Legionella pneumonia presenting with bilateral flank pain, hyponatraemia and acute renal failure

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Abstract

Legionnaires' disease (LD) is an often overlooked but a possible cause of sporadic community acquired pneumonia. High fever, cough and gastrointestinal symptoms are non-specific symptoms. Hyponatremia is more common in LD than pneumonia linked with other causes. A definitive diagnosis is usually confirmed by culture, urinary antigen testing for *Legionella* species. Macolide or quinolone antibiotic is the treatment of choice. We describe a case of Legionella pneumonia presenting with high fever, bilateral flank pain and oliguria. It is important for clinicians to be aware of this diagnosis when managing patients with flank pain. The case highlights the problems in differentiating LD from renal colic and the importance of proper history, physical examination with laboratory tests for appropriate management.

Introduction

Legionnaires' disease is a type of pneumonia caused by *Legionella* bacteria. The bacterium was first identified in 1976 after many people at an American Legion convention in Philadelphia suffered an outbreak of this disease. To date, there are at least 48 species and 70 serogroups of *Legionella* species in environment.¹ Risk factors for community-acquired and travel-associated legionellosis include old age, male sex, smoking, alcoholism, diabetes, chronic lung disease, malignancy, end-stage renal disease, immunosuppression and HIV/AIDS. There are between 120 and 200 cases each year in the U.K.² The classic presentations of LD include malaise, myalgia, anorexia, diarrhea, weakness, cough, confusion and headache. Distinctive features of LD include headache, diarrhoea, arthralgia or myalgia, confusion, fever, purulent sputum, hyponatremia, hepatic dysfunction, creatine phosphokinase elevation, hypophosphatemia, proteinuria and hematuria. Occasionally patients may present with predominantly gastrointestinal, urological

and neurological symptoms. However, pulmonary manifestation is the most common clinical presentation.³ A rapid test that detects *Legionella* antigens in the urine has a sensitivity of 80% and specificity in excess of 95%.⁴ Appropriate medical treatment has a major impact on recovery. We report a patient who presented with flank pain. Due to misinterpretation of clinical presentations and laboratory results, the diagnosis was delayed.

Case report

A 44-year-old man presented with a 7-day history of bilateral loin pain, fever, sweating, rigors, headache and general malaise.

Two days prior to admission, he attended the Accident and Emergency Department (A & E) with dysuria and frequency. His clinical examination, including chest, was normal. Urine on dipstick analysis revealed leucocytes and blood. He was discharged on a course of trimethoprim for a suspected urinary tract infection (UTI).

He was admitted to a urology ward with bilateral flank pain for further investigation. His medical history included mild asthma. His initial assessment revealed oxygen saturations of 94%, slight tachycardia at 97/minute. On admission, he was pyrexial (38.6°C), respiratory rate was 24/min and blood pressure was stable at 132/75 Hg. Clinical examination revealed tenderness bilaterally in the lumbar region and supra-pubic area. Chest examination showed only some scattered wheeze and good air entry. No other remarkable findings were found.

His preliminary blood results were recorded (Table 1). His urine dipstick was positive for nitrates in his blood and protein. Mid-stream urine (MSU) collected at the A & E was negative. A routine electrocardiogram showed sinus rhythm with no abnormality and chest x-ray was unremarkable. The initial diagnosis of an ongoing UTI with pyelonephritis was made. He was treated with intravenous fluids to correct his dehydration, antibiotics, analgesia and anti-emetics and a renal ultrasound scan was requested.

