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Fluoroquinolone therapy could influence the clinical signs of pulmonary coccidioidomