Q Fever Pneumonia in Southwest Germany: Radiographic and Clinical Findings

Q-Fieber-Pneumonie im Südwesten Deutschlands: Radiologische und klinische Befunde

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Bibliography

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ZUSAMMENFASSUNG

Ziel Q-Fieber ist eine weltweit vorkommende Zoonose, deren klinisches Bild von milden Erkältungssymptomen bis hin zur schweren Pneumonie und Hepatitis reichen kann. Diese retrospektive Arbeit untersucht die radiologischen und klinischen Befunde bei Patienten mit akuter Q-Fieber-Pneumonie im Südwesten Deutschlands.

Patienten und Methoden Vierzig Patienten mit IgM-positiver Q-Fieber-Pneumonie die in den Jahren von 2006 bis 2016 in unserem Krankenhaus behandelt wurden, konnten retrospektiv identifiziert werden. Neben den klinischen Daten wurden die Labordaten analysiert. Die Röntgen-Thorax-Aufnahmen wurden von zwei Radiologen anhand eines standardisierten Protokolls beurteilt.

Ergebnisse Frauen und Männer waren etwa gleich häufig betroffen. Das mittlere Alter lag bei 44,9 ± 15,7 Jahren. Ungefähr die Hälfte der Patienten (45 %) erwarb die Infektion im zweiten Quartal des Jahres. Die Hauptbeschwerden waren Fieber, Husten und Dyspnoe. Während die Leukozytenzahl bei den meisten Patienten nicht erhöht war, zeigte sich eine deutliche CRP-Erhöhung. Eine Q-Fieber assoziierte Hepatitis fand sich bei 63 % der Patienten. Die vorwiegende radiologische Veränderung, die alveoläre Verschattung, zeigte sich bei 27 (82%) der Patienten. Der typische Röntgen-Thorax-Befund war eine einzelne segmentale Verschattung, allerdings fanden sich auch mehrere segmentale oder fleckförmige Verschattungen. Ein lobäres Infiltrat fand sich nur bei 2 (6%) Patienten.

Schlussfolgerung Einseitige, nur einen Lappen betreffende segmentale Verschattungen sind die typischen radiologischen Befunde bei der Q-Fieber-Pneumonie. Da diese Veränderungen aber auch bei anderen Pneumonien auftreten können, ist eine Differenzierung anhand der Thoraxaufnahme nicht sicher möglich. Auf jeden Fall sollte aber bei jüngeren Patienten mit segmentalen Infiltraten die in einem Endemiegebiet leben an eine Q-Fieber-Pneumonie gedacht werden.

Kernaussagen

- Einseitige, auf einen Lappen beschränkte segmentale Verschattungen sind die wichtigsten Befunde bei der Q-Fieber-Pneumonie.
- Lobäre, fleckige sowie multisegmentale Verschattungen können ebenfalls auftreten.
- Die Röntgenthorax Aufnahme erlaubt nicht die Differenzierung von Q-Fieber von anderen Pneumonien.

ABSTRACT

Purpose Q fever is a worldwide zoonosis that causes clinical symptoms ranging from mild flu-like symptoms to severe pneumonia and/ or hepatitis. This retrospective study was conducted to describe the radiographic and clinical signs in patients with acute Q fever pneumonia in Southwest Germany.

Patients and Methods 40 patients with IgM-positive Q fever-related pneumonia who were treated in the years 2006 to 2016 in our hospital were retrospectively identified. Clinical and laboratory data were analyzed. Chest radiographs were reviewed by two radiologists and interpreted using a standardized protocol.

Results Females and males were equally affected. The mean age was 44.9 ± 15.7 years. About half of the patients (45%) acquired their infection in the second quarter of the year. The main complaints were fever, cough and dyspnea. While the white cell blood count was in the normal range in most of the patients, the CRP value was markedly elevated. Q fever-related hepatitis was found in 63% of the patients. Air space opacification was the predominant radiographic sign and was found in 27 of the patients (82%). The typical chest radiographic pattern was a single segmental opacity. However, multiple segmental opacities and patchy opacities were also found. Lobar opacities were found in only 2 (6%) of the patients.

