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Marta Díaz-Menéndez^{a,*}, Eduardo Malmierca^b

^a La Paz – Carlos III University Hospital-IdiPAZ, National Referral Unit for Imported Tropical Diseases, Tropical & Travel medicine Unit, Infectious Diseases Department, Madrid, Spain

^b Infanta Sofía University Hospital, Infectious Diseases Department, Universidad Europea de Madrid, Madrid, Spain

* Corresponding author.

E-mail address: marta.diazmenendez@salud.madrid.org (M. Díaz-Menéndez).

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Erythema nodosum: An uncommon manifestation of Rickettsiosis



Eritema nodoso: una manifestación infrecuente en las rickettsiosis

Erythema nodosum (EN) is a well defined cutaneous syndrome that can be primary or secondary to systemic and autoimmune diseases, inflammatory bowel disease, pregnancy, neoplastic diseases, drugs or infections.¹ Between infectious agents, Streptococci and *Mycobacterium tuberculosis* are the most common causes in developed and developing countries, respectively. Many other microorganisms have been involved in EN, but *Rickettsia* spp. have only been related in very few case reports.^{2,3}

A 30-year-old woman without any previous diseases, had a property vaccinated dog and lived in a rural area. In mid-autumn she began suffering fevers of up to 38 °C, headache, stiff neck and vomiting, so she went to the Emergency Department of our hospital. Upon arrival, blood pressure was 110/78 mmHg, heart rate 124 beats per minute and oxygen saturation by pulse-oximetry was 100%. At physical exploration, neurological examination was normal; she had a black, scabby and painless skin lesion on her scalp, as well as multiple red, indurated and painful lesions on palpation in both lower limbs, suggestive of EN. A blood test was performed: CRP of 270 mg/L, procalcitonin of 1.41 ng/mL, neutrophilia of 8710/μL

with lymphopenia of 770/μL and discrete prolongation of prothrombin time (15.5 s). CSF analysis was normal, and CSF, blood and urine cultures were all negative. Chest x-rays and abdominal ultrasound were normal too. The patient was admitted to the Infectious Diseases Unit. A skin biopsy from one of the lesions in the lower limbs was taken (Fig. 1).

On the day after admission, the patient referred blurred vision. An Ophthalmologist found mild vitritis, retinal vasculitis, patchy retinitis and severe papillitis in her right eye, as well as mild patchy vasculitis in the posterior pole of her left eye.

ANA, antiDNA and ENA antibodies were all negative. Serologies for *Coxiella burnetii*, HIV, VEB and CMV were negative but *Rickettsia* spp's serology was positive IgM and negative IgG (Chemiluminiscent immunoassay or CLIA; *Rickettsia conorii* Virclia, Vircell®: Moroccan strain ATCC VR-141). At that moment, doxycycline 100 mg every 12 h was initiated for 7 days, along with corticosteroids to treat the ocular disease. The patient became afebrile 36 h after starting doxycycline. She improved quickly and could be discharged home. New serologies were made against *Rickettsia* spp in successive weeks: positive IgM and negative IgG persisted 2 weeks later; 3 months later, serology was still IgM positive by CLIA but undetermined IgM (1/40; *Rickettsia conorii* IFA IgM, Vircell®: Moroccan strain ATCC VR-141) and positive total antibodies by immunofluorescence assay (IFA).

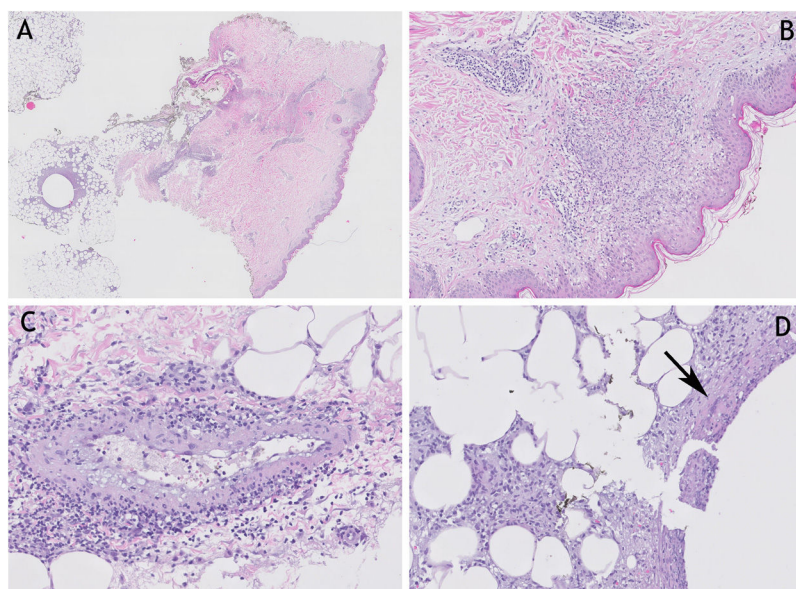


Fig. 1. (A) (H&E 20×) cutaneous punch in which superficial, deep dermis and adipose panniculus are appreciated. (B) (H&E 200×) detail of lichenoid dermatitis with vacuolar degeneration of basal epidermal layer, and underlying granulomatous reaction. (C) (H&E 200×) medium-sized vessel with vacuolated endothelium and enveloping lymphocytic inflammatory infiltrate. (D) (H&E 400×) lobular and septal panniculitis with presence of giant multinucleated cell (arrow). H&E: hematoxylin and eosin.

