Meningoencefalitis por virus varicela-zóster: una entidad infrecuente de síndrome confusional agudo en el anciano

Meningoencephalitis due to varicella-zoster virus: an uncommon problem of acute confusional syndrome in the elderly

Sr. Editor:

La reactivación del virus varicela-zóster (VVZ) latente en los ganglios dorsales tras la primoinfección resulta en una erupción cutánea denominada herpes zoster; el riesgo estimado de aparición a lo largo de la vida es de alrededor de 10-20%[1]. La alteración de la inmunidad celular es un factor de riesgo bien conocido, bien sea secundaria a neoplasia, trasplante, tratamiento inmunosupresor o infección por el VIH. Asimismo, la edad también desempeña un papel importante en dicha reactivación, objetivándose en mayores de 75 años una incidencia 5 veces mayor que la población general, presumiblemente por la pérdida de inmunidad celular asociada al envejecimiento[2]. Si bien lo habitual es la presencia de una reactivación limitada a una erupción cutánea, bien sea localizada o generalizada, en ocasiones se presenta asociada a complicaciones. Aproximadamente en el 10% de los casos (mayoritariamente inmunodeprimidos) existe afectación visceral, ya sea pulmonar, hepática o del SNC[3,4], conociéndose entonces como infección diseminada por VVZ, caracterizada por una elevada morbimortalidad (20-30%)[5].

Presentamos el caso de un varón inmunocompetente de 80 años previamente sano, que acude al servicio de urgencias por cuadro de malestar general, disuria, sensación distérmica y fiebre de 48 h de evolución. En el examen físico presentaba un regular estado general, fiebre de 38,5 °C y tiritona, aunque eupneico y hemodinámicamente estable. No se apreció semiología relevante en la exploración por aparatos. Se objetivó leucocitosis con desviación izquierda, así como más de 100 leucocitos/campo y abundantes gérmenes en el análisis de orina; el resto de las pruebas básicas eran normales. Se decidió ingreso con el diagnóstico de infección de tracto urinario complicada y se inició tratamiento con ceftriaxona. A posteriori, tanto en el urocultivo como los hemocultivos se aislaría *Escherichia coli* multisensible. A las 48 h de ingreso, el paciente permanece hemodinámicamente estable y afebril, con mejoría del estado general aunque desorientado en tiempo y espacio, y con alteración del patrón vigilia-sueño. A las 72 h presenta lesiones cutáneas de contenido claro sobre base eritematosa, algunas de centro necrótico, diseminadas en el tórax y las extremidades. Se realizó inmunofluorescencia directa que resultó positiva para VVZ (confirmada posteriormente por cultivo) siendo diagnosticado de herpes zóster generalizado e iniciándose tratamiento con aciclovir por vía intravenosa. En el quinto día de ingreso se aprecia un mayor deterioro neurológico, con marcada agitación nocturna, con subsiguiente somnolencia, estupor y bajo nivel de conciencia. Desde el punto de vista serológico, fue negativo para VIH y lúes, y positivo para IgG VVZ e IgG virus del herpes simple. Una TC toraco-abdominal descartó neoplasia subyacente. Se realizó una TC craneal que tan sólo mostró leucoencefalopatía arterioesclerótica hipertensiva por lo que se procedió a la realización de una punción lumbar, que arrojó un líquido cefalorraquídeo (LCR) de predomino mononuclear (295 leucocitos/98% linfocitos), proteínas elevadas (386 mg/dl) y glucosa normal (65 mg/dl) con una ADA de 32,4. Se realizó un diagnóstico de presunción de meningoencefalitis por VVZ, si bien la elevación marcada de ADA planteaba un más que razonable diagnóstico diferencial con tuberculosis. Los resultados de LCR mostraron posteriormente cultivo y gramnegativos, Lowenstein negativo, citología negativa y PCR para VVZ positiva. Se realizó una resonancia magnética cerebral que no mostró signos encefalitis, aunque el estudio fue técnicamente limitado. Se completaron 15 días de tratamiento con ceftriaxona y 21 días de aciclovir. El paciente presentó una mejoría lenta pero progresiva. Se realizó una nueva PL que mostró mejoría de todos los parámetros, incluido una ADA de 10. El paciente es dado de alta tras un mes de ingreso. En el seguimiento en consultas se constató recuperación neurológica completa.

Con nuestro caso pretendemos resaltar la necesidad de descartar organicidad (en especial, infección de SNC) en el síndrome confusional agudo del anciano, describiéndose una meningoencefalitis VVZ en paciente añoso inmunocompetente, con la particularidad de presentar altos niveles de ADA en LCR, dato sugestivo de tuberculosis, aunque ya descrito previamente en la literatura asociado a infecciones herpéticas de SNC[6].

