Learning from errors

Swine flu: false-positive rapid flu swab with resulting misdiagnosis of a case of Legionella pneumonia

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Summary

A 59-year-old man presented with a severe flu-like illness and widespread pulmonary infiltrates on chest x-ray. A rapid influenza direct test was positive and the patient was nursed in isolation. On subsequent review, a diagnosis of probable atypical pneumonia was made, which was confirmed with positive urinary serology for *Legionella pneumophila* and treatment with appropriate antibiotics was started. A real-time PCR test for influenza A and B was negative at 72 h. The patient made a slow but full recovery and was discharged after 14 days.

BACKGROUND

During the present H1N1 (swine flu) pandemic, local and national healthcare organisations have attempted to write protocols for the diagnosis and management of this condition.^{1 2} However, the symptoms of swine flu are protean and the differential diagnosis for such cases is wide. Rapid influenza direct testing (RIDT) is described as being highly sensitive and specific for detection of swine flu. However, in this case, the false positive test result led to an initial misdiagnosis and, therefore, a delay in administering

antibiotic treatment.³ In cases of *Legionella pneumonia*, such delay can be associated with worsened morbidity and mortality.³ We feel this case emphasises the need for vigilance and awareness of alternative diagnosis during the present pandemic.

CASE PRESENTATION

A 59-year-old man presented to the accident and emergency department with a 6-day history of 'flu-like symptoms'—hot/cold sweats and high fever. For 3 days

Figure 1 Chest x-ray on admission.

prior to admission, he also complained of breathlessness, productive cough, palpitations and diarrhoea. He gave a history of foreign travel to Portugal approximately 12 weeks previously.

Initial observations showed a pyrexia of 40.2, SpO₂ 93% on room air, respiratory rate 25/min, heart rate 170 bpm, blood pressure 110/70 mm Hg. Bibasal crepitations were present on chest auscultation with dullness to percussion at the right base. An ECG confirmed atrial flutter with a rapid ventricular response. The chest x-ray showed widespread pulmonary infiltrates (figure 1).

The patient was given a stat dose of metoprolol intravenously and subsequently reverted to sinus rhythm. Oral beta blocker was maintained thereafter.

Swine flu was diagnosed on the basis of symptoms and a positive RIDT. Initial treatment was with oseltamivir 75 mg twice daily and the patient moved to an isolated side room as per hospital infection policy.

On review 24 h later, a diagnosis of probable atypical pneumonia was made and treated with rifampicin and clarithromycin initially pending the result of a urinary legionella antigen (subsequently positive). A real time PCR test for swine flu was negative at 72 h. Oseltamivir was discontinued. His antibiotics were subsequently changed to ciprofloxacin when his liver function tests became abnormal. On further questioning, the patient gave a history of recently cycling to work for 3 weeks prior to his presentation. On arriving, he would shower in the work's changing rooms—a facility that was not widely used. Suspecting this as the source of his infection, Public Health and the occupational health at the patient's work were informed. Culture of the shower heads at his work revealed growth of *Legionella pneumophila* serogroup 1, monoclonal antibody subgroup 'Benidorm', identical to the serogroup isolated from the patient. The patient continued to spike a high pyrexia intermittently, but this gradually resolved and he made a full but slow recovery and was discharged at 14 days.

INVESTIGATIONS

Chest X-ray: widespread pulmonary infiltrates; ECG: atrial flutter with rapid ventricular response; echocardiography: normal left ventricular systolic function, no pericardial effusion, normal valves; positive RIDT: Remmel X-pect Flu A&B rapid testing kit; real time PCR influenza A and B: negative; legionella urine rapid test: positive; and *Legionella pneumophila* serotype 1 antigen test: positive.

DIFFERENTIAL DIAGNOSIS

Community acquired pneumonia of alternative aetiology.

TREATMENT

Initial treatment was with oseltamivir 75 mg twice daily, metoprolol 5 mg intravenously and 50 mg orally stat—atrial fibrillation reverted to sinus rhythm and subsequent treatment was bisoprolol 5 mg once daily and enoxaparin 40 mg once daily subcutaneously.