Table 1. Serial laboratory data of patient

Blood test	Normal range	On admission	Day 1	Day 2	Day 5	Day 7	Day 9	Day 11
Hemoglobin	13-18 g/dL	14.3	13.6	12.8	12.5	12.7	13.8	13.5
White cell count	4-11 10 ⁹ /L	6.9	4.81	4.96	14.30	10.4	9.15	9.8
Platelets	135-400 10 ⁹ /L	122	148	203	244	251	232	223
Neutrophils	2-7.5 10 ⁹ /L	5.97	3.73	4.23	11.4	7.59	5.99	6.69
Lymphocytes	1.5-4.0 10 ⁹ /L	0.54	0.71	0.43	1.94	1.79	2.24	2.42
Sodium	136-145 mmol/L	123	128	136	140	140	138	136
Potassium	3.5-5.1 mmol/L	3.9	3.9	4.8	4.0	4.8	4.3	4.3
Urea	2.5-7.0 mmol/L	23.1	14.7	7.8	6.7	5.8	7.2	6.3
Creatinine	60-120 µmol/L	332	180	85	88	94	103	102
Albumin	35-50 g/L	28		20	26	29	33	31
Alkaline phosphatase	40-120 u/L	167		197	271	303	316	233
Alanine transaminase	0-56 u/L	86		72	428	596	540	274
Bilirubin	0-22 µmol/L	8		7	9	9	10	7
Amylase	23-125 u/L	62						
C-reactive protein	0-9 mg/L	414	138	<5				
Ferritin	20-300 µg/L				2490	2168	1062	

Few hours after admission, he became agitated and short of breath. His oxygen saturations dropped to 84% and his chest sounded wheezy, but otherwise his vital signs were stable. The patient's condition improved after he was given 6 L of oxygen and salbutamol nebulizers. A second MSU showed protein and granular casts and no growth. A renal ultrasound scan demonstrated normal size, non-hydronephrotic kidneys with normal shape and echotexture and no evidence of renal tract calculi. In view of negative ultrasound findings, a medical review was requested. The medical team made a diagnosis of urinary sepsis, either post-strep glomerular nephritis or inflammatory nephritis. An urgent chest x-ray and arterial blood gas were requested and the routine bloods were repeated. Further investigations were requested including: Ig, ANCA, RhF, ANA, GBM, HBV, HCV, a throat swab, and catheter urine specimen and blood cultures. Blood gas results revealed arterial blood pH 7.48, pO₂ 9.4 kPa, HCO₃⁻ 18 mmol/L, BE -3 mmol/L, and pCO₂ 3.3 kPa while he was on 6 L of oxygen. The repeat full blood count and urea and electrolytes results were normal, apart from serum sodium of 123 mmol/L and creatinine of 260 µmol/L.

He continued to complain of difficulty in breathing, and became more short of breath in the afternoon, with left pleuritic chest pain, which he admitted was the same pain he had presented with. He had a temperature of 40.3°C, oxygen saturations was 90% on 4 L of oxygen, a blood pressure of 105/80 mm Hg, and a heart rate of 80 pulse/min. The chest examination revealed left basal rhonchi with widespread coarse crackles throughout his left lung. A repeat blood gas on 15 L of oxygen analysis showed a pH 7.45, pCO₂ 3.3 kPa, pO₂ 15.3 kPa, HCO₃⁻ 17 mmol/L, and BE -5 mmol/L. The medical team made a clinical diagnosis of community

acquired pneumonia. Additional investigations included sputum sample, culture and polymerase chain reaction (PCR) for Legionella and urine sample for legionella and pneumococcal antigen. The chest x-ray showed significant left upper lobe consolidation and the patient was taken over by the respiratory team.

He was transferred to the respiratory ward. Further management included adding clarithromycin, while continuing cefotaxime. The diagnosis of LD was confirmed by legionella Ag in the urine 10 days after admission. The patient also reported that he recently traveled to London and stayed in a hotel; the hotel was contacted and the case was reported.

