

Q fever pneumonia: a review of 164 community-acquired cases in the Basque country

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ABSTRACT: One hundred and sixty four cases of Q fever pneumonia are reviewed. *Coxiella burnetii* is responsible for 18.8% of pneumonias acquired in the community in our region with an extremely high seasonal variation. 91% of the cases occur between January and June. 88.5% of the patients are less than 40 yrs of age and 77% are male. The most common clinical symptoms are high fever, cough, cephalalgia and myalgias. 46.5% of the patients have no respiratory symptoms although 34% of the cases report pleural pain. The radiological signs are nonspecific. With regard to laboratory data, it is often observed that the white blood cell count (WBC) is normal and the liver enzymes are abnormal (45%). Treatment with doxycycline reduces the fever more quickly than erythromycin.

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Q fever is a zoonosis prevalent worldwide caused by *Coxiella burnetii* [1]. This micro-organism is an infrequent cause of community-acquired pneumonia [2, 3]. On the other hand, descriptions of epidemics of Q fever include numerous cases in which the lungs are not affected [4-6]. This has led to Q fever pneumonia not being a widely described disease entity. In the Basque Country, it is a common cause of community-acquired pneumonia since the first cases were described in 1982 [7, 8]. In this study, we review 164 cases of Q fever pneumonia that have been admitted to our service since 1982.

Materials and methods

The study included 164 cases of Q fever pneumonia acquired in the community and admitted to our pulmonary service from July 1982 to December 1986 (fig. 1). The clinical diagnosis is based on the existence of an acute onset with fever and chest X-ray findings compatible with pneumonia. The diagnosis of Q fever was based on the fourfold increase in phase II, *C. burnetii* antibody titre assayed by complement fixation (141 patients, 86%) or by the presence of a stable titre $\geq 1/128$ (23 patients, 14%) [9]. The two serum samples were obtained at intervals spaced four weeks apart.

The X-rays were checked by two observers. One hundred and twenty four X-rays were obtained. Pneumonia site, existence of pleural effusion, air bronchogram, laminar atelectasis, radiological progression, and size (larger, equal to, or smaller than segment) were recorded. For the 40 cases in which no X-rays were obtained, site

and existence of pleural effusion were obtained from the clinical history. The statistical analysis was performed using the Mann-Whitney test.

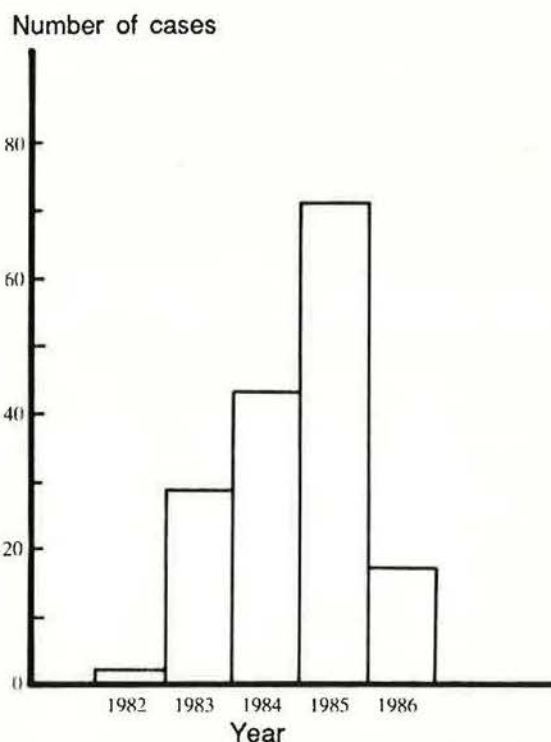


Fig. 1. - Annual incidence of community-acquired Q fever in our service.

Results

The annual incidence of Q fever pneumonia has varied widely; 1985 being the year of greatest incidence with 71 cases (fig. 1). During this year, a prospective study of community-acquired pneumonias was carried out in our service. Of 378 patients admitted for community-acquired pneumonia, 71 were caused by Q fever (18.8%). There is a pronounced seasonal variation, with 91% of cases occurring between the months of January and June (table 1). The average age of the patients was 30 ± 10.5 yrs. Only 19 patients were over 40 yrs. 46% of the patients lived in a rural environment, although only 18% of the patients (13/71) had direct contact with animals.

Table 1. — General and epidemiological characteristics of 164 patients with community-acquired Q fever pneumonia

Characteristic	n	%
Age <40 yrs	145	88.5
Sex: male	126	77
Period:		
January–April	109	66.5
January–June	149	91
Epidemic presentation	87	53
Inhabitants of rural areas	75	46
Direct contact with animals	13*	18

* Data available in 71 patients.