Bibliografía

1. Gnann JW, Whitley RJ. Herpes zoster. N Engl J Med. 2002;347:340–6.
2. Schmader K. Herpes zoster in older adults. Clin Infect Dis. 2001;32:1481.
3. Gilden DH, Kleinschmidt-DeMasters BK, Laguardia JJ, Mahalingam R, Cohrs RJ. Neurologic complications of the reativation of varicella-zoster virus. N Engl J Med. 2000;342:635–45.
4. Mueller NH, Gilden DH, Cohrs RJ, Mahalingam R, Nagel MA. Varicella zoster virus infection: clinical features, molecular patogénesis of disease, and Latency. Neurol Clin. 2008;26:675–97.
5. Yawn BP, Saddier P, Wollan PC, St Sauver JL, Kurland MJ, Sy LS. A population-based study of the incidente and complication rates of herpes zoster befote zoster vaccine introduction. Mayo Clin Proc. 2007;82:1341.
6. Lopez-Gomez M, López-Ruz MA, Jiménez-Alonso J. High levels of adenosine deaminase in a patient with herpetic encephalitis and inicial negative PCR results. Clin Infec Dis. 2003; 37, 137-148.

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Chlamydia pneumoniae Infection Associated to Acute Fibrinous and Organizing Pneumonia

Infección por Chlamydia pneumoniae asociada a neumonía aguda fibrinosa y en organización

To the Editor:

Pneumonia with a mild prolonged course is the most frequent clinical presentation of the lower respiratory tract infection by *Chlamydia pneumoniae*.[1] However, severe, life-threatening pneumonia has been reported, mainly in elderly hosts and those with chronic-associated conditions, but in previously healthy patients as well.[1–5] Acute Fibrinous and Organizing Pneumonia (AFOP) is a histologic pattern associated with a clinical picture of acute lung injury which differs from the classic presentations of diffuse alveolar damage (DAD), bronchiolitis obliterans with organizing pneumonia (BOOP), and eosinophilic pneumonia (EP).[1] Like these patterns, however, AFOP can occur in an idiopathic setting or in association with a wide spectrum of clinical conditions.[6] The dominant histological finding in AFOP is the presence of intra-alveolar fibrin in the form of "fibrin balls" within the alveolar spaces.[6]

AFOP has a poor prognosis, with an overall mortality rate of about 50%.[6]

Here we present a case of *Chlamydia pneumoniae* infection associated with AFOP, respiratory failure, multi-organ dysfunction, and death. A 69-year-old woman with a history of hypertension, type II diabetes mellitus and chronic liver disease consulted for a four-day history of arthromyalgias, rhinorrhea, dry cough, fever, and progressive shortness of breath. She reported no relevant epidemiological history, such as exotic travel or contact with animals. She had received the influenza vaccine annually and pneumococcal vaccine the previous year. Her usual treatment was an ACE inhibitor and glibenclamide. At hospital admission, she was tachypneic (32 breaths min^{-1}); oxygen saturation was 92% breathing room air, blood pressure 120/60 mmHg, pulse 111 beats min^{-1}, and axillary temperature 37.9 °C. Respiratory auscultation revealed crackles in both lower hemithoraces. Room air arterial blood gas determination showed acute respiratory hypoxia with an arterial oxygen tension (PaO_2) of 8.3 kPa (62 mmHg), and arterial carbon dioxide tension ($PaCO_2$) of 2.7 kPa (20 mmHg), a pH of 7.5, and oxygen saturation of 95.4%. Other notable laboratory findings were platelet count 34,000 cells mm^{-3} (34.0 cells $\times$ $10^9 \cdot L^{-1}$), white blood cell count 3,900 cells mm^{-3} (3.9 cells $\times$ $10^9 \cdot L^{-1}$) with 87% neutrophils, and Na^+ 129 mmol L^{-1}. Chest radiography revealed an alveolar consolidation in the right-middle and right-lower lobes and the lingula (Fig. 1). A sputum sample could not be obtained for examination. Urinary antigen detection by immunochromatography was negative for both *Legionella pneumophila* and *Streptococcus pneumoniae*. With the diagnosis of community-acquired pneumonia, the patient was treated with intravenous ceftriaxone (1 g/day) and levofloxacin (500 mg/day) for 24 hours, followed by levofloxacin after establishing that urinary antigen for *S. pneumoniae* was negative. During the following two days, the patient's clinical condition deteriorated; consolidation on chest radiograph progressed and respiratory failure ensued, requiring transfer to the intensive care unit, invasive mechanical ventilation, and systemic corticosteroids. A chest computed tomographic scan showed areas of consolidation and ground glass opacities in the lower lobes. Studies for mycobacteria, fungi, conventional bacterial culture and viral cultures (Adenovirus, Influenza, Respiratory Syncytial Virus, Herpes simplex 1/2, Cytomegalovirus and Varicella Zoster) from a bronchoalveolar lavage were negative. Transbronchial biopsy showed an inflammatory process with a predominance of alveolar fibrin exudate in the form of "fibrin balls" without formation of hyaline membranes, and signs of organization compatible with AFOP (Fig. 2). Immunology was negative for vasculitis (anti-proteinase 3, anti-myeloperoxidase, and

