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Procalcitonin in severe acute respiratory syndrome (SARS)

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KEYWORDS
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Summary *Objective and methods.* The role of procalcitonin (PCT) in severe acute respiratory syndrome (SARS) has not been highlighted so far. We described retrospectively eight cases of sepsis from pneumonia of various microbiological aetiologies including two due to SARS, compared their PCT concentrations and provided further descriptors of SARS as a viral pneumonia.

Results. Like any viral pneumonia, patients with SARS had low PCT levels in contrast to bacterial or fungal pneumonia.

Conclusions. In the setting of pneumonia with a finding of low PCT, testing for SARS should be considered, especially if there is a positive travel or contact history. During a SARS epidemic, we also strongly advocate isolating all suspected community acquired pneumonia with a low PCT level.

Introduction

Procalcitonin (PCT) is a recently described innovative marker of severe sepsis.[1] Concentration increases in bacterial infections but remains low in viral infections making it a useful marker for distinguishing between bacterial and viral infections.[2,3] Severe acute respiratory syndrome (SARS) had been documented to be due to a novel coronavirus which has caused a rapidly progressive pneumonia in all age sectors in an epidemic manner with high fatality rate.[4,5] Rapid and accurate diagnostic tools are critical in the management of this potentially fatal disease. There are limitations to the current existing diagnostic tools. A low PCT level may provide an additional useful case definition to this deadly viral pneumonia.

Method and materials

PCT concentrations were measured for patients on admission to our medical intensive care unit (MICU) for severe sepsis from community-acquired pneumonia according to the American College of Chest Physicians/Society of Critical Care Medicine criteria. These patients presented during the peak SARS outbreak period in our country from March to July this year. In vitro PCT levels were measured in serum samples by use of KRYPTOR immunoanalyser (DYAMED Biotech) available in a service laboratory

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Table 1 Summary of case series

Case no.	Age (yr)/ gender	Comorbidities	Diagnosis	Radiological finding	Microbiology results	PCT level (ng/ml)	Mechanical ventilation[a]
1	71/Female	Diabetes, autoimmune hypothyroidism	SARS	Bilateral lower lobe ground glass opacification	Nasopharyngeal aspirate SARS-CoV RT-PCR and anti-SARS-CoV Ig G titer positive	0.11	Yes
2	43/Female	Hypertension	SARS	Bilateral lower lobe consolidations	See[b]	0.74	Yes
3	65/Male	Gastric non-Hodgkin lymphoma 2001 with gastrectomy and chemotherapy	*Klebsiella pneumonia*	Airspace shadowing in right mid and upper zones	Sputum and blood cultures positive for *Klebsiella pneumoniae*	All >10, highest 27	Yes
4	76/Male	None	Pulmonary tuberculosis	Bilateral patchy fluffy infiltrate with cavitation	AFB smear positive	5.42	Yes
5	33/Male	Type 1 diabetes on insulin, melioidosis with meningitis and osteomyelitis 2002	Melioidosis	Multilobar consolidations	Blood and respiratory cultures positive for *Burkholderia pseudomallei*	79.24	Yes
6	55/Male	Renal transplant 1988	PCP pneumonia[c]	Bilateral diffuse groundglass consolidation predominantly in the perihilar regions	Bronchoalveolar lavage cytology positive for PCP	2.58	Yes
7	47/Male	Bronchial asthma, newly diagnosed HIV positive	? CMV[d] pneumonia	Fine alveolar infiltrate in the perihilar regions bilaterally	Low grade CMV viraemia. Bronchoscopic lavage negative	0.07	No
8	45/Female	Migraine	*Mycoplasma pneumonia*	Infiltrate in left mid lung field obscuring left cardiac border	Significant rise in serum mycoplasma titre	<0.06	No

[a] Mechanical ventilation was indicated for severe type 1 respiratory failure from acute respiratory distress syndrome or severe pneumonia.
[b] All investigations were negative. Postmortem was not performed due to possible high infectious risk. Diagnostic kit for coronavirus was also not available in our hospital at that time. However, we think she likely had SARS as a healthcare worker who had performed a bronchoscopic lavage on her fell ill 3 days after the contact and was subsequently confirmed to have SARS serologically.
[c] Pneumocystis carinii pneumonia.
[d] Cytomegalovirus.

at National University Hospital, Singapore. The upper limit of normal was 0.5 ng/ml.

