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Influenza-Associated Parotitis During the 2014–2015 Influenza Season in the United States

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Abstract

Background.—During the 2014–2015 influenza season in the United States, 256 cases of influenza-associated parotitis were reported from 27 states. We conducted a case-control study and laboratory investigation to further describe this rare clinical manifestation of influenza.

Methods.—During February 2015–April 2015, we interviewed 50 cases (with parotitis) and 124 ill controls (without parotitis) with laboratory-confirmed influenza; participants resided in 11 states and were matched by age, state, hospital admission status, and specimen collection date. Influenza viruses were characterized using real-time polymerase chain reaction and next-

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generation sequencing. We compared cases and controls using conditional logistic regression. Specimens from additional reported cases were also analyzed.

Results.—Cases, 73% of whom were aged <20 years, experienced painful (86%), unilateral (68%) parotitis a median of 4 (range, 0–16) days after onset of systemic or respiratory symptoms. Cases were more likely than controls to be male (76% vs 51%; $P = .005$). We detected influenza A(H3N2) viruses, genetic group 3C.2a, in 100% (32/32) of case and 92% (105/108) of control specimens sequenced ($P = .22$). Influenza B and A(H3N2) 3C.3 and 3C.3b genetic group virus infections were detected in specimens from additional cases.

Conclusions.—Influenza-associated parotitis, as reported here and in prior sporadic case reports, seems to occur primarily with influenza A(H3N2) virus infection. Because of the different clinical and infection control considerations for mumps and influenza virus infections, we recommend clinicians consider influenza in the differential diagnoses among patients with acute parotitis during the influenza season.

Keywords

influenza; parotitis

Acute parotitis is a classic sign of mumps virus infection [1]; however, parotitis can be caused by other viral pathogens including adenovirus, Coxsackie A viruses, echoviruses, Epstein-Barr virus, human herpes virus 6, human immunodeficiency virus, lymphocytic choriomeningitis virus, and parainfluenza viruses 1 and 3 [2]. Acute viral parotitis is typically uncomplicated and resolves with supportive care [3].

Parotitis with influenza A virus infection was described among 12 patients with illnesses during the 1975–1976 influenza season in the United States [4] and in reports of sporadic cases occurring in the United States [5, 6], Canada [7, 8], Chile [9], and Spain [10]. These cases involved uncomplicated illness and occurred among children and adults. However, the frequency of occurrence, risk factors for development, and clinical manifestations of influenza-associated parotitis are not well described.

During December 2014, 5 cases of parotitis among patients with laboratory-confirmed influenza were reported to the Centers for Disease Control and Prevention (CDC). Surveillance activities for non-mumps parotitis were established by multiple state health departments, and patients with non-mumps parotitis were tested for influenza and other respiratory viruses. From these case-finding activities, 256 cases of influenza-associated parotitis occurred during October 2014–March 2015 and were reported to the CDC. During February 2015, we initiated a multistate case-control study to describe the clinical, epidemio-logic, and viral risk factors for influenza-associated parotitis.

METHODS

Case Ascertainment and Epidemiologic Investigation

On 9 January 2015, the CDC notified state and local health departments of the occurrence of influenza-associated parotitis using notifications sent to the Epidemic Information Exchange and requested that states notify the CDC's Influenza Division when a case was identified.

We defined a case as acute parotitis in a patient with laboratory-confirmed influenza virus infection with clinical diagnosis of parotitis from 1 October 2014 through 31 March 2015 (the study interval).

States identified cases in multiple ways, including unsolicited reports of cases from healthcare providers and Health Alert Network notifications asking healthcare providers to notify health departments if they saw patients fitting the case definition. Also, 2 states set up enhanced laboratory testing for nonmumps viruses among specimens submitted to state public health laboratories for mumps testing. In addition, the CDC also received unsolicited reports of cases from healthcare providers.