Conclusion Unilobar, unilateral, segmental opacities are the key feature of Q fever pneumonia chest radiographs. Definitive radiographic differentiation from other community-acquired pneumonias is not possible, but Q fever pneumonia should be considered in middle-aged patients with segmental opacities living in an endemic area.

Key points

- Unilobar, unilateral, segmental opacities are the key feature of Q fever pneumonia.
- Lobar and patchy as well as multisegmental opacities are also found.
- Chest radiography does not allow the differentiation of Q fever from other pneumonias.

Introduction

Q fever is a zoonosis with a worldwide distribution that is caused by the bacterium Coxiella burnetii [1]. 25 to 100 cases of Q fever are annually reported in Germany [2] with the highest incidence of the disease in the state of Baden-Württemberg in Southwest Germany. The bacteria are found in feces, urine and milk of infected animals. However, the most important route is the shedding of C. burnetii into the environment during parturition [3]. Humans are infected by the ingestion of unpasteurized milk or milk products or by the inhalation of contaminated dust. The clinical signs of acute infection range from asymptomatic infections and mild flu-like symptoms to severe pneumonia and hepatitis [4]. In 1 – 5% of patients with acute, untreated Q fever, a chronic disease with valvular heart disease, arterial aneurysms and osteomyelitis develops [1]. About 50% of infected patients become symptomatic [5]. The signs and symptoms of acute illness include a flu-like syndrome with fever, cough, myalgia and headaches [6]. The onset is usually abrupt. Q fever-related hepatitis is found in around 85% of patients with an elevation of liver enzymes from 2 to 10 times normal values. There is a high regional heterogeneity in the incidence of Q fever-related hepatitis. While hepatitis is common in Southern Europe, it is infrequent in North America. Hepatitis is more common in younger patients, while pneumonia is more common in older patients [7].

The diagnosis is made using an immunofluorescence assay (IFA) or an enzyme-linked immunosorbent assay (EIA). Blood cultures are typically sterile, since C. burnetii does not grow in routine blood cultures [8]. In very early infections the antibody level might not be detectable or may be very low. In these cases PCR can be used to detect C. burnetii [8].

The reported radiologic findings in patients with Q fever pneumonia on chest radiographs or CT scans vary and the available literature is sparse [9, 10]. To our knowledge, there is no study that systematically describes the radiographic findings of Q fever pneumonia on chest radiographs in Germany.

The purpose of this study is the characterization of patients with Q fever pneumonia and analysis of the findings on chest radiographs in Southwest Germany.

Patients and methods

Between 2006 and 2016, the charts of all patients who were treated for Q fever pneumonia at the Zollernalb Klinikum were retrospectively analyzed. The Zollernalb Klinikum is located in the southern part of Baden-Württemberg, Germany and receives patients from a rural area with approximately 250 000 inhabitants.

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The diagnosis of acute Q fever pneumonia was based on both serologic and clinical criteria. Serology was done using an enzyme-linked immunosorbent assay (EIA, Vireon\Sereon GmbH, Würzburg, Germany). An acute infection was diagnosed if the titer of anti-phase II was ≥ 110 U/ml for IgM or an at least fourfold increase in IgG titers in two consecutive assays. In addition, two or more of the following clinical symptoms had to be present: body temperature > 38 °C, respiratory symptoms (dyspnea, cough, chest pain), pneumonia or hepatitis-like symptoms with a more than two-fold increase in serum levels of alanine and aspartate aminotransferase (AST, ALT levels, respectively). Applying the above mentioned criteria, we identified 40 patients with an acute O fever pneumonia. We were able to retrieve the chest radiographs of 33 patients. In three of the patients an initial CT scan was done and therefore plain X-ray radiographs were not available for analysis. In the remaining patients, chest radiographs were done in other radiologic institutes before admission and we were not able to retrieve the original chest X-ray radiographs.