Results

All patients with viral pneumonia including two patients with SARS had low PCT level of less than 1 ng/ml (Table 1). In contrast, PCT concentrations were raised in bacterial and fungal neumonia with the exception of mycoplasma pneumonia.

Discussion

Procalcitonin, a 14-kDa protein encoded by the

Calc-1 gene along with calcitonin and kataclacin, is an innovative diagnostic parameter with kinetics different from other presently available indicators of the inflammatory response.[6] In the animal model, hyperprocalcitoninemia was an early systemic marker of sepsis which correlated closely with severity of acute illness and mortality.[7] Studies of its behavior in patients with bacterial sepsis have found it to be a useful marker of systemic bacterial infection, with greater specificity and sensitivity than acute phase proteins such as C-reactive protein, interleukin-6 and lactate levels even in a medical intensive care unit setting.[8,9]

The excellent specificity and negative predictive value at a cut-off point of 0.5 ng/ml suggests that this test might be a useful parameter in the management of infectious diseases.[10] PCT can help to identify an infectious cause or complication in patients with systemic inflammatory response syndrome (SIRS).[11] It has also been used to distinguish infectious from non-infectious causes of acute respiratory distress syndrome (ARDS).[12] It is moderately increased in local bacterial infection (pneumonia, pyelonephritis), parasitic and fungal infections and is unchanged or only slightly increased in even severe viral infections.[13–18] A serum PCT level of <0.4 ng/ml accurately rules out the diagnosis of bacteraemia.[19] Children with bacterial pneumonia had significantly higher PCT than those with sole viral aetiology.[20] PCT has also similarly high diagnostic value in both immunosuppressed and non-immunosuppressed patients with sepsis or severe infections.[21–23]

SARS is an emerging infectious disease by a novel coronavirus—SARS-CoV which is associated with pneumonia with global impact.[24] It is notable that nearly 40% of the patients developed respiratory failure that required assisted ventilation. In the ICU setting, SARS is essentially ARDS plus intensified respiratory isolation.[25] The clinical presentation and radiologic features of SARS bear some resemblance to the syndrome commonly referred to as 'atypical pneumonia'. The high incidence of altered liver function, leucopenia, severe lymphopenia, thrombocytopenia, and subsequent evolution into adult respiratory distress syndrome suggest a severe systemic inflammatory damage induced by this human pneumonia-associated coronavirus.[26] The constellation of absence of upper respiratory symptoms, the presence of dry cough, and minimal auscultatory findings with consolidations on chest radiographs may alert the clinician to the possible diagnosis of SARS. However, the clinical and radiographic characteristics of atypical pneumonia are not useful in differentiating these pathogens from usual bacterial pathogens such as *S. penumoniae* and *H. influenzae*. Clinical diagnosis also becomes particularly problematic once the association with travel or case contact is lost. The difficulty of making a firm diagnosis until chest radiographic changes appear has important implications for healthcare personnel and for surveillance.

Early diagnosis by virus isolation or serological testing is essential to halt the spread of SARS. Rapid diagnosis of SARS for infection-control measures and potential treatment will require very sensitive and specific methods. There is still no reference standard (gold standard) test for SARS. Three diagnostic tests are currently available, but all with their limitations.[27,28]

We have reported two cases of patients with SARS and low PCT levels. This is consistent with the current evidence that SARS is just another viral pneumonia. High initial levels of PCT may be used to exclude SARS to a certain degree of accuracy whereas low PCT in relevant clinical context may prompt further testing for SARS. We recommend that PCT concentrations be determined for every patient presenting with community-acquired pneumonia.

Conclusions

In the setting of pneumonia with a finding of low PCT, with or without a positive contact history for SARS or relevant travel history, testing for SARS should be considered. This may be an additional screen to help narrow the number of patients that require specific SARS testing. However, the true validity of this test requires further prospective testing.

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