Cases with an available respiratory or oral specimen (nasopharyngeal, oropharyngeal, or buccal swab) obtained while the individual was symptomatic were eligible to participate in the case-control study. We defined a control illness as laboratory-confirmed influenza in a patient without acute parotitis during the study interval and with an available respiratory or oral specimen. Controls were selected among patients with influenza reported through annual influenza surveillance activities conducted by state public health departments. We aimed to match 3 controls to each case by age group (<2, 2–4, 5–13, 14–19, 20–49, and ≥50 years), state of residence, outpatient or inpatient status, and date of specimen collection (±3 weeks). Based on statistical power calculations to detect a 20% difference in exposure frequency, we aimed to enroll 50 cases and 150 matched controls. Study participation was open to all states; 11 states participated (Kansas, Maine, Michigan, Minnesota, Missouri, New Hampshire, New Jersey, Texas, Virginia, West Virginia, and Wisconsin). Among states that had identified more than 10 eligible cases, we randomly enrolled 10 into the study. The CDC deemed the proposed activities to be part of a public health response.

We developed a questionnaire to collect information regarding patient demographic features; signs and symptoms of illness; vaccine, travel, and illness history; as well as exposure to antivirals, antibiotics, and over-the-counter medications within 2 weeks of illness onset. During February 2015–April 2015, we interviewed cases and controls, or parents/guardians for those aged <18 years, by phone after obtaining verbal informed consent.

Laboratory Testing and Analysis

To be eligible for the case-control study, cases and controls needed to have laboratory-confirmed influenza detected using any test recommended for routine patient diagnosis, including polymerase chain reaction (PCR)–based molecular testing, rapid diagnostic tests, or viral culture [11]. Influenza virus infection was confirmed and subtyped for all case and control specimens at the CDC using real-time (RT)-PCR, with standard protocols.

CDC Influenza Division laboratories conducted next-generation sequencing of case and control specimens. Briefly, we extracted RNA from specimens using the QIAmp Viral RNA extraction kit according to protocol (Qiagen, Hilden, Germany) and amplified full influenza genomes [12] using the Superscript III One-Step RT-PCR kit (Invitrogen, Carlsbad, California). After quality control and normalization procedures, we prepared and indexed paired-end Illumina libraries using the Nextera XT sample preparation kit (Illumina, San Diego, California). We then pooled up to 96 libraries (92 samples, 1 positive control, and 3

negative controls) and generated sequences using a MiSeq platform (Illumina). We assembled sequences with at least 20× coverage into genomes using the Iterative Refinement Meta Assembler [13]. We compared study sequences to viral reference sequences and sequences from other circulating viruses. Additionally, we used LABEL [14] to determine the genetic group of the hemagglutinin (HA) gene of influenza A(H3N2) viruses and conducted phylogenetic analysis using MEGA 6 [15].

Statistical Analyses

We compared cases and controls using conditional logistic regression, with maximum likelihood methods, on matched case-control sets. We used a conditional logistic regression with exact methods to estimate the odds ratios (ORs) for the comparison of influenza subtypes and influenza A(H3N2) HA genetic groups, because of low frequencies of some genetic groups. We conducted statistical analyses with SAS, version 9.3 (SAS Institute, Cary, North Carolina) and considered *P* values < .05 to be statistically significant.

RESULTS

Description of Cases

During October 2014–March 2015, 256 cases of influenza-associated parotitis were reported to CDC from 27 states (California, Hawaii, Illinois, Indiana, Kansas, Kentucky, Maine, Maryland, Massachusetts, Michigan, Minnesota, Missouri, New Hampshire, New Jersey, New York, North Carolina, Oregon, Pennsylvania, Rhode Island, South Carolina, Texas, Utah, Vermont, Virginia, Washington, West Virginia, and Wisconsin). Among patients with sufficient data, the median age was 13 years (73% of 234 patients aged <20 years) and 69% (155/224) were male.

Among the 50 cases interviewed, parotid swelling was described as unilateral (68%), painful (86%), and lasting a median of 4 days (interquartile range [IQR], 3–6 days among 36 patients reporting symptom duration). Thirty-seven patients (74%) self-reported being tested for mumps while ill with parotitis; all tests were negative at state public health laboratories. The majority of cases (78%) had symptoms consistent with influenza, including chills, cough, muscle aches, sore throat, and feeling feverish, prior to onset of parotitis (median, 4 days prior; IQR, 1–7 days; range, 1–16 days). Eleven cases (22%) reported seeing a healthcare provider prior to the onset of parotitis. One patient reported a complication of illness (ear infection) and 1 patient reported testicular pain during his illness. Among 7 cases (14%) hospitalized, 2 patients were admitted to an intensive care unit, including 1 who was hospitalized prior to symptom onset. None of the patients died.

