

BRIEF ORIGINAL

INCIDENCE OF *BARTONELLA HENSELAE* INFECTION
DURING THE PERIOD 2009-2012 IN THE VALENCIAN COMMUNITY, SPAIN

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ABSTRACT

Background: *Bartonella henselae* is the causative agent of the disease caused by cat scratches and it has a worldwide distribution. The objective of the study was to investigate its incidence in the Valencian Community during the period 2009-2012.

Methods: A study of the chosen microbiological tests for *B. henselae* during four years was carried out. Patients with serology (IgM and IgG), culture, or PCR positive were considered case studies. Data from the Red de Vigilancia Microbiológica Valenciana (RedMIVA) depending on the "General Direction of Public Health" (Dirección General de Salud Pública) was used as the source of information.

Results: During the studied period, 14 cases were detected. The incidence rates were: 0,07 per 10⁵ inhabitants and year of the Valencian Community, 0,10 per 10⁵ inhabitants/year in the province of Alicante, with marked differences in relation to Valencia of 0,06 per 105 inhabitants/year and Castellón (with no cases). The temporal distribution of the cases were: 4 in 2009, 4 in 2010, 3 in 2011, and 3 in 2012. 64% of the cases were women and 36% men. The median age was 21 years (range 1-65 years). Predominant age groups arose between 1-10 years (42%) and 31-40 years (28%).

Conclusions: The incidence of *B. henselae* in the Valencian Community is low. The data obtained suggest that its distribution varies depending on the geographical area in the Community. There is a predominance of young people.

Keywords: *Bartonella henselae*. Epidemiology. Spain.

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RESUMEN

Incidencia de la infección por *Bartonella henselae* en la Comunidad Valenciana durante el periodo 2009-2012

Fundamentos: *Bartonella henselae* es el agente causal de la enfermedad por arañazo de gato y su distribución es mundial. El objetivo del trabajo fue conocer la incidencia de esta infección en la Comunidad Valenciana durante el periodo 2009-2012..

Métodos: Se realizó el estudio sobre las pruebas microbiológicas solicitadas para *B. henselae* durante cuatro años. Se consideró "caso" al paciente con serología (IgM e IgG) cultivo o PCR positivos. Como fuente de información se utilizaron los datos procedentes de la Red de Vigilancia Microbiológica Valenciana (RedMIVA) dependiente de la Dirección General de Salud Pública.

Resultados: Durante el periodo estudiado se detectaron 14 casos. Las tasas de incidencia fueron: 0,07 por 10⁵ habitantes y año en la Comunidad Valenciana, 0,10 por 10⁵ habitantes/año en la provincia de Alicante, 0,06 por 105 habitantes/año en Valencia y ningún caso en la provincia de Castellón. La distribución temporal de los casos fue: 4 en 2009, 4 en 2010, 3 en 2011 y 3 en 2012. El 64% fueron mujeres y el 36% hombres. La mediana de edad fue de 21 años (rango de 1-65 años). Los grupos etarios predominantes se presentaron entre 1-10 años (42%) y 31-40 años (28%).

Conclusiones: La incidencia de infección por *B. henselae* en la Comunidad Valenciana es baja. Los datos obtenidos sugieren que varía su distribución según el área geográfica dentro de la Comunidad. Se observa un predominio de casos entre la población infantil.

Palabras clave: *Bartonella henselae*. Epidemiología. España

INTRODUCTION

Bartonella henselae is a fastidious gram negative bacterium. It has a worldwide distribution and cats are the main reservoir. Fleas are the most common vectors between animals, although there is also evidence of ticks transmitting the illness¹. Human is an accidental host after bite or scratch of infected cats.

Several studies in EEUU, Japan and France suggest that the incidence is highest in Autumn with a decrease in Spring²⁻⁴. Cat Scratch Disease (CSD) affects immunocompetent young people and rarely causes complications. It can also occur in immunocompromised individuals as HIV-infected, HCV-infected or transplanted patients⁵.

In a study performed in Catalonia (Spain), the *B. henselae* antibody population prevalence was 6.4%-7.9%; the highest age-specific was 0-14 and 30-44 years⁶. In Catalonia HIV-infected patients, the prevalence reached 22.3%⁷. The prevalence of IgG antibodies in a healthy population in Sevilla was 24.7%. These data arise that *B. henselae* infections are frequent in these areas and most of them subclinical⁸.