Discussion

The differential diagnosis for the patient's symptoms is wide, including musculoskeletal, mechanical, kidney calculus/obstruction, pneumonia, testicular torsion, prostatitis and fibromyalgia. Abdominal pain with pneumonia is a type of referred pain and it occurs in 23% of patients with this disease.⁵

This case illustrates that patients do not always present in a classical manner and a wide list of differentials should be considered, especially when there are some unknown factors. Looking at the initial investigations, we found that he was hyponatraemic for which there was no explanation. His oxygen saturation was low on admission, particularly potentially serious in a young asthmatic patient, which was essentially ignored. A red herring to complicate matters further was the granular casts in his urine; this was highly suggestive of renal disease. After further investigations, the diagnosis had still not been reached. Initially, it was thought

that he had a urological problem because he was experiencing loin pain with a history of a possible UTI which would be consistent with pyelonephritis. However, a UTI in a young male is unlikely. The renal impairment suggested that an obstructive uropathy may have been responsible, but a normal renal ultrasound scan rules this out.

This educational case suggests that, in a young patient, acute flank pain, fever, chest symptoms, hyponatremia and normal kidney size on ultrasound may suggest a wrong diagnosis of urolithiasis or pyelonephritis.

Legionnaires' disease is caused by *Legionella* species, which are Gram-negative bacteria, which typically spread in the warm environment of air conditioning systems. *Legionella* species are responsible for 1% to 5% of cases of community-acquired pneumonia (CAP).^{3,4,6} It has a high mortality with a fatality between 10 and 15%.⁷ Some cases of Legionnaire's disease are sporadic and some are related to outbreaks.

The clinical manifestations of LD are nonspecific and are similar to those of an atypical pneumonia. The incubation period is 2 to 10 days after exposure. The onset is often acute and starts with non-specific symptoms, including fever, malaise, headache, diarrhea cough and confusion. Diarrhea may cause hyponatremia because of the loss of sodium and water. Other abnormalities include hepatic dysfunction, hypophosphatemia, thrombocytopenia, hematuria and moderate elevation of serum levels of creatine kinase.⁸ A Winthrop-University Hospital (WUH) scoring system was developed to diagnose LD (Table 2).⁹ This is a weighted point score system for the presumptive clinical diagnosis of LD (legionella CAP probability); more than 15 points indicates that legionella is very likely, 5 to 10 points indicate that legionella is likely, and less than 5 points indicates that legionella is an unlikely cause of CAP. Our patient score was 37, suggesting very likely diagnosis of LD. In a recent article, Cunha and colleagues suggested that the diagnosis of LD should be considered in hospitalized adults with CAP with extrapulmonary findings and relative bradycardia, accompanied by any three of the following symptoms (otherwise unexplained relative lymphopenia, early/mildly elevated serum transaminases (SGOT/SGPT), highly increased ferritin levels ($\geq 2 \times n$) or hypophosphatemia). The diagnostic LD triad provides clinicians with a rapid way to clinically diagnose LD, pending legionella antigen test results.¹⁰

Gupta and colleagues reported 78% to 87% sensitivity and 50% to 65% specificity for the WUH score in diagnosing LD.¹¹ Miller suggested that within 24 hours of admission, any three of the following four features are strongly suggestive of LD: (1) prodromal "viral" illness; (2) dry cough or confusion or diarrhea; (3) lymphopenia without marked neutrophilia; and (4) hyponatremia.¹²

Sopena and colleagues showed that male sex and chronic lung disease prevailed in sporadic cases and that these

patients were more likely to present with respiratory symptoms and blood chemistry alterations, including hyponatremia, raised urea and a low oxygen partial pressure.¹³ Despite the patient's recent hotel stay, he had many of the features of sporadic Legionellosis.

