (Table 1).
- The male to female ratio was 5:1 and the median age was 11.6 years (range 1.7-13.9 years). The median time from influenza diagnosis to hospital admission was 4.5 days (range 1-6 days).
- Four patients were previously healthy, and two patients were at higher-risk for influenza-associated complications (1 due to age 6-59 months and 1 due to asthma).
- Patients had a wide range of head and neck infections: orbital cellulitis (3), retropharyngeal abscess (2), Lemierre's syndrome (1), peritonsillar abscess (1), Pott's puffy tumor (1), and subdural empyema (1); 4 also had sinusitis (Figures).
- All patients required a surgical procedure: endoscopic sinus surgery (ESS) (3), incision and drainage of abscess (2), or craniotomy with washout (1).
- A causative pathogen was found in 4 cases: methicillin-resistant *Staphylococcus aureus* (MRSA), *Streptococcus anginosus* group, *S. pyogenes*, and *S. intermedius*.

- Two patients had polymicrobial infections: *Prevotella* with *Peptostreptococcus* and *S. mitis*; *Prevotella* with GAS
- Two patients were bacteremic: 1 with MRSA (positive cultures for 2 days) and 1 with *S. intermedius*.
- The median duration of hospitalization was 22 days (range 5-35 days) and 3 patients required intensive care.
- Treatment duration ranged from 3.5 – 6 weeks.
- All patients completed antibiotic treatment successfully and had favorable outcomes.

**Figure 1.** Computed tomography (CT) neck with contrast of a patient with Lemierre's syndrome and retropharyngeal abscess extending from nasopharynx to C5.



**Figure 2.** Maxillofacial CT with contrast of a patient with Pott's puffy tumor, extensive sinusitis, and orbital cellulitis.



**Table 1.** Characteristics of pediatric patients with severe bacterial head or neck infections following infection with influenza virus, 2017-2018 season

Case	Sex, age (years)	2017 Influenza vaccination, Prior influenza vaccination	Pneumococcal vaccination	Time from influenza diagnosis to admission (days)	Clinical Presentation	Diagnoses	Pathogen	Procedure	Definitive Treatment	Treatment Duration (weeks)
1	M, 11.2	No, No	PCV7, 4 doses PCV13, 1 dose	1	R eye pain, swelling, erythema	Sinusitis, Orbital cellulitis	Unknown	ESS	linezolid, ceftriaxone, metronidazole	3.5
2	F, 1.7	No, No	PCV13, 4 doses	5	R neck swelling	Lemierre's syndrome, RPA	MRSA	I&D	vancomycin	6
3	M, 12	No, Yes	PCV7, 4 doses	4	L eye pain and swelling, forehead swelling	Sinusitis, Pott's puffy tumor, orbital cellulitis	<i>Streptococcus anginosus</i> group <sup>a</sup>	ESS	ceftriaxone, metronidazole	5
4	M, 5.3	No, No	PCV13, 4 doses	3	L eye pain, swelling	Sinusitis, orbital cellulitis	Unknown <sup>b</sup>	ESS	vancomycin, ceftriaxone	4
5	M, 13.9	Yes, Yes <sup>c</sup>	PCV7, 4 doses	6	Neck pain and stiffness	RPA and peritonsillar abscesses	<i>S. pyogenes</i> <sup>d</sup>	I&D	penicillin	3
6	M 12.6	No, Unknown	Unavailable	5	L facial droop	Sinusitis, subdural empyema	<i>S. intermedius</i>	Craniotomy	ceftriaxone	4

Abbreviations: ESS endoscopic sinus surgery, I&D incision and drainage, MRSA methicillin resistant *Staphylococcus aureus*, RPA retropharyngeal abscess

<sup>a</sup>Patient had a polymicrobial infection with *Peptostreptococcus*, *Prevotella*, and *S. mitis*; <sup>b</sup>Patient had a Gram-stain positive for gram-positive cocci in pairs and gram-negative rods; <sup>c</sup>Patient received influenza vaccination in 2006, 2007, 2009, 2012, 2014, and 2015; <sup>d</sup>Patient had a polymicrobial infection with *Prevotella*.

## CONCLUSIONS

- We report 6 children hospitalized with severe head and neck infections following infection with influenza virus during the 2017-2018 influenza season at a large pediatric referral hospital.
- Of our 6 patients, only 1 had received seasonal influenza immunization.
- The disease burden of children hospitalized with influenza underscores the importance of prevention and treatment of influenza infection.
- We suggest that serious or complicated bacterial head and neck infections may represent an under recognized co-infection or secondary complication of infection with influenza virus.