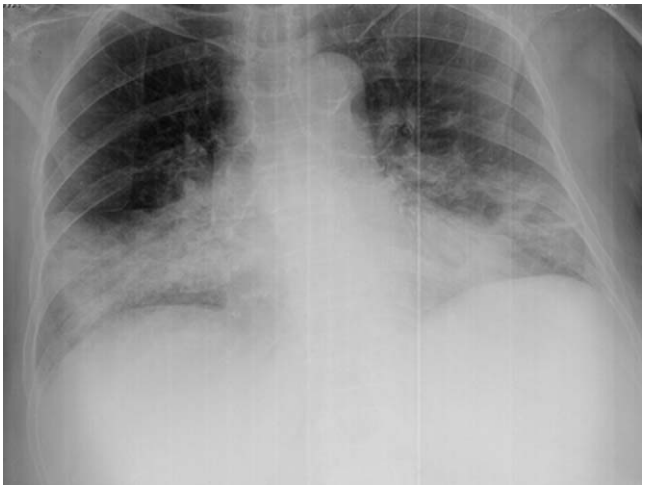

Figure 1. Chest radiography: alveolar consolidation in the right-middle and right-lower lobes and the lingula.

Table 1
Main characteristics of the four cases of *C. pneumoniae* infection associated with either BOOP or AFOP.

Patient num (reference)	Age/gender	Comorbidity	Chest radiography	PaO_2 mmHg (FiO_2 21%)	Serology *C. pneumoniae*		Treatment	Histology	Outcome
					First	Second			
1 (7)	65/M	Wegener's granulomatosis Immunosuppressive treatment Renal failure/ hemodialysis Diabetes Alcohol abuse/chronic pancreatitis	Diffuse reticulonodular and patchy opacities	58	Positive*	Positive*	Doxycycline Prednisone	BOOP	Recovered
2 (8)	70/M	-	Infiltration right lung	47	IgM: negative IgG: 1/2,048	4096	Doxycycline Prednisone (1 mg/kg)	BOOP	Recovered
3 (9)	70/M	-	Migratory infiltrates	54	IgM negative IgG 1/256	2048	Minocycline	BOOP	Recovered
4 (present case)	69/F	Diabetes Chronic liver disease (HCV)	Bilateral consolidation	62	IgM negative IgG 1/32	IgM inconclusive IgG 1/512	Levofloxacin Prednisone (1 mg/kg)	AFOP	Died

BOOP: Bronchiolitis Obliterans with Organizing Pneumonia; AFOP: Acute Fibrinous and Organizing Pneumonia.
* IgM and IgG titles are not detailed.

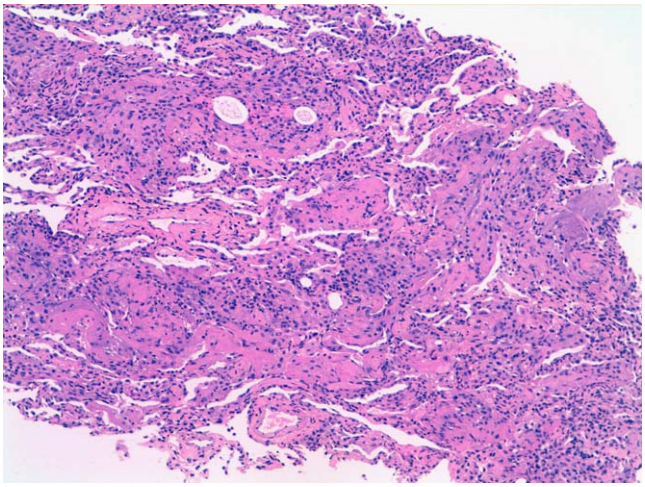

Figure 2. Transbronchial biopsy: intra-alveolar "fibrin balls" and fibroblastic tissue without hyaline membranes (hematoxylin-eosin ×100).

anti-glomerular basement membrane antibodies), and an echocardiography showed good global contractility and a pulmonary artery pressure of 4.9 kPa (37 mmHg). In spite of high doses of corticosteroids, respiratory distress and multiorgan dysfunction ensued and the patient died after 20 days of admission. Autopsy was not performed because it was not authorized by the family.

Serologies for *Mycoplasma pneumoniae*, *Coxiella burnetti* and *Legionella pneumophila* were negative. *Chlamydia pneumoniae* serology anti-IgG, using indirect microimmunofluorescence techniques (MIF, Focus Diagnostics) and Enzyme immunoassay (EIA, Savyon Diagnostics), showed a four-fold rise in IgG titers (1:32-1:512) between the first and second serum samples extracted 13 days apart. IgM detection was inconclusive by EIA.