The chest radiographs were done using a computed radiography (CR) system. The imaging plate (Agfa, CR MD 4.0 cassette) contains a photostimulable phosphor imaging plate. The readout of the imaging plate was done using an Agfa CR 30X system.

All chest radiographs were reviewed by two experienced radiologists (A.B. and M.B.). In the case of discrepancies, the findings were discussed and a consensus was reached. The radiologic findings were analyzed following a standardized protocol: On the basis of the predominant type of parenchymal abnormality, the radiographic patterns were classified as either alveolar or reticular. The number and distribution characteristics of the lesions were assessed. The definition of the air space lesions was as follows: lobar, if one or more lobes were involved; segmental, if one or more segments were affected; patchy, if subsegments of one or more segments were involved. Additional findings like pleural effusion were also assessed.

Results

Patient characteristics are given in ► **Table 1**. The mean age of the patients at presentation was 44.9 years. Females (48 %) and males (52 %) were almost equally affected. Direct and close contact to animals was reported by none of the patients. Half of the patients (50 %) presented with dry cough. Headache or myalgia was present in 23 % and 15 % of patients, respectively. 23 patients (58 %) had a body temperature > 38.5 °C. 30 % of the patients complained of dyspnea. Oxygen saturation of 94 % or below was obtained in 30 % of the patients. About half of the patients (45 %) acquired their infection in the second quarter of the year. The remaining patients acquired their infection almost equally distributed.

Table 1 The table shows the clinical and laboratory data of the 40 patients with Q fever pneumonia. For each parameter the number of patients with values outside the reference range is given. The mean values as well as the standard deviations of these patients are given.

Tab. 1 Die Tabelle zeigt die klinischen und laborchemischen Daten der 40 Patienten mit Q-Fieber-Pneumonie. Für jeden Parameter wurde die Anzahl der Patienten angegeben, bei denen die Werte außerhalb des Referenzbereich lagen. Von diesen Patienten wurden die Mittelwerte und die Standardabweichungen bestimmt.

patients, n=40	patients with pathologic values (n)		reference values
sex (male)		21	
age (years)		44.9 ± 15.7	
body temperature °C	31	38.9±0.8	36.3 – 37.4 °C
white blood cell count (G/I)	7	14.4±4.2	4.2 – 10.8 G/I
oxygen saturation (sO_2) n = 27	9	89.1±3.7	94 – 97 %
C-reactive protein (mg/dl)	40	20.0 ± 10.0	< 0.5 mg/dl
procalcitonin (ng/ml) n = 15	4	2.4 ± 2.3	< 0.5 ng/ml
AST (U/I)	16	109.4 ± 76.7	< 50 U/I
ALT (U/I)	14	144.0 ± 87.0	< 50 U/I
gGT (U/I)	17	115.8 ± 75.9	< 60 U/I
alkaline phosphatase (U/I)	9	233.9±71.6	< 130 U/I

uted in the other three quarters of the year. 25 (63%) of the patients had Q fever-related hepatitis. The white cell count was elevated in only 7 patients (18%). Procalcitonin was measured in 15 patients and was elevated in only 4 patients (27%). In contrast, the levels of C-reactive protein were elevated in all 40 patients. The infection had no impact on platelet count, renal function and liver function (as determined by normal bilirubin and INR levels).

The findings in the three patients in whom initial CT scans of the thorax were performed revealed single consolidations in the left lung in all patients. In one patient there were patchy consolidations in the apex of the left lung, in one patient there were patchy consolidations paracardial, and in the third patient a segmental consolidation in the left lower lobe was seen.

Chest radiographs on admission were available in 33 of the 40 patients. Of the 33 chest radiographs, 2 were without pathological findings.