Once pneumonia was diagnosed, the appropriate diagnostic tests were sent, including culture, PCR and the urine antigen. A study to assess the sensitivity of legionella detection after initiation of antibiotic therapy found that respiratory samples of legionella PCR should be obtained before or early after initiating antimicrobial therapy otherwise it limits the assay.¹⁴ However, LD has a high mortality and there should be no delay in starting antibiotics even before a definite diagnosis has been made. Erythromycin has been the treatment of choice, although fluoroquinolones have been found to be as effective and have been associated with shorter hospital stay.¹⁵

Conclusion

Since prompt diagnosis of LD, especially the non-pneumophila species, is extremely difficult, alertness to this diagnostic option and early empirical initiation of appropriate aggressive antibiotic treatment is critical. Awareness of the threat of LD must be maintained among clinicians and hospital epidemiologists because it is unlikely that the problem of nosocomial LD will disappear.

Since the clinical presentation of LD is nonspecific, a definitive diagnosis can be delayed. The triad suggested by Cunha and colleagues may help in early identification.¹⁰ This case illustrates the importance of considering non-renal causes in the differential diagnosis of flank pain. Critical analyses of clinical presentations, good physical examination coupled with methodical assessment of blood results are vital. Due to diagnostic difficulties, *Legionella* might be the cause of CAP, and empiric anti-legionella treatment should be included in the initial management of all patients with CAP requiring in-patient treatment.¹⁶ In this case, low oxygen saturation, hyponatremia and granular cast in the urine were unexplained and this resulted in some delay in correct diagnosis.

Competing interests: None declared.

This paper has been peer-reviewed.

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Table 2. Adapted from Winthrop-University Hospital Infectious Disease Division's weighted point system for diagnosing Legionnaires' disease†

	Qualifying conditions	Point score	Illustrative case's point score
Clinical features			
Temperature >102°F*	With relative bradycardia	+5	+5
Headache	Acute onset	+2	
Mental confusion/lethargy*	Not drug induced	+4	+4
Ear pain	Acute onset	-3	
Non-exudative pharyngitis	Acute onset	-3	
Hoarseness*	Acute not chronic	-3	
Sputum (purulent)	Excluding AEBCB	-3	
Hemoptysis	Mild/moderate	-3	
Chest pain (pleuritic)		-3	-3
Loose stools/watery diarrhea*	Not drug induced	+3	
Abdominal pain*	With/without diarrhea	+1	+5
Renal failure*	Acute (not chronic)	+3	+3
Shock/hypotension*	Excluding cardiac/pulmonary causes	-5	
Splenomegaly	Excluding non-CAP causes	+5	
Lack of response to β-lactam antibiotics	After 72 h (excluding viral pneumonias)	+5	
Laboratory features			
Chest x-ray	Rapidly progressive asymmetric infiltrates (excluding severe influenza/SARS)*	+3	+3
↓ pO ₂ with ↑ A-a gradient (>35)*	Acute onset	-5	
↓ Na ⁺	Acute onset	+1	+1
Hypophosphatemia	Acute onset	+5	
↑ SGOT/SGPT (early, mild/transient)*	Acute onset	+2	+2
↑ Total bilirubin	Acute onset	+1	
↑ LDH (>400)*	Acute onset	-5	
↑ CPK	Acute onset	+4	
↑ CRP (>30)	Acute onset	+5	+5
↑ Cold agglutinins (≥1:64)	Acute onset	-5	
Severe relative lymphopenia (<10%)*		+5	+5
↑ Ferritin (>2 × n)		+5	+5
Microscopic hematuria*	Excluding trauma, BPH, Foley catheter, bladder/renal neoplasms	+2	+2
Likelihood of legionella		Patient's point score	
Total point score		37	
		>15 Legionella very likely	
		5–15 Legionella likely	
		<5 Legionella unlikely	

AEBCB: acute exacerbation of chronic bronchitis; BPH: benign prostatic hyperplasia; SARS: severe acute respiratory syndrome; SGOT/SGPT: serum glutamate oxaloacetate transaminase/serum glutamate pyruvate transaminase; LDH: lactate dehydrogenase; CPK: creatine phosphokinase; CRP: C-reactive protein. *Otherwise unexplained (acute and associated with the pneumonia). †In adults, otherwise unexplained, acute and associated with the pneumonia.

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