

Neurological symptoms and complications of influenza in the elderly.

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Abstract

BACKGROUND: An in-depth study of neurological symptoms and complications of influenza in elderly patients. This population group is more susceptible to complications of the disease and these complications are more likely to end in death.

METHODS: A retrospective analysis of patient data was performed. All patients aged 65 years and older were included in the study. The study period was from the 1st of January, 2018 to 31st of December, 2021. All symptoms and complications of influenza were analyzed. Especially neurological and general symptoms were analyzed. Data were extracted from the complete medical records of the patients.

RESULTS: The most common symptoms of influenza in the elderly were fever in 218 cases (83.52%), cough in 189 patients (72.41%), general weakness in 182 (69.73%) and fatigue in 166 patients (63.6%). Myalgias were experienced by 106 patients (40.61%) and arthralgias by 101 patients (38.7%). Headache occurred in only 21 patients (8.06%). Encephalopathy was observed in 7 elderly patients (2.68%) during hospitalization. Influenza encephalitis was noted in 2 cases.

CONCLUSION: The most common neurological symptoms of influenza in more than half of the elderly are general weakness and increased fatigue. Myalgias are common, headache less often. Nausea is not uncommon. Of the complications, encephalopathy is the most common. Cases of influenza encephalitis have also been reported. We have not encountered a stroke. Concerning other complications, bacterial pneumonia was the most common.

INTRODUCTION

Influenza is an infectious disease caused by influenza viruses that belong to the orthomyxovirus family. Influenza A and B viruses are responsible for epidemics with approximately 3-5 million severe cases and about 300,000 deaths worldwide each year. The European Centre for Disease Control estimates that influenza causes more than 38,000 deaths in Europe each year (Preaud *et al.* 2014). Mortality rates

are not significantly different between influenza A and B. It is approximately 16% for the former and 10% for the latter (Asai *et al.* 2017). Rather than from influenza itself, most patients die from its complications. The more common complication of influenza is bacterial pneumonia. Bronchitis and sinusitis can also occur in the respiratory tract. Dangerous complications of influenza can also involve the heart. These are mainly myocarditis and pericarditis. Up to

90% of pericarditis in developed countries is idiopathic, which could be related to viral disease (Maisch et al. 2004). Among neurological symptoms, headache, muscle and joint pain dominate. General weakness and increased fatigue tend to be an integral part of the spectrum of symptoms in the elderly. Neurological complications include encephalopathy and, rarely, encephalitis. Stroke may also occur.

MATERIAL AND METHODS

Retrospective analysis of patient data. The study population consisted of all patients over 65 years of age who were diagnosed with influenza at the University Hospital Pilsen between 1st of January 2018 and 31st of December 2021. Retrospectively, data were obtained from the electronic medical records of the patients in WinMedicalc software (Medicalc Software, s. r. o., Plzeň, Czech Republic). We observed the history and nature of the health difficulties, symptoms at the initial examination, laboratory results, microbiological test results, complications and final status. We focused mainly on neurological symptoms and complications. We also monitored information on influenza vaccination. Data was processed in Excel 2016 spreadsheet editor (Microsoft Corporation, Redmond, USA).

RESULTS

During the period under review, the diagnosis of influenza A was confirmed in 602 patients. Of these, 261 patients were elderly (43.36%), 286 patients (47.51%) were of working age and 55 were children (9.13%). In the elderly group there were 143 women and 118 men. The mean and median age was 77.48 years and 76 years respectively, with a minimum and maximum age of 65 and 99 years respectively. The peak of diagnosed influenza illnesses among the elderly was during the month of February.