Subsequent treatment with rifampicin 600 mg twice daily orally and clarithromycin 500 mg twice daily (intravenously) subsequently changed to ciprofloxacin 500 mg twice daily.

OUTCOME AND FOLLOW-UP

Recovery, with discharge at 14 days. Well at 6 weeks' follow-up. Now back at work.

DISCUSSION

The current recommendations from the Health Protection Agency for diagnosing pandemic H1N1 influenza are solely based on clinical suspicion.⁴ The clinical diagnostic criteria are found in box 1.

Box 1. Health Agency guidelines⁴

- ▶ Fever (pyrexia > 38C) or a history of fever
- ▶ AND
- ▶ Influenza-like illness, classified as >2 of the following symptoms:
 - ▶ Cough; sore throat; rhinorrhoea; limb or joint pain; headache; vomiting or diarrhoea
- ▶ OR
- ▶ Severe and/or life-threatening illness suggestive of an infectious process.

These symptoms are obviously not specific to influenza. Current recommendations advise that further confirmatory testing in the community is unnecessary unless hospital admission is required.⁵ Beyond clinical diagnosis, RT-PCR is the gold standard laboratory test for confirmation of influenza A, but this has a turnaround time of 48–96 hours.^{6,7}

For early diagnosis and appropriate isolation of suspected cases in patients admitted to hospital, rapid influenza antigen testing is now available and recommended by WHO.⁸

In our institution, potential swine flu cases are immediately swabbed using the Remmel X-pect Flu A&B (REMEL Inc, Lenexa, KS, USA) rapid testing kit.^{9–11} This result is available in 15 min and positive results are sent for confirmation using PCR. To date, studies have suggested a very high sensitivity (78–97.8%) and specificity (95–100%).^{9–11} However, in this patient's case, the result proved to be a false-positive. We believe this case describes one of the first reports of a false-positive result with this assay. At the time of submission we are aware of an isolated case of *Legionella pneumonia* misdiagnosed as swine flu publicised on the internet but not yet as a case report. Other reports describe misdiagnosis of meningitis during an influenza pandemic and the role of decision support algorithms.^{12–14} These cases have all been in the community and in patients who have been diagnosed on a clinical basis without recourse to laboratory or point of care rapid testing. We are unaware of any report describing a positive rapid care test for swine flu with a subsequent negative real-time PCR test that has manifested *Legionella pneumonia*.

Both morbidity and mortality in *Legionella* infection are adversely affected by delayed treatment.³ We believe that this patient's initial misdiagnosis as a case of H1N1 influenza A was largely due to the protean nature of the presenting symptoms and a positive rapid swab test (in keeping with current guidelines.) Therefore, commencement of appropriate antibiotic treatment was delayed, although fortunately in this instance the patient made a full recovery. We feel that this case emphasises the need for vigilance during the influenza pandemic.

Table 1 Comparison of available influenza diagnostic tests⁷

Influenza diagnostic tests	Method	Availability	Typical processing time	Sensitivity for 2009 H1N1 influenza	Distinguishes 2009 H1N1 influenza from other influenza A viruses?
Rapid influenza diagnostic tests	Antigen detection	Wide	0.5 h	10–70	No
Direct and indirect immunofluorescence assays	Antigen detection	Wide	2–4 h	47–93	No
Viral isolation in tissue cell culture	Virus isolation	Limited	2–10 days	–	Yes
Nucleic acid amplification tests (including rRT-PCR)	RNA detection	Limited	48–96 h (6–8 h to perform test)	86–100	Yes

Learning points

- ▶ The symptoms of swine flu are non-specific and common to many other conditions associated with a systemic inflammatory response.
- ▶ Be aware of differential diagnosis in patients admitted to hospital with 'swine flu' and investigate appropriately.
- ▶ Rapid point of care testing is a useful clinical adjunct but is an imperfect test.
- ▶ The gold standard test for influenza is real time PCR.

Competing interests None.

Patient consent Obtained.

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