Clinical findings

Respiratory symptoms were absent in 46.5% of the cases, although one third of the group reported pleural pain (table 2). The combination of purulent sputum and pleural pain is present in 9% of the cases. Cephalalgia was a common neurological symptom, whilst confusion appeared in only one patient. Diarrhoea was observed in only two cases.

Table 2. — Clinical characteristics upon hospital admission in 164 patients with Q fever pneumonia

Characteristic	n	%
Fever $\geq 38^\circ\text{C}$	158	96
Cough	88	53.5
Expectoration	55	33.5
Haemoptysis	17	10.5
Pleuralgia	56	34
Purulent sputum and pleuralgia	15	9
Myalgias	88	53.5
Cephalalgia	91	55.5
Nausea/vomiting	12	7
Crepitus	96	58.5
Hepatomegaly	11	6.7
Mortality	0	0

High fever was the most frequently observed alteration during the baseline examination. A fever of 39°C or higher was observed in 35 patients (21.5%). Duration of fever from onset of symptoms was 8.3 ± 2.7 days. This time was no longer in patients aged over 40 yrs. 58% of the patients had crepitus, whilst signs of consolidation were observed in only eleven cases. Skin rash was observed in only one patient. None of the 164 patients died.

Radiological findings

There was a predominance of images in the lower lobes (table 3) and bilateral involvement or the existence of pleural effusion was uncommon. In general, the radiological images were small, affecting less than one segment. The presence of laminar atelectasis or radiological progression in the days following admittance to hospital was rare.

Table 3. — Radiological characteristics in 164 patients with Q fever pneumonia

Characteristic	n	%
Bilateral	21	12.8
Lower lobes	100	61
Air bronchogram	50	40*
Pleural effusion	20	12
Size (< one segment)	80	64.5*
Radiological progression	3	2.4*
Laminar atelectasis	3	2.4*

* Results in 124 cases.

Laboratory findings

Common laboratory findings are shown in table 4. It was common for the white blood cell count (WBC) to be normal. Respiratory insufficiency, arterial oxygen tension (Pao_2) < 8 kPa, was observed in twelve cases.

Table 4. — Laboratory findings upon hospital admission in 164 patients with Q fever pneumonia

Characteristic	n	%
Leucocytes $5-10 \times 10^9 \cdot l^{-1}$	136	83
Leucocytes $> 10 \times 10^9 \cdot l^{-1}$	22	13
Erythrocyte sedimentation rate	71	43
> 50 mm in 1 h		
Platelets $< 100 \times 10^9 \cdot l^{-1}$	1	0.6
Altered liver function*	74	45
Albumin $< 25 \text{ g} \cdot l^{-1}$	10	6
$\text{Pao}_2 < 9.3$ kPa	87	53
Presence of proteinuria and/or haematuria	17	10.4

*: increased activity of one or more enzymes; Pao_2 : arterial oxygen tension.

Treatment

During this survey, antibiotic therapy was not controlled. 97 patients were treated with erythromycin, 37 with doxycycline and the other 30 with various antibiotics, alone or in association.

Fever evolution varies, depending on the antibiotic treatment used. While there was no difference in fever duration prior to admittance (4.7 ± 2.2 days for the doxycycline group vs 5 ± 2.5 days for the erythromycin group), once treatment had started, fever disappeared more rapidly in the patients treated with doxycycline (2.4 ± 1.4 days vs 3.6 ± 2 days, $p < 0.01$).

On comparing clinical, radiological and analytical features between the two treatment groups, it is observed that only pleural effusion is more common in the group treated with erythromycin (9 cases vs 0 cases in the doxycycline group). If these nine patients are excluded from the statistical study, there is still a difference in the time to disappearance of the fever (2.4 ± 1.4 days for the doxycycline group vs 3.5 ± 2 days, for the erythromycin group, $p < 0.05$).

Discussion

Q fever is a rare cause of community-acquired pneumonia, accounting for less than 5% of cases [2, 3], with the exception of Nova Scotia, where Q fever accounts for 21.8% of community-acquired pneumonias [10]. In the Basque Country, it is the second cause of pneumonia, after *S. pneumoniae*, which leads one to assume an endemic nature for the infection [8]. The annual variations found in our study are directly related to the epidemic nature of the infection and, in 1985, to a systematic investigation of the cases. In fact, the higher frequency of Q fever pneumonia recorded during the first months of the year coincides with the oestrous cycle of sheep. Epidemiological studies have shown that a large number of the flocks were infected. Of the 103 flocks examined, 30 (29.7%) were infected with Q fever [11]. Other frequently infected animals in our region are rabbits, goats, and dogs [11]. The higher incidence of Q fever pneumonia in young patients and males is well documented [4-6]. Due to the great infective power of *Coxiella burnetii*, the inhalation of just one micro-organism would probably result in infection [12]. In most cases, patients are infected by inhalation of aerosol particles in the contaminated atmosphere [1]. This would explain the low percentage of patients in direct contact with animals.

