

## CLINICAL VIGNETTE

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# Asymptomatic Influenza Presenting with Bradycardia and other EKG Changes

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One hundred years after the great Spanish flu pandemic of 1918, which caused at least 20-50 million deaths world-wide, Influenza remains a significant cause of morbidity and mortality, with some annual estimates falling between 12,000 and 56,000 deaths<sup>1</sup> and the total annual economic burden of influenza at \$87.1 billion.<sup>2</sup> Influenza viruses, single-stranded RNA viruses belonging to Orthomyxoviridae family, are highly contagious and spread easily in close quarters and open communities. This is compounded by the current culture of vaccine aversion leading to a poor vaccination rate. The 2017-2018 seasonal Influenza outbreak was among the worst in recent years in terms of clinical burden, hospitalization, morbidity and mortality.<sup>3</sup> Influenza remains especially deadly for the immunocompromised, those burdened with chronic illness and older adults. Most clinicians are aware of the common or typical complications of influenza, which are generally secondary to bronchitis or pneumonia. However, in this report, we present a case of an older man who was asymptomatic of influenza infection and whose only clinical sign was bradycardia.

### *Case Presentation*

A 92-year-old nursing home resident with a history of schizophrenia, coronary heart disease, and peripheral artery disease was found to have a new bradycardia. He had had a non-ST elevation myocardial infarction (NSTEMI) 3 years prior while recovering from a left above-knee amputation. His post-operative course was also complicated by long runs of ventricular tachycardia (VT). During that time, his health-care proxy expanded his previous Do Not Resuscitate order to include no cardiac catheterization or ICU treatments and so he was maintained on a low dose of metoprolol at 12.5mg twice a day. Subsequent to those events, he continued to do well despite the initial poor prognosis heralded by his NSTEMI.

During a flu outbreak in the nursing home, he was noted by the nursing staff to have a slow heart rate at 38 beats per minute (bpm), which was found incidentally while checking vitals prior to giving his beta blocker. Review of records show his baseline heart rate to be about 60 beats per minutes. On assessment, it was felt he had rapid breathing and it was recorded at 22 breaths per minute. He had no other complaints – no fever, no sore throat, no cough, no gastrointestinal symptoms and was otherwise at baseline and comfortable. Other vitals were blood pressure of 125/69mm Hg, oral temperature of 98°F, and oxygen saturation of 93% on room air. Supplemental O<sub>2</sub> was started at 2 liters nasal cannula which increased his O<sub>2</sub> saturation to 97%. He was sent to the emergency department (ED),

where he was noted to be pleasant and comfortable. Upon arrival, he was not noted to be short of breath. He continued to be afebrile but now with a pulse of 81 beats per minute, a blood pressures of 108/72 mmHg, and stable oxygenation of 96% on 2L nasal cannula. His white blood cell count was 5.97 k/uL. Troponin was 0.04 ng/mL. Chest X-ray (CXR) showed no acute process.

Emergency department providers noted on EKG that he was having premature atrial and ventricular contractions (PAC/PVC) with a stable 1st degree AV block seen on previous EKGs. He was also noted to have a new incomplete Left Bundle Branch Block (LBBB) compared to prior EKGs. After ruling him out for an ischemic event, the providers did not feel he met admission criteria and he was discharged back to his nursing home with a diagnosis of asymptomatic bradycardia.

During follow up evaluation, he was noted to be comfortable and without complaints. In the morning, he did not require supplemental O<sub>2</sub>, but was still bradycardic. Given the concomitant flu outbreak, the patient was swabbed for influenza. He patient had been previously vaccinated. He was also on oseltamivir (Tamiflu) prophylaxis as per Centers for Disease Control (CDC) protocol as he had roomed with one of the nursing home's sentinel cases. By the afternoon, he was noted to have slightly increased respiratory rate of 24 with increased work of breathing and evidence of hypoxia with O<sub>2</sub> saturations now drifting down to 80%. Paramedics were called and he was sent to the ED.

On repeat presentation to the ED, he was found to be hypoxic off supplemental O<sub>2</sub> to 80%, but increased to 95% after oxygen supplementation via nasal cannula. Other vitals were: temperature of 97.2°F, pulse of 33 beats per minute, and respiratory rate of 24, with a blood pressure of 142/64mmHg. Labs revealed a white blood cell count of 7.67 k/uL. Troponin was 0.05 ng/mL, then 0.04 ng/mL on recheck. Lactate was 2.3mmol/L. Chest x-ray showed a new left lower lobe infiltrate. Influenza swab taken in the morning resulted positive for Influenza A. He was admitted to the inpatient ICU, put on Bilevel Positive Airway Pressure (BiPAP) and was noted to have a ventricular bigeminal rhythm, frequent runs of non-sustained ventricular tachycardia (NSVT) and premature ventricular contractions possibly confounding as bradycardia. He appeared to recover after a 4-day admission, but was sent back to ED a day later with heart rate of 28 bpm repeated as 38bpm manually. On re-admission, he was again found to be in NSVT with ventricular bigeminy and a run of VT at about 180 beats per minute as well as periods

of sinus bradycardia. At that point, Cardiology specialists increased his oral metoprolol to 25mg twice a day, and started amiodarone 200mg a day. He was discharged after a 3-day admission and continued to maintain a heart rate between high 50 and low 70 beats per minute, although this may be related to these additional medications.