Of the 261 patients over 65 years of age, only 43 were treated as outpatients, all of whom were free of risk factors and complications; the other 218 were hospitalized. Of the 218 hospitalized elderly patients, 163 (74.77%) were treated in a standard bed, 40 (18.35%) required a stay in a first or second level intensive care bed, and the condition of 15 patients (6.88%) required resuscitative care of a higher type in a third level intensive care bed. In terms of the patient's first contact with a physician since the onset of the difficulty, the largest group was the elderly who were examined by a physician on the 3rd day after the onset of difficulties. There were 121 such patients (46.36%) out of 261.

Fever was the most common flu symptom in 218 cases (83.52%). Cough occurred in 189 seniors (72.41%). Cough and fever together occurred in 160 patients (61.3%). The most frequent neurological symptoms were general weakness in 182 (69.73%) of the patients and fatigue in 166 (63.6%)

of the elderly patients. Myalgias were reported by 106 patients (40.61%) and arthralgias by 101 patients (38.7%). Headache was reported by only 21 patients (8.06%) in the elderly population. Nausea as a partially perceived neurological symptom and nuisance was present in 37 patients (14.18%). The prevalence of all the perceived symptoms of influenza in patients in our cohort is shown in Table 1.

The mean number of leukocytes, erythrocytes and platelets in the blood count at the first sampling was $9.23 \times 10^9/l$, $4.31 \times 10^{12}/l$ and $188.14 \times 10^9/l$, respectively. All patients were monitored for C-reactive protein level. The mean value in elderly patients with uncomplicated course was 51 mg/l, in patients with complications it was 90.79 mg/l. Renal function parameters were also monitored. In patients without complications, the values of urea and creatinine were within normal limits, but in patients with complications of influenza, the mean value of urea was 11.2 mmol/l and creatinine was 126.59 mmol/l. In the whole cohort, the mean values of sodium, chloride and potassium in the ionogram were 138.95 mmol/l, 101.54 mmol/l and 4.0 mmol/l respectively.

No complications were observed in 69 seniors. Encephalopathy was observed in 7 seniors (2.68%). All cases were male patients. Encephalitis was noted in 2 patients. Influenza virus was detected by PCR in both of them after lumbar puncture. We did not observe stroke as a complication of influenza in our cohort. Concerning other complications, 114 elderly patients (43.68%) had pneumonia. Bacterial etiology superimposed on influenza-like illness was found in 48 cases. *Klebsiella pneumoniae* and *Streptococcus pneumoniae* were the most common. Acute cardiac decompensation occurred in 69 elderly cardiac patients. Acute respiratory insufficiency was observed in 72 patients (27.59%). Of these, oxygen therapy with mask or higher oxygen flow nasal prongs was sufficient in 49 patients, 8 were connected to HFNO, 5 required temporary non-invasive pulmonary ventilation in the intensive care bed and in another 10 patients it was necessary to secure the airway by tracheal intubation and perform artificial pulmonary ventilation. Acute deterioration of renal function was observed in 41 patients (15.71%). In addition to pneumonia, acute bronchitis was observed in 37 cases in our cohort of elderly patients. In 14 patients we observed exacerbation of chronic obstructive pulmonary disease. The next most common infectious complication of influenza, apart from respiratory tract infection, was urinary tract infection. This occurred in 20 patients (7.66%) in our cohort. An overview of the complications of influenza in our cohort of patients is shown in Table 2.

226 out of 261 seniors (86.59%) in our cohort were treated with oseltamivir. No other antiviral agent effective against influenza viruses was used. In the case of only 11 seniors it was proved that they have been

Tab. 1. Symptoms of influenza in elderly

group of symptoms	symptom	elderly patients (n = 261)	
		n	%
general	fever	218	83.52
	chill	41	15.71
	nausea	37	14.18
	fatigue	166	63.60
head and neck	headache	21	8.05
	nasal congestion	30	11.49
	rhinorrhea	11	4.21
	sore throat	23	8.81
	hoarseness	9	3.45
neuromuscular	myalgia	106	40.61
	arthralgia	101	38.7
	weakness	182	69.73
gastrointestinal	chest pain	20	7.66
	abdominal pain	11	4.21
	vomiting	19	7.28
	diarrhea	33	12.64
	flatulence	19	7.28
pulmonary	cough	189	72.41
	hemoptysis	5	1.92
	pleural pain	14	5.36

vaccinated with influenza vaccination, as an effective prevention of the disease. Hospitalization was necessary in 6 of them because of complications within the respiratory system. None of these patients died. 105 patients were found not to have been vaccinated, while the remaining 145 elderly patients could not be traced back in their medical records.