Case-Control Study

We enrolled 50 cases and 124 matched controls. Thirty-one cases were matched with 3 or more controls each and 19 cases were matched to at least 1 control each. Cases and controls did not differ in race/ethnicity; however, cases were significantly more likely to be male (Table 1). Significantly fewer cases self-reported influenza-like illness than controls (Table 2). Significantly more cases than controls self-reported facial swelling, gland swelling, and ear pain. Cases were less likely than controls to have received an influenza antiviral

medication (27% vs 64%; OR, 0.2; 95% confidence interval [CI], 0.1, 0.4) but more likely to have received an antibiotic during their illness (65% vs 22%; OR, 9.9; 95% CI, 4.1, 23.9). Cases and controls did not differ significantly regarding the presence of underlying medical conditions and exposures to over-the-counter medications, influenza vaccination, mumps vaccination, or histories of travel, illness, or hospitalization (Table 3).

Five cases (11% of 47 respondents) and 2 controls (2% of 118 respondents) reported having prior mumps virus infection (OR, 9.3; 95% CI, 1.8, 68.8). This association remained when adjusted for male sex (OR, 6.2; 95% CI, 1.0, 37.2) and may be age dependent, as 4 of the 5 cases with prior mumps were adults.

While all control specimens were nasopharyngeal or oropharyngeal swabs, most case specimens (66%) were buccal swabs. Influenza A(H3N2) viruses were the only identified influenza virus from cases (100% of 50 specimens) and the most common among controls (95% of 123 specimens; Table 4). Thirty-two (63%) case and 108 (92%) control specimens had complete or partial sequences from next-generation sequencing for further analysis. Phylogenetic analysis identified influenza A(H3N2) viruses in the 3C.3 and 3C.2a HA genetic groups; 3C.2a HA genetic group viruses were detected among all cases and most controls, which was not statistically significantly different. Within the HA gene, we did not identify any nucleotide changes in the case sequences compared with sequences from controls. Nucleotide changes seen between case sequences and influenza reference sequences were characteristic of the 3C.2a HA genetic group [16].

Laboratory Testing Among Additional Cases

In addition to the 50 cases included in the case-control study, CDC received reports of 163 other cases of influenza-positive parotitis that occurred in patients who provided either laboratory information or specimens for further testing. Of these additional case reports, 162 with subtyping information were all reported as influenza A(H3N2) virus infections. One patient had parotitis associated with RT-PCR–confirmed influenza B virus infection.

Next-generation sequencing was performed on 80 specimens from the additional cases not included in the case-control study; complete or partial sequences were available from 61 (76%) specimens. Among these, all had A(H3N2) viruses detected, including 58 (95%) classified as 3C.2a, 1 (2%) classified as 3C.3, and 2 (3%) classified in the 3C.3b HA genetic group—both reported among cases from Pennsylvania. Together with the 32 sequences from the case-control study case specimens, 90 (97%) of the A(H3N2) viruses from patients with parotitis were classified in the 3C.2a genetic group.

DISCUSSION

During the 2014–2015 US influenza season, 256 cases of influenza-associated acute parotitis occurred among residents of 27 states and were reported to CDC. Reported cases ranged widely in age but occurred primarily among school-aged children. Patients described painful facial swelling, consistent with acute parotitis, which developed shortly after the onset of systemic or respiratory symptoms. Swelling lasted a median of 4 days before

resolving. Seven cases were hospitalized during their illness, including 2 patients who were admitted to the intensive care unit.

Prior to the 2014–2015 influenza season, only 18 cumulative cases of influenza-associated parotitis were reported during the 1975–1976, 1984–1985, 2004–2005, and 2007–2008 influenza seasons in the United States, Canada, Chile, and Spain [4–10]. Additional laboratory testing revealed influenza A(H3N2) virus infections in all cases tested (15/15). Furthermore, the predominant influenza viruses during these seasons were influenza A(H3N2) viruses [17–20]. Additionally, circulating viruses characterized during these seasons had evidence of antigenic differences (drift) from prior circulating influenza A(H3N2) viruses [18–20].