### **Discussion**

**Atypical presentations of influenza in the elderly** - Diagnosis of influenza is often made challenging in the nursing home by the fact that older adults are well known to have atypical presentations, poor response to vaccination,<sup>4</sup> and inability to mount a “true” fever or immune response.<sup>5,6</sup> The elderly may instead present with no symptoms or perhaps just fatigue and a less alert mental status, which can be non-specific in older adults. Thus, infections in older adults may be difficult to diagnose. In addition, an influenza infection specifically may present in confounding and atypical ways and thus be more difficult to detect and contain. Paradoxically, while influenza is overall quite deadly in older adults and those with multiple chronic diseases, in our nursing home we have seen several cases of veterans over 90 years in age present with no symptom other than a dry cough, while younger roommates are ill with influenza for days. Because of the deadly and far-ranging consequence of missing an influenza infection in the close quarters of a nursing home, it is important to be aware of the especially subtle presentations of influenza to aid early detection.

**Influenza Remains Undetected at High Rates** - Fever and malaise are generally felt to be part of “Influenza-Like Illness” (ILI), but in fact, cough is likely the most common presenting symptom and fever does not present in adults as commonly as in children.<sup>7,8</sup> However, rates of asymptomatic influenza may be as high as 33% and these patients may have subtle clinical signs, sometimes difficult to detect in a busy ED.<sup>9</sup> More and more attention is being paid to detecting asymptomatic influenza infections in hospitalized and ICU patients.<sup>10</sup> In fact, in one study during the flu season, one third of ICU patients tested positive for tracheal aspirate even though influenza was not suspected in half of the patients.<sup>11</sup> Despite this, patients presenting with flu-like symptoms are still under-tested.<sup>12</sup> In addition, it is possible that at least 25% of all patients presenting to the ED with community-acquired pneumonia or severe symptoms that are not necessarily flu-like during epidemic periods are influenza positive.<sup>13</sup> Furthermore, many of these studies use nasopharyngeal swabbing, which may be less sensitive than tracheal samples, as one study detected 92% of flu cases by nasal swab but 100% via tracheal aspirate.<sup>14</sup>

**Complications of Influenza** -Pulmonary complications of influenza are well documented and include viral pneumonia and, possibly a more pernicious, superinfection bacterial pneumonia. Non-pulmonary complications of influenza, however, can be wide-ranging and multi-systemic, and often the presentation of these are not accompanied by typical symptoms expected in influenza infection. These can include neurological complications and musculoskeletal disorders, as well as ocular,

hematological, endocrine and renal disorders.<sup>15</sup> However, the deadliest can be cardiac complications, such as heart failure, myocarditis, and ischemic heart disease.<sup>16</sup> Main-stream media communication of this last complication may have caused a surge in vaccination rates this season, likely because heart attacks are a well-recognized deadly event by the general public, as opposed to some of the other possibly less well understood complications. In addition, influenza infection has been associated with EKG changes, myocarditis, and increase in cardiac enzymes.<sup>17</sup>

**Bradycardia and other EKG changes in Influenza** – Bradycardia in influenza is noted in the literature as early as 1899 in an article published the Lancet. That article described several cases in young adults. In one case, the treatment recommended was “Champagne ... in large doses and brandy ... given at regular intervals” to increase the heart rate. It was postulated that the effect was the result of “immediate action on the pneumogastric nerve or on the ganglia of the heart by the influenza toxins.”<sup>18</sup> In the nearly 120 years since the Lancet article, there has been much documentation of the effect of influenza on the conduction system of the heart which can lead to various EKG changes and arrhythmias.

These cardiac abnormalities are likely the result of viral myocarditis ranging from mild subclinical myocarditis to necrosis of the heart muscle. Subclinical myocarditis presenting as “EKG myocarditis” may be as high as 10%. This may present with various EKG changes ranging from ST segment disruption and T wave changes and/or dysrhythmias such as atrial fibrillation or sinus bradycardia.<sup>19</sup> These are rarely accompanied by troponin abnormalities and usually resolve within a few weeks.<sup>20</sup> Fulminant myocarditis is likely due to necrosis of the heart muscle in response to the influenza infection. It is a rare consequence and may present with arrhythmia, or more severely as cardiogenic shock with rapid progression to death. Whether the cause is the result of direct viral involvement versus immune mediated response to the virus remains unclear.

It is important to be aware of the cardiac complications of influenza, not only because supportive treatment may be necessary while the infection remains active, but also because overlooking a diagnosis of influenza can contribute to its spread with severe implications in frail older adults.

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Submitted September 5, 2018