Out of 261 elderly patients, 47 people (18.01%) died of influenza and its complications. Most of these patients had severe pneumonia with acute respiratory insufficiency. In some patients, severe heart failure occurred concurrently or separately. One patient developed acute colitis with subsequent ileus. Decompensation of other chronic diseases in elderly patients was standardly observed.

DISCUSSION

The elderly are one of the high-risk groups with high probability of influenza complications and are therefore recommended to be vaccinated annually (Ghebrehewet *et al.* 2016, Rolfes *et al.* 2019). Symptoms of influenza in the elderly are varied and involve the respiratory tract, digestive tract, musculoskeletal system, as in working-age adults and children, and the classic general symptoms of viral illness are also observed. These often

include fever, cough, myalgia, respiratory-dependent chest pain, headache, sore throat and chills (Savulescu *et al.* 2010, Shahid *et al.* 2010). However, fever and cough are the most commonly reported ones (Lam *et al.* 2016). The results of our study also confirm this. Fever occurred in 83.52% and cough in 72.41% of the elderly. Together, these symptoms occurred in 61.3% of our cohort. However, some results show that fever and cough have a significantly lower predictive value for influenza in the elderly than in the working-age adult population. Some authors point out that in the elderly we may more often than in young adults encounter absence of fever, mild systemic symptoms, but more often qualitative changes in consciousness (Monmany *et al.* 2004). We may also more often encounter only fever and impaired consciousness, especially if pneumonia is present simultaneously as a complication of influenza (Falsey *et al.* 2006).

In general, it is necessary to state that in times of increased incidence of influenza, an automated system for measuring body temperature at the time of admission to the emergency room can increase the detection of patients with this disease. An increase in the number of persons with elevated body temperature captured correlates with an increased incidence of influenza in a given region (Bordonaro *et al.* 2016). Even

Tab. 2. Complications of influenza in the elderly

complications	elderly patients (n = 261)	
	n	%
acute sinusitis	10	3.83
acute tonsillitis	5	1.92
acute bronchitis	37	14.18
pneumonia	114	43.68
acute respiratory insufficiency	72	27.59
heart failure	69	26.44
myocarditis	4	1.53
acute renal failure	41	15.71
urinary tract infection	20	7.66
encephalopathy	7	2.68
encephalitis	2	0.77
myositis	2	0.77
ileus	1	0.38

during the influenza season, the possibility of infection with SARS-CoV-2 should not be forgotten. Coinfection with covid-19 during influenza has been documented repeatedly. It is more commonly associated with elderly patients or persons with other risk factors (Brenner *et al.* 2020, Jing *et al.* 2021). Influenza should also be kept in mind in case of patients with pulmonary embolism during the epidemiologically relevant period. As with covid-19, factors that increase the risk of pulmonary embolism in influenza include male gender, older age, and higher D-dimer levels (Števík *et al.* 2023).