Influenza A(H3N2) viruses were also the predominant viruses circulating during the 2014–2015 influenza season in North America and Europe. The majority of circulating A(H3N2) viruses were antigenically and genetically drifted from the influenza A(H3N2) component in the 2014–2015 Northern Hemisphere influenza vaccine and from prior circulating A(H3N2) viruses [21]. Further genetic characterization of A(H3N2) viruses in the United States demonstrated that the majority of the drifted viruses were in a newly emerged HA genetic group, labelled 3C.2a. Other HA genetic groups of the A(H3N2) viruses also circulated during the season, including 3C.2b, 3C.3, 3C.3a, and 3C.3b, with local variability [22]. The 3C.3 and 3C.3b viruses are closely related, yet distinct, from 3C.2a viruses in phylogenetic analysis, with several amino acid changes at antigenic sites [16, 22, 23].

In addition to the cases reported to the CDC, cases of influenza-associated parotitis were also reported in Canada, England, Scotland, and separately in Pennsylvania during the 2014–2015 influenza season [24–27]. Combined with our report, 99% (258/261) of all patients with influenza-associated parotitis reported during the 2014–2015 influenza season had influenza A virus infections and 95% (246/258) were infected with A(H3N2) viruses. Though infrequent during the 2014–2015 season, parotitis was also described in 1 patient after influenza A(H1N1pdm09), reported from Scotland [25], and in 1 patient with B virus infection, reported here. Of the 246 A(H3N2) viruses, 114 were further sequenced and 96% (109/114) were classified in the 3C.2a HA genetic group. Our case ascertainment efforts identified 2 patients infected with A(H3N2) viruses in the 3C.3b HA genetic group, both reported from Pennsylvania, which had a greater proportion of 3C.3b viruses circulating than other parts of the country [22], and 1 patient infected with an A(H3N2) virus from the 3C.3 HA genetic group.

Our case-control study revealed a significant association of parotitis with male sex. We are not aware of anatomical differences in male and female parotid glands that could account for this association [28], and male predominance among patients with mumps parotitis, to our knowledge, has not been described [29–31]. The recent report from British Columbia, Canada, noted 88% (14/16) of cases were males [24]. Additionally, we found an association between a history of prior mumps infection and influenza-associated parotitis, mainly among adults; the etiology and clinical relevance of this finding is unclear. Patients with influenza-associated parotitis, more so than controls, were less likely to receive influenza antiviral therapy but were more commonly given an antibiotic during their illness, possibly

because healthcare providers were concerned about bacterial etiologies of parotitis. We do not know for certain whether antibiotics were appropriate for a patient; however, nationally we see that antibiotics tend to be overprescribed for patients with influenza [32].

Our investigation is subject to limitations. First, interview responses may be subject to recall errors because most participants were interviewed 1–3 months after their illnesses, and misclassification might occur with self-reported exposures. Second, no cases had laboratory evidence of mumps infections; however, detection of mumps virus in buccal and serum specimens is challenging, particularly among vaccinated persons [33–35]. So, while unlikely given that none of the cases had epidemiologic links to mumps outbreaks, we could not definitively rule out mumps. Third, we used different strategies to find cases and controls, and this differential ascertainment might have contributed to observed differences in self-reported symptoms. Fourth, case specimens were primarily buccal swabs, and control specimens were nasopharyngeal or oropharyngeal swabs. Buccal swabs are currently not an approved specimen type for clinical influenza diagnostic testing; however, low cycle threshold values from case buccal swabs tested by RT-PCR suggest a large amount of influenza virus was present (median cycle threshold, 29.1, range, 19.1–38.5 among 98 specimens). Fifth, while influenza A(H3N2) virus was detected in all subtyped case specimens, fewer case than control specimens had complete genetic sequences. Next-generation sequencing has a lower limit of detection than RT-PCR; therefore, it is likely that case specimens that could not be sequenced contained lower viral loads. This might result from physiologic differences in viral shedding from the parotid gland or with the timing of specimen collection during the course of illness. Finally, additional sequencing investigations of case buccal specimens are ongoing to determine what bacterial pathogens may be codetected and whether these pathogens may contribute to the propensity to develop parotitis with influenza virus infection [36].