The dermatological manifestations of rickettsiosis can be diverse. An eschar with epidermal necrosis at the site of inoculation is characteristic (tache noire). In addition, this infection can cause generalized vasculitis with involvement of the intima and media with vascular and perivascular infiltration of polymorphonuclear cells, lymphocytes and histiocytes. Other findings rarely seen are blood extravasation in petechial lesions, vacuolization of basal epidermal layers, and even intraepidermal vesicles with inflammatory infiltrate in the papillary dermis; EN is very uncommon. Cutaneous lesions in the form of a maculopapulopetechial rash with palmoplantar involvement are very characteristic of *Rickettsia conorii*, although we could not confirm the species in our patient.⁴

Rickettsiosis usually have a good prognosis, and disease tend to be limited to 10–20 days without sequelae. Complications are usually related to delays in treatment, advanced age and comorbidities. There is also a “malignant” rickettsial form of the disease characterized by multi-organic failure, especially kidney failure, disseminated intravascular coagulation with purpuric exanthema, severe hepatic injury, pulmonary infiltrates and altered consciousness.^{5,6}

The basis of diagnosis is serology, being limited by cross reactions between members of the group of spotted fevers and those of the typhus group, leading to false positive results.⁶ Indirect immunofluorescence is the most sensitive and specific of all serological tests. Polymerase chain reaction (PCR) can also be performed in a eschar biopsy or blood sample and has the advantages of high specificity and being positive in the acute phase of disease.⁷

Between rickettsial species, *Rickettsia conorii* and *Rickettsia sibirica mongolitimonae* are the most frequent between May and September. *Rickettsia slovaca* and *Rickettsia rioja* are much more frequent in other times of the year and their eschars are commonly located on the scalp.⁸ Although in the south of Spain the autumns are getting warmer, either *Rickettsia slovaca* or *Rickettsia rioja* could be the causative agents of our case report.

Another recently described tick-borne infection that must be included in the differential diagnosis is the one caused by ‘*Candidatus Neorhlichia mikurensis*’. It is transmitted by *Ixodes ricinus* ticks and it causes an inflammatory disease affecting predominantly patients with underlying diseases.⁹

Some cases of EN labeled as idiopathic might be secondary to Rickettsial infections in endemic regions.^{2,3,10} Our case reports an uncommon manifestation of a relatively frequent infection in our country. Rickettsiosis could manifest just with fevers and dermatological manifestation like EN, so we suggest performing at least an initial serology and another one two weeks later in every patient

presenting this dermatological sign in order to rule out an easy to treat infection.

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Conflict interest

All authors declare no conflicts of interest.

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José Antonio Peregrina-Rivas^a, Emilio Guirao-Arrabal^{b,*}, Francisco Manuel Ramos-Pleguezuelos^c, José Hernández-Quero^b

^a Unidad de Medicina Interna, Hospital Universitario San Cecilio, Granada, Spain

^b Unidad de Enfermedades Infecciosas, Hospital Universitario San Cecilio, Granada, Spain

^c Unidad de Anatomía Patológica, Hospital Universitario San Cecilio, Granada, Spain

* Corresponding author.

E-mail address: emilio.guirao@gmail.com (E. Guirao-Arrabal).

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Baja sensibilidad de los test rápidos antigénicos como método de cribado en un brote de infección por SARS-CoV-2 en prisión



Low sensitivity of rapid antigenic tests as a screening method in an outbreak of SARS-CoV-2 infection in prison

Sr. Editor:

Actualmente, el «estándar oro» para el diagnóstico de la infección por SARS-CoV-2 es la detección de ARN viral mediante una PCR en tiempo real (rt-PCR) o una técnica molecular equivalente. En España pueden utilizarse los test rápidos antigénicos (TRA)

debidamente validados (sensibilidad $\geq 80\%$ y especificidad $\geq 97\%$) en los 5 primeros días de la aparición de síntomas en pacientes que no sean grandes inmunodeprimidos o no tengan criterios de ingreso en la UCI¹. El TRA tiene menos sensibilidad que la rt-PCR en todos los estadios de la infección, y todavía menos en casos asintomáticos, pero su uso en ausencia de síntomas no está descartado en todos los escenarios^{1–3}. Un reciente informe del European Centre for Disease prevention and Control (ECDC) aconseja emplearlos en pacientes con o sin síntomas si se prevé una proporción de pruebas positivas $\geq 10\%$ ². También los recomienda en entornos de alto riesgo para identificar rápidamente a los infectados y aplicar medidas de prevención y control que eviten la transmisión, aunque aconseja que los casos negativos se confirmen con una prueba rt-PCR^{1–3}.