Q fever pneumonia rates among clinically described atypical pneumonias [13]. Nevertheless, these descriptions are fairly biased, as they were performed during epidemics in which not all the patients had pneumonia [4-6, 14]. This would explain the fact that the frequency of pleuralgia or haemoptysis in our study is larger than that described in the literature [4, 6, 14], and about 10% of the cases of Q fever pneumonia present with a "typical" clinical picture. Unlike other authors [4], we have not found the duration of fever or the incidence of

pneumonia to be greater in patients aged over 40 yrs. These factors complicate the clinical diagnosis due to the lack of specific data. Radiologically, the location in the lower lobe, the low incidence of pleural effusion and the extent of the pneumonia (generally confined to a single segment) have been described previously [4, 15, 16], but constitute factors which are useless in distinguishing Q fever from other bacterial or atypical pneumonias [17]. Laminar atelectasis, described in other studies as indicative of Q fever [16], was not recorded in our study. Neither do the alterations in laboratory findings reveal any specificity. The frequency and types of alterations observed, including the sole reported case of thrombocytopenia, have been described previously [4, 6, 14].

The absence of specific clinical, radiological or laboratory findings hamper diagnostic orientation for Q fever pneumonia. This difficulty is increased by the danger of isolating the micro-organism and the late appearance of complement fixation [1]. Even when the IgM antibodies were determined by indirect immunofluorescence assay, only half of the cases were diagnosed in the first week [18]. In these circumstances, diagnostic suspicion should be based on epidemiological criteria. In the Basque Country, this aetiology should be considered for all young patients with community-acquired pneumonia during the first six months of the year, especially in the case of an epidemic. Establishing the diagnosis, albeit late, is essential because even though Q fever pneumonia is a self-limiting disease with a good prognosis [5, 14], late complications (especially endocarditis) have an appreciable mortality [1].

Q fever diagnosis by complement fixation is assured if there is a fourfold increase in the baseline titre. However, the reliability of a stable titre is proportional to the rate of infection in the general population. In the Basque Country, only 3 out of 1,286 healthy people examined had a titre $\geq 1/128$ [11]. Therefore, an acute pneumonia associated with a stable titre $\geq 1/128$ seems to be sufficient to diagnose Q fever pneumonia.

Erythromycin is the antibiotic habitually used in clinical practice in the treatment of atypical pneumonias [13], and is also effective against *Legionella pneumophila*. *In vitro* studies show that this antibiotic is ineffective against Q fever infection, although its possible efficacy *in vivo* has recently been described [20, 21]. The effectiveness of an antibiotic is difficult to evaluate *in vivo*, especially in self-limiting diseases such as Q fever pneumonia. In fact, our patients treated with other ineffective antibiotics recovered without complications. Fever is the most objective clinical finding, and diminished fever is generally associated with clinical improvement [22]. However, if the days with fever prior to treatment are not taken into account, the beneficial effect of this antibiotic may coincide with the patient's recovery. Our results showed a quicker remission of fever symptoms with doxycycline than with erythromycin, thus leading to doubts as to the latter's efficacy. In fact, the *in vivo* efficacy of erythromycin is based on four patients. Of the three cases treated by ELLIS and DUNGAR [20], one had been ill for six days before treatment, and information was not provided for the other two cases. The patients described by D'ANGELO

[21] had fever for two days before admittance, which persisted 48–72 h after beginning treatment. With regard to tetracycline, despite the difficulties described in its evaluation, it reduced fever more rapidly than when antibiotics were not used [14] or when compared with penicillin [22].

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Pneumonie dans le cadre d'une fièvre Q: revue de 164 cas acquis dans la communauté, dans le Pays Basque. V. Sobradillo, P. Ansola, F. Baranda, C. Corral.

RÉSUMÉ: Etude de 164 cas de pneumonie dans le cadre de la fièvre Q. *C. burnetii* est responsable de 18.8% des pneumonies dans la collectivité de notre région, avec une variation saisonnière extrêmement importante, 91% des cas survenant entre janvier et juin. L'âge des patients est inférieur à 40 ans dans 88.5%, et le sexe est masculin dans 77% des cas. Les symptômes cliniques les plus courants sont une fièvre élevée, de la toux, des céphalées et des myalgies. Les symptômes respiratoires sont défaut chez 46.5% des patients; 34% des cas font état de douleurs pleurales. Les signes radiologiques sont non spécifiques. En ce qui concerne les données de laboratoire, on observe fréquemment que la leucocytose est normale et que les enzymes hépatiques sont perturbés (45% des cas). Le traitement à la doxycycline fait baisser la fièvre plus rapidement que celui à l'érythromycine. *Eur Respir J.*, 1989, 2, 263–266.