Various diagnosis criteria has been proposed^{5,9}. For diagnosis serological criteria (serum IgG and IgM) are commonly used, although the detection of bacterial genome by polymerase chain reaction (PCR) in tissue samples or abscesses is more sensitive and specific.

There are no large series of epidemiological studies of *B. henselae* in the Valencian Community. The assessment of microbiological data in a wide population such as an autonomous community could make a good estimation of the incidence of the disease. The Red de Vigilancia Microbiológica Valenciana (RedMIVA) depending on the Dirección General de Salud Pública is a source of data which collects microbiological results of hospitals, store and analyze them in a centralized system to afterwards spread the generated information.

The aim of this study was to determine the incidence of the disease through analysis of microbiological determinations performed in patients with clinical suspicion of *B. henselae* infection, during 2009-2012.

METHODS

A descriptive study of positive microbiological tests for *B. henselae* of Valencian Community patients, during four years, was carried out. The following variables were collected from RedMIVA: test solicited, place of origin, age and sex. Tests for *B. henselae* detection were specific to each laboratory attached to RedMIVA.

Patients with serology (IgM and IgG), culture, or PCR positive were considered case studies. 491 serological tests for *B. henselae* in the Valencian Community (Valencia, Alicante, Castellón) was requested. The total census was 5.113.209 inhabitants.

A descriptive analysis of the characteristics of patients (sex, age and place of residence) was performed. The incidence in the Valencian Community was calculated, comparing this data on the province and year using Poisson's distribution. P values higher than 0.05 were considered no statistically significant.

RESULTS

14 cases were confirmed with positive IgG and IgM antibodies serology against *B. henselae*. All of them had titers higher than 1/64 with positive IgM. No culture or PCR assay were performed. 64% were women and 36% men. The median age was 21 years (range 1-65 years). The predominant age groups were 1-10 years (42%) and 31-40 years (28%) (table 1).

Of the total amount of cases, 8 belonged to Alicante and 6 to Valencia. No cases were detected in Castellón. The overall incidence rate in the Valencian Community for the period was 0.07 per 10⁵ inhabitants/year. The higher

Table 1
Sex and age cases distribution

| Age | % | Men | Women |
|-------|------|-----|-------|
| 0-10 | 42 | 3 | 3 |
| 11-20 | 7.1 | - | 1 |
| 21-30 | | - | - |
| 31-40 | 28 | 1 | 3 |
| 41-50 | 14.2 | 1 | 1 |
| 51-60 | | - | - |
| 61-70 | 7.1 | - | 1 |
| Total | 100 | 5 | 9 |

incidence was detected in Alicante: 0.10 per 10⁵ inhabitants/year, followed by Valencia with 0.06 per 10⁵ inhabitants/year. No significant differences rates ($p > 0.05$) between provinces and years, using Poisson regression, were observed. The temporal distribution of cases was 4 in 2009, 4 in 2010, 3 in 2011 and 3 in 2012. There was a decrease over the years but no significant differences. 42% of the were detected in spring (March, April and May), 21% in autumn and winter and 14% in summer.

DISCUSSION

The incidence of the disease through IgG and IgM positive serology for *B. henselae* in Valencian Community patients is low compared to other countries as Denmark and USA. Thus, in USA the annual incidence of CSD was 0.8 per 10⁵ inhabitants/year for inpatient, rising to 9.3 per 10⁵ inhabitants/year for outpatients². In Europe, Denmark has reported an incidence of 2.6 per 10⁵ inhabitants/year¹⁰.

The results suggest that the distribution may vary in the Community depending on each geographical area which may be related to epidemiological factors, a low warning level to the disease by the medical personnel or a limited use of microbiological testing as confirmation.

The predominant group of age was between 0-10 and 31-40 years, which may be a result of increased contact with the pet at these ages, especially in children⁶. Different studies^{2,5,6,11} match this data. Connecticut provides an incidence of 3,7 per 10⁵ inhabitants/year, noting that this is increased in

patients younger than 10 years to 9.3 per 10⁵ inhabitants/year¹¹.