Additional investigations of influenza-associated parotitis are warranted to better understand the etiology and epidemiologic features of this uncommon clinical finding. After finding few epidemiologic risk factors in our study, we focused on describing the sequence differences in the influenza virus. Specifically, we looked for differences in the virus's HA gene because of this gene's role in viral attachment to host epithelial cells and its propensity for genetic change. We did not identify any changes in the HA gene that were specific to case viruses; however, detailed sequence analysis of the 7 other influenza gene segments might help further explain differences in the case and control influenza viruses. Furthermore, there may be host cell polymorphisms, environmental factors, or unmeasured exposures that may be risk factors for influenza-associated parotitis. Further studies would also be helpful to understand how influenza viruses interact with epithelial cells on the parotid gland and whether influenza viruses circulating in 2014–2015 had different tropism to the parotid gland.

We believe that this outbreak is reflective of increased occurrence during the 2014–2015 season rather than an artifact of enhanced surveillance and case finding efforts. Multiple independent reports from public health departments and clinicians were received by CDC's Influenza Division and Division of Viral Disease's mumps investigation team prior to setting up nationwide active case finding. However, it is possible that influenza-associated parotitis

was detected more often because targeted mumps investigations and reductions in mumps incidence during the past few decades has made non-mumps parotitis easier to detect. Efforts to establish population-based surveillance of influenza-associated parotitis could help describe its incidence, associated complications, and the public health impact during influenza seasons.

In conclusion, this outbreak of influenza-associated parotitis is the largest ever reported. Compared with recruited controls and broader virologic surveillance in the United States, influenza-associated parotitis seems to occur primarily with influenza A(H3N2) virus infection, although it does not appear to be exclusively associated with the newly emerged 3C.2a HA genetic group of A(H3N2) viruses. Our findings suggest that including influenza in the differential diagnoses among patients who present with acute parotitis may be prudent during influenza season, particularly during seasons dominated by influenza A(H3N2) virus infection and when respiratory symptoms precede parotitis. Testing for influenza would support appropriate treatment with influenza antiviral treatment, according to treatment guidelines [37], and may also reduce inappropriate use of antibiotics. Additionally, differentiating mumps-associated parotitis from influenza-associated parotitis is important from a public health perspective. Currently, mumps is relatively uncommon and prone to outbreaks. When mumps is suspected in a person, an intensive public health response may be warranted, including contact tracing, vaccination clinics, and patient isolation. In the United States, we experience annual widespread epidemics of influenza, and such a public health response is not generally needed. Due to these substantial differences, public health officials should consider influenza virus infection when investigating occurrences of parotitis during the influenza season.

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Table 1.

Demographic Characteristics of Cases and Controls, Multistate Investigation of Influenza-Associated Parotitis, United States, 1 October 2014–31 March 2015

	Cases (n = 50)		Controls (n = 124)			
Characteristic	**Respondents**	**n (%)**	**Respondents**	**n (%)**	**Odds Ratio [95% Confidence Interval][a]**	***P* Value[a]**
Age, years	50		124			
<2	…	0 (0)	…	0 (0)	…	…
2–4	…	2 (4)	…	6 (5)	…	…
5–13	…	21 (42)	…	61 (49)	…	…
14–19	…	13 (26)	…	26 (21)	…	…
20–49	…	11 (22)	…	23 (19)	…	…
≥50	…	3 (6)	…	8 (6)	…	…
Sex	50		124			
Male	…	38 (76)	…	63 (51)	3.0 [1.4, 6.3]	.005
Female	…	12 (24)	…	61 (49)	Reference	…
Race	50		124			
Black	…	3 (6)	…	9 (7)	1.3 [0.3, 4.9]	.74
White	…	42 (84)	…	110 (89)	Reference	…
Other/unknown	…	5 (10)	…	5 (4)	0.5 [0.1, 2.1]	.34
Ethnicity	50		124			…
Hispanic	…	7 (14)	…	18 (15)	1.3 [0.4, 3.8]	.66
Non-Hispanic	…	43 (86)	…	106 (85)	Reference	…

[a]Odds ratios, 95% confidence intervals, and *P* values from conditional logistic regression. No statistical comparison of age group was done because age group was used to set up the matched case-control pairs.