▶ Table 2 shows the distribution of the affected lobes. In the majority of patients, the lower lobes were affected (70%). The left lung was more affected than the right lung, 48% and 30%, respectively. Involvement of both lungs was seen in 5 patients (15%).

The radiographic patterns are given in \triangleright **Table 3**. Air space opacification was the predominant sign and was found in 27 of the patients (82 %). Mass-like changes (\triangleright **Fig. 1**) were found in 3 of the patients (9%). In the majority of patients only one lobe was affected (70%). 2, 3, 4 and all 5 lobes were affected in 12%, 6%, 3% and 3% of the patients, respectively. 23 of the patients had a segmental pattern (\triangleright **Fig. 2**, 70%), 5 patients (15%) had patchy changes (\triangleright **Fig. 3**) and 2 patients (6%) had a lobar infiltrate (\triangleright **Fig. 4**). Micronodular as well as reticular changes were seen in none of the patients. Pleural effusions (\triangleright **Fig. 1**) were found in 4 patients (12%).

Table 2 The table shows the affected lobes in the 33 patients with Q fever pneumonia for whom the chest radiographs were available.

► Tab. 2 Die Tabelle zeigt die betroffenen Lungenlappen der 33 Patienten mit Q-Fieber-Pneumonie bei denen eine Röntgenthoraxaufnahme vorlag.

affected lobe	n	%
right upper	8	24%
right middle	6	18%
right lower	8	24%
left upper	9	27%
left lower	15	45 %

Discussion

In our paper, we describe the clinical, radiologic and laboratory findings of patients with Q fever pneumonia in Southwest Germany. Whereas three studies described a male preponderance [11 – 13], Caron et al. [14] described a male-to-female ratio of 1:3.4. In contrast to these authors, we did not find any gender-specific preponderance but rather a balanced female-to-male ratio. Our laboratory findings are consistent with the data of other groups who reported a normal white cell count in most of the patients with Q fever pneumonia [3, 8, 15] whereas the CRP values were markedly elevated in the patients. In contrast, the mean procalcitonin (PCT) levels were only slightly elevated. Unfortunately, the PCT levels were available in 16 patients only. Of these patients, two had markedly elevated PCT levels and the remaining patients had normal or almost normal PCT levels. It remains unclear why

Table 3 The table shows the radiographic pattern of 33 patients with Q fever pneumonia.

Tab. 3 Die Tabelle zeigt die radiologischen Befunde der 33 Patienten mit Q-Fieber-Pneumonie.

radiographic pattern	patients (n)	%
air space opacities	27	82 %
 lobar 	2	6%
 segmental 	23	70%
 patchy 	5	15%
nodular findings	2	6%
 micronodular (0.5 – 0.9 cm) 	0	0 %
 macronodular (1.0 – 2.9 cm) 	0	0 %
■ mass-like (≥ 3 cm)	3	9%
reticular findings	0	0 %
pleural effusion	4	12%



▶ Fig. 1 Posteroanterior chest radiograph of a 22-year old man presenting with a 10-day history of fever and cough. IgM titer against C. burnetii was 306 and IgG was 207 U/ml. These findings make an infection of more than two weeks likely. The radiograph shows a pleural effusion that was later diagnosed as pleural emphysema and a mass-like lesion in the right middle lobe.

▶ Abb. 1 Posterior-anteriorer Röntgen-Thorax eines 22-jährigen Mannes der sich mit Fieber und Husten seit 10 Tagen vorstellte. Der IgM Titer gegen C. burnetii war 306 und IgG betrug 207 U/ml. Dies lässt auf eine Infektion die länger als zwei Wochen geht schließen. Die Aufnahme zeigt einen Pleuraerguss, der laborchemisch einem Emphyem entsprach sowie eine solide Läsion im rechten Mittellappen.



▶ Fig. 2 Chest radiograph of a 64-year-old man presenting with fever and cough. IgM titer against C. burnetii was >500. The posteroanterior view shows a segmental opacity in the lingula.