Accurate and early diagnosis of influenza is essential in the elderly, as they are at risk of developing serious complications (Lang *et al.* 2012). The most common complications include pneumonia, invasive bacterial co-infections, myositis and exacerbations of chronic diseases (Jani *et al.* 2018). Among chronic diseases, these are mainly cardiovascular diseases, chronic respiratory diseases, renal, hepatic and hematological diseases (Grohskopf *et al.* 2017). Also in our patient cohort, we observed pneumonia as the most common complication. This occurred in 43.68% of the elderly patients. Influenza viruses themselves can cause severe pneumonia. However, mortality is significantly increased mainly by secondary bacterial pneumonia (Kash *et al.* 2015). This is the case in normal epidemics, and has been even more pronounced in most pandemics in documented history (Tognotti *et al.* 2009, Weinberger *et al.* 2012). The most common pathogen causing bacterial pneumonia in influenza-like illness is *Streptococcus pneumoniae* (Short *et al.* 2012, Ishiguro *et al.* 2019). *Staphylococcus aureus* is also reported more frequently, including MRSA (Dawood *et al.* 2014). In our study, *Klebsiella pneumoniae* and *Streptococcus pneumoniae* were the most frequently implicated bacteria. Among

the respiratory tract complications, we observed acute bronchitis, exacerbation of chronic respiratory diseases and acute respiratory insufficiency in greater numbers. Acute cardiac decompensation was not infrequently encountered as a complication. Acute deterioration of renal function, sometimes of a higher degree, was also observed more frequently, which is commonly described and is not a rare complication of influenza-like illness (Bagshaw *et al.* 2013).

The laboratory findings were not different from the usual findings in respiratory viral diseases. Mostly leukocytosis was observed in the blood count. C-reactive protein levels were also consistent with findings in common viruses. A secondary finding of our study is that interleukin-6 is not routinely screened in patients with influenza in our hospital, although it is an important predictor of influenza severity and its further development (Zhang *et al.* 2020). The same is true for respiratory disease covid-19, for example (Gao *et al.* 2020, Tjendra *et al.* 2020).

The interval of first contact with a physician from the onset of symptoms was often crucial for the patient's future prognosis. No patient sought medical attention on the first day of difficulty. In the interval of 2-5 days from the onset of difficulties 96.43% of patients came to the University Hospital, the rest came on the 6th day of persistent difficulties. Among the elderly, 54% of patients visited the emergency room on day 2-5 after the onset of difficulties (Lam *et al.* 2016). Even later, 29% of elderly patients did so. We consider it important to note that all patients over 65 years of age who died of influenza and its complications in the University Hospital during the study period came into contact with a physician no earlier than day 3 after the onset of difficulties.

Oseltamivir was administered to 226 of 261 elderly patients (86.59%) in our cohort, usually twice a day orally at a dose of 75 mg. The possible development of resistance to oseltamivir described in the literature was not observed in any of the observed cases (Baz *et al.* 2009, Roussy *et al.* 2013). Corticosteroids were no longer routinely administered to patients, as many studies have shown that their administration increased mortality (Delaney *et al.* 2016, Li *et al.* 2017) and more complications occurred (Linko *et al.* 2011, Lee *et al.* 2015). Prolonged release of influenza virus has also been described (Lee *et al.* 2008). Effective vaccination with the tetravalent vaccine remains an essential component of disease prevention. Seasonal vitamin D supplementation should also be part of prevention in all population groups, as low serum 25-hydroxyvitamin D levels have been repeatedly shown to correlate with higher susceptibility to acute respiratory infections (Simanek *et al.* 2024).

CONCLUSION

The elderly are a fragile group with many chronic diseases and smaller body reserves. The most common symptoms, and thus predictors of illness, during the influenza season are the rapid onset of fever and dry cough. Neurological symptoms such as muscle and joint pain are more common in the elderly; headaches are less common. General weakness is more prevalent, sometimes with increased fatigue. Influenza in the elderly is often accompanied by many complications. Neurological complications include encephalopathy and encephalitis. It may also be associated with the development of ischaemic stroke. In our cohort of patients, pneumonia was the most common complication. Acute heart failure and renal impairment also required treatment more frequently. The mortality rate in our cohort was 18.01%. The most effective prevention of the development of influenza and its complications in the elderly is still available vaccination, which is fully covered by public health insurance in the Czech Republic for patients over 65 years of age.

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