Table 2.

Clinical Characteristics and Symptoms of Illness Among Cases and Controls, Multistate Investigation of Influenza-Associated Parotitis, United States, 1 October 2014–31 March 2015

	Cases (n = 50)		Controls (n = 124)			
Characteristic	**Respondents**	**n (%)**	**Respondents**	**n (%)**	**Odds Ratio [95% Confidence Interval][a]**	***P* Value[a]**
Influenza-like illness[b]	49	25 (51)	122	109 (89)	0.15 [0.06, 0.35]	<.001
Self-report of testing for influenza	45	30 (67)	124	123 (99)	0.003 [<0.001, 0.05]	<.001
Self-report of testing for strep throat	43	18 (42)	113	50 (44)	0.8 [0.3, 1.7]	.53
Self-reported symptoms						
Fever/feverish[c]	49	32 (65)	122	115 (94)	0.1 [0.05, 0.4]	<.001
Chills	49	24 (49)	115	87 (76)	0.3 [0.2, 0.7]	.002
Muscle ache	47	18 (38)	119	83 (70)	0.3 [0.1, 0.6]	<.001
Headache	48	30 (63)	119	86 (72)	0.6 [0.3, 1.3]	.23
Cough	50	32 (64)	122	106 (87)	0.2 [0.1, 0.6]	.001
Wheezing	49	5 (10)	121	36 (30)	0.2 [0.07, 0.6]	.004
Shortness of breath	49	4 (8)	120	33 (28)	0.2 [0.05, 0.6]	.007
Sore throat/difficulty swallowing	49	27 (55)	121	79 (65)	0.6 [0.3, 1.2]	.17
Runny nose	46	23 (50)	121	75 (62)	0.6 [0.2, 1.2]	.12
Ear pain	48	19 (40)	119	26 (22)	2.3 [1.1, 4.8]	.03
Rash	49	5 (10)	122	10 (8)	0.9 [0.2, 3.4]	.87
Facial swelling	50	34 (68)	122	2 (2)	41.7 [10.0, 174.6]	<.001
Gland swelling	50	36 (72)	113	29 (26)	5.9 [2.7, 13.0]	<.001
Tongue swelling[d]	47	1 (2)	121	4 (3)	…	…
Discomfort with acidic foods	40	4 (10)	92	8 (9)	1.1 [0.2, 4.7]	.95

[a]Odds ratios (ORs), 95% confidence intervals, and *P* values from conditional logistic regression. Reference group for OR is absence of symptom or condition.

[b]Influenza-like illness defined as fever (≥100°F) or feeling feverish and cough and/or sore throat.

[c]Temperature ≥100°F or self-report of feeling feverish.

[d]OR for frequency of tongue swelling in cases compared with controls could not be estimated from the model.

Table 3.

Clinical History and Epidemiologic Exposures Among Cases With Influenza-Associated Parotitis and Controls, Multistate Investigation of Influenza-associated Parotitis, United States, 1 October 2014–31 March 31 2015