The laboratory method for diagnosis is the IgG and IgM specific detection. Numerous studies show that the sensibility and specificity of both tests are low^{5,9,12-14}. Bergmans et al studied the kinetics IgM and IgG production and concluded that the response of each patient is different; some patients with cat scratch disease produced high levels of IgG and IgM, others IgM only and others had low levels of both¹³. In addition to this there are other factors that determine the low sensibility and specificity. The low specificity can be explained by the seroprevalence in general population and cross reaction with other species such as *B. quintana*, *Coxiella burnetii*, *Chlamydochloa*, especially when IgG detection is performed.

Another limitation of this study is the absence of clinical data in cases evaluation, since microbiological and some epidemiological data (location, age, sex) are analyzed. In addition, Bartonella infection is not a notifiable disease resulting in incomplete available information, particularly in the clinical assessment of patients.

Since it is a rare disease, data from the present study cannot be extrapolated to the general population of Spain. Further studies outside Valencian Community would be useful to provide comparative data.

The incidence of *B. henselae* infection in the Valencian Community compared with data from other geographic areas could suggest that it is a low incidence disease, rarely suspected or scarcely microbiological confirmed. However it should be considered in the Valencian Community, especially in pediatric patients and middle-age.

BIBLIOGRAPHY

1. Jacomo V, Kelly PJ, Raoult D. Natural history of Bartonella infections (an exception to Koch's postulate). Clin Diagn Lab Immunol. 2002; 9:8-18.

2. Jackson LA, Perkins BA, Wenger JD. Cat scratch disease in the United States: An analysis of three national databases. *Am J Public Health.* 1993; 83: 1707-1711.
3. Tsukahara M. Cat scratch disease in Japan. *J Infect Chemother.* 2002; 8: 321-325
4. Sanguinetti-Morelli D, Angelakis E, Richet H, Davoust B, Rolain JM, Raoult D. Seasonality of Cat Scratch disease, France, 1999-2009. *Emerg Infect Dis.* 2011; 17: 705-707.
5. Spach D, Kaplan S. Microbiology, epidemiology, clinical manifestations, and diagnosis of cat scratch disease. 2014. [cited septiembre 2014]. Available en: <http://www.uptodate.com/contents/microbiology-epidemiology-clinical-manifestations-and-diagnosis-of-cat-scratch-disease>
6. Pons I, Sanfeliu I, Cardeñosa N, Nogueras MM, Font B, Segura F. Serological evidence of *Bartonella henselae* infection in healthy people in Catalonia, Spain. *Epidemiol Infect.* 2008; 136: 1712-7165.
7. Pons I, Sanfeliu I, Nogueras MM *et al.* Seroprevalence of *Bartonella spp.* infection in HIV patients in Catalonia, Spain. *BMC Infect Dis.* 2008; 8: 58-63
8. Garcia-Garcia JA *et al.* Prevalencia de anticuerpos séricos frente a *Bartonella spp.* en una población sana del área del sur de la provincia de Sevilla. *Rev Clin Esp.* 2005; 11:541-544.
9. Hansmann Y, DeMartino S, Piémont Y *et al.* Diagnosis of cat scratch disease with detection of *Bartonella henselae* by PCR: a study of patients with lymph node enlargement. *J Clin Microbiol.* 2005; 43: 3800-3806.
10. Blomgren M, Hardt-Madsen M. Cat-scratch disease: an overlooked disease in Denmark? *Ugeskr Laeger.* 1997; 159: 2876-2877.
11. Hamilton DH, Zangwill KM, Hadle, JL *et al.* Cat-scratch disease—Connecticut 1992-1993. *J Infect Dis.* 1995; 172: 570-573
12. Vermeulen MJ, Verbakel H, Notermans DW *et al.* Evaluation of sensitivity, specificity and cross-reactivity in *Bartonella henselae* serology. *J Med Microbiol.* 2010; 59: 743-745
13. Bergmans A, Peeters M, Schellekens J, Vos M, Sabbe L, Ossewaarde J *et al.* Pitfalls and fallacies of cat scratch disease serology: evaluation of *Bartonella henselae*-based indirect fluorescence assay and enzyme-linked immunoassay. *J Clin Microbiol.* 1997; 35:1931-1937.
14. Abarca K, Winter M, Marsac D, Palma C, Contreras AM, Ferrés M. Exactitud y utilidad diagnóstica de la IgM en infecciones por *Bartonella henselae*. *Rev Chil Infectol.* 2013; 30: 125-128.