Severe respiratory infection by *C. pneumoniae* occasionally has been associated with histological features of BOOP, which appeared to be secondary to the pulmonary infection.[7-9] However, to our knowledge, no cases of *C. pneumoniae* infection associated with AFOP have been reported to date. Table 1 shows the main characteristics of the four cases of *C. pneumoniae* infection associated with BOOP reported in the literature, and the present case, associated with AFOP. All four patients were around the seventh decade of life: two of them had associated comorbidities and the other two were previously healthy. Chest radiographic findings differed slightly in the four cases, but alveolar infiltrates were always present. Three patients were treated with prednisone at doses 1 mg/kg, in combination with an appropriate antimicrobial agent. All of them developed respiratory failure. The subsequent course was satisfactory under treatment in the three cases with BOOP. Despite appropriate antibiotic treatment and steroids, the clinical course of our patient was unsatisfactory and she died of respiratory failure. Treatment with steroids is almost always successful in BOOP, but are frequently less effective in AFOP due to the presence of fibrin in the alveolar spaces.[10,11]

The case presented here illustrates that *C. pneumoniae*-associated AFOP should be considered in cases of atypical pneumonia with an unfavorable clinical evolution and that appropriate serological tests should be part of the etiological search in cases of BOOP or AFOP of unknown origin.

Bibliografía

1. Balis E, Boufas A, Iliopoulos I, Legakis NJ, Zerva L. Severe Community-Acquired Pneumonia with Acute Hypoxemic Respiratory Failure Due to Primary Infection with *Chlamydia pneumoniae* in a Previously Healthy Adult. Clin Infect Dis. 2003;36:e155–7.
2. Marik PE, Iglesias JI. Severe community-acquired pneumonia, shock and multiorgan dysfunction syndrome caused by *Chlamydia pneumoniae*. J Intern Med. 1997;241:441–4.
3. Gnarpe J, Gnarpe H, Nissen K, Haldar K, Nääs J. *Chlamydia pneumoniae* infection associated with multi-organ failure and fatal outcome in previously healthy patient. Scand J Infect Dis. 1998;30:523–4.
4. Panagou P, Tsipra S, Bouros D. Adult respiratory distress syndrome due to *Chlamydia pneumoniae* in a young adult. Respir Med. 1996;90:311–3.
5. Córdoba A, Monterrubio J, Bueno I, Corcho G. Neumonía comunitaria grave por Chlamydia pneumoniae. Emergencias. 2006;18:263–4.
6. Beasley MD, Franks TJ, Galvin JR, Gouchuico B, Travis WD. Acute Fibrinous and Organizing Pneumonia. A histologic Pattern of Lung Injury and Possible Variant of Diffuse Alveolar Damage. Arch Pathol Lab Med. 2002;126:1064–70.
7. Case records of the Massachusetts General Hospital. Weekly clinicopathological exercises. Case 48-1990. A 65-year-old man with pulmonary infiltrates after treatment for Wegener's granulomatosis. N Engl J Med. 1990;323:1546-55.
8. Diehl JL, Gisselbrecht M, Meyer G, Israel-Biet D, Sors H. Bronchiolitis obliterans organizing pneumonia associated with chlamydial infection. Eur Respir J. 1996;9:1320–2.
9. Imokawa S, Yasuda K, Uchiyawa H, Sagisaka S, Harada M, Mori K, et al. Chlamydial Infection Showing Migratory Pulmonar Infiltrates. Nippon Naika Gakkai Zasshi. 2007;46:1735–8.
10. Tzouvelekis A, Koutsopoulos A, Oikonomou A, Froudarakis M, Zaragoulidis P, Steiropoulos P, et al. Acute Fibrinous and Organizing Pneumonia: a case report and review of the literature. J Med Case Reports. 2009;3:74.
11. Gary R, Epler MD. Bronchiolitis Obliterans Organizing Pneumonia. Arch Intern Med. 2001;161:158–64.

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Hidatidosis esplénica: 5 casos de esta rara localización

Splenic hydatidosis: 5 cases of this location

Sr. Editor:

La hidatidosis es una zoonosis causada por la larva del *Echinococcus granulosus* infectando al ser humano como huésped intermediario. Su afección esplénica es una rara entidad que afecta al 0,5-6% de las localizaciones abdominales, siendo la tercera localización en frecuencia tras la hepática (50-80%) y pulmonar (25%). El diagnóstico sincrónico, hepático o peritoneal se observa en el 20-30% de los pacientes. En áreas endémicas el 50-80% de los quistes esplénicos son de origen hidatídico[1]. El primer caso fue descrito en 1790 por Bertelot, siendo Sabadini quien publicó la primera serie.