	Cases (n = 50)		Controls (n = 124)			
Characteristic	**Respondents**	**n (%)**	**Respondents**	**n (%)**	**Odds Ratio [95% Confidence Interval][a]**	***P* Value[a]**
Experienced complication from illness[b]	46	1 (2)	123	9 (7)	0.2 [0.03, 2.2]	.21
Has an underlying medical condition	49	21 (43)	124	56 (45)	0.9 [0.4, 2.0]	.81
Underlying medical conditions						
Asthma	49	11 (22)	123	30 (24)	1.0 [0.4, 2.5]	.97
Chronic obstructive pulmonary disease or chronic lung condition	49	2 (4)	124	3 (2)	1.6 [0.2, 15.0]	.71
Cardiovascular condition	49	3 (6)	124	2 (2)	5.2 [0.7, 39.2]	.11
Diabetes	49	3 (6)	124	5 (4)	1.3 [0.2, 7.1]	.76
Renal condition	49	0 (0)	124	3 (2)	…	…
Immunosuppressive condition	49	0 (0)	124	4 (3)	…	…
Chemotherapy in past year	49	0 (0)	123	4 (3)	…	…
Neurologic/neurodevelopmental condition	48	4 (8)	124	7 (6)	1.4 [0.3, 5.7]	.66
Rheumatoid arthritis	48	0 (0)	124	1 (1)	…	…
Sjogren’s syndrome	49	0 (0)	124	0 (0)	…	…
Other condition[c]	47	0 (0)	124	1 (1)	…	…
Vaccination history						
Influenza vaccine: 2013–2014 season	47	29 (62)	118	78 (66)	1.1 [0.5, 2.5]	.78
Influenza vaccine: 2014–2015 season[d]	44	18 (41)	121	49 (40)	1.1 [0.5, 2.3]	.91
Measles-mumps-rubella vaccination[e]	46	46 (100)	110	103 (94)	…	…
History of mumps virus infection	47	5 (11)	118	2 (2)	9.3 [1.8, 68.8]	.03
History of parotitis	46	3 (7)	120	5 (4)	2.3 [0.4, 11.7]	.33
Strep throat in past year	46	8 (17)	115	18 (16)	1.2 [0.4, 3.5]	.70
Skin/soft tissue infection in past year	49	3 (6)	123	3 (2)	2.7 [0.4, 18.5]	.30
Respiratory syncytial virus or mononucleosis in past year	48	0 (0)	123	1 (1)	…	…
Hospitalization for other illness in past year	46	3 (7)	119	10 (8)	0.7 [0.2, 2.9]	.58
Dentist/oral surgeon visit within 2 weeks before illness[f]	48	3 (6)	123	5 (4)	1.7 [0.4, 8.6]	.50

Characteristic	Cases (n = 50) Respondents	Cases (n = 50) n (%)	Controls (n = 124) Respondents	Controls (n = 124) n (%)	Odds Ratio [95% Confidence Interval][a]	*P* Value[a]
Sinus procedure within 2 weeks before illness	48	1 (2)	123	0 (0)	…	…
Travel within 2 weeks before illness	46	5 (11)	122	11 (9)	1.0 [0.3, 3.6]	.98
Aware of others with parotitis/mumps	42	2 (5)	115	3 (3)	1.8 [0.3, 12.6]	.57

[a] Odds ratios (ORs), 95% confidence intervals, and *P* values from conditional logistic regression. Reference group for OR is absence of symptom or exposure. ORs and *P* values could not be estimated for exposures that were not observed in or observed for 100% of either cases or controls.

[b] Self-reported complication in the case was ear infection and among controls included pneumomediastinum, pneumonia, bronchitis, bronchiectasis, persistent cough, and hallucination with fever.

[c] Other conditions included hepatic disease.

[d] Received influenza vaccine at least 2 weeks before symptom onset.

[e] Reported receiving at least 1 dose of the measles–mumps–rubella vaccine.

[f] Patient saw dentist/oral surgeon for procedure other than routine cleaning.

Table 4.

Virologic Characteristics of Influenza Virus Infection Among Cases With Influenza-Associated Parotitis and Controls, Multistate Investigation of Influenza-associated Parotitis, United States, 1 October 2014–31 March 2015

Virologic Characteristic	Cases, n (%)	Controls, n (%)	Odds Ratio [95% Confidence Interval][a]	*P* Value[a]
Influenza subtype[b]				
A(H3N2)	50 (100)	117 (95)	3.3 [0.6, >999]	0.28
A(H1 N1)pdm09	0 (0)	1 (0.8)	Reference	…
B	0 (0)	5 (4)	Reference	…
Genetic group of influenza A(H3N2) viruses[c]				
3C.2a	32 (100)	105 (97)	3.8 [0.7, >999]	0.22
3C.3	0 (0)	3 (3)	Reference	…
3C.3a	0 (0)	0 (0)	Reference	…
3C.3b	0 (0)	0 (0)	Reference	…

[a]Odds ratios (ORs) and *P* values from conditional logistic regression using exact methods to estimate the OR. For the model of influenza subtype, we defined a common reference group of influenza A(H1N1)pdm09 and B virus infections. For the model of influenza A(H3N2) genetic groups, we defined a common reference group of 3C.3, 3C.3a, and 3C.3b virus infections.

[b]Subtyping could not be performed on specimens from 1 control.

[c]Of the influenza A(H3N2) viruses detected, sequencing was successful for 32 case and 108 control specimens.