 Abb. 2 Röntgenthorax eines 64-jährigen Mannes der sich mit Fieber und Husten vorstellte. Der IgM Titer gegen C. burnetii war
 500. Die posterior-anteriore Ansicht zeigt eine segmentale Verschattung in der Lingula.



▶ Fig. 3 Chest radiograph of a 32-year-old woman presenting with fever, myalgia and headache. IgM titer against C burnetii was > 500. The posteroanterior view shows patchy infiltrates in all five lobes.

Abb. 3 Röntgen-Thorax einer 32-jährigen Frau, die sich mit Fieber, Myalgien und Kopfschmerzen vorstellte. Der IgM Titer gegen C. burnetii war > 500. Die posterior-anteriore Ansicht zeigt fleckige Infiltrate in allen fünf Lappen.



▶ **Fig. 4** Chest radiograph of a 21-year-old man presenting with fever and cough. IgM titer against C burnetii was 394. The postero-anterior view **a** as well as the lateral view **b** show a lobar infiltrate in the middle lobe.

Abb. 4 Röntgen-Thorax eines 21-jährigen Mannes, der sich mit Fieber und Husten vorstellte. Der IgM Titer gegen C. burnetii betrug 394. Die posterior-anteriore Ansicht a sowie das Seitbild b zeigen ein lobäres Infiltrat im Mittellappen.

Q fever – in contrast to other bacterial pneumonias –is not associated with an increase in the white cell count and PCT in most patients. Hence, we conclude that PCT and the white cell count are not valuable markers in the diagnosis of Q fever pneumonia. In addition, and in line with a large retrospective study from the Netherlands [15], we did not find an abnormal platelet count nor did we find an abnormal creatinine level. As expected, more than half of our patients had elevated liver enzymes as an indicator of Q fever-related hepatitis. This is described by several other authors [3, 14, 16, 17]. The presence of elevated liver enzymes in patients with acute Q fever shows a regional heterogeneity with a high percentage in southern Europe and a low percentage in North America. Our results are strengthened by the results of the retrospective analysis from the Netherlands [15] that compared patients with Q fever pneumonia to patients with pneumonia from other pathogens. Even though they found elevated liver enzymes in both groups, liver enzymes were significantly higher in the Q fever group than in the control group.

The radiographic findings in our patients were not specific for Q fever pneumonia. Unilateral, single segmental opacities were the most common findings. The lower lobes were more affected than the upper lobes. The mostly unilateral, segmental pattern was also shown by other studies [9, 18 - 20] and seems to be the typical but not unique pattern of Q fever pneumonia. Two of the three studies [18, 20] described the lower lobes to be more often affected than the upper lobes, which is congruent with our findings. In contrast to the above mentioned studies, Millar et al. [10] found multiple round opacities and linear atelectasis in 68% and 50% of the patients, respectively.

Previous studies [9, 19] described the radiographic changes in Q fever pneumonia as slowly resolving, compared to other pneumonias. As our study was retrospective, systematic follow-up chest radiographs of the patients were not available. Nevertheless, the available follow-up chest radiographs of some of the patients did support these findings.

In conclusion, the radiographic findings in our study did not allow the definite differentiation of Q fever pneumonia from other community-acquired pneumonias. Segmental and/or lobar opacities are seen in both entities. However, in young to middle-aged patients in an endemic area presenting with segmental opacities, clinicians should at least consider Q fever pneumonia and initiate the appropriate diagnostic workup.

Summary

Patients with acute Q fever pneumonia usually present with cough, fever and myalgia. Typical laboratory findings are a normal white blood count and a high CRP level. About two-thirds of the patients have Q fever-related pneumonia. Unilobar, unilateral, segmental opacities are the common findings of chest radiographs in Q fever pneumonia. However, patchy and lobar infiltrates are also found in some patients. In young to middle-aged patients with segmental opacities living in an endemic area, the differential diagnosis should include Q fever pneumonia and the appropriate diagnostic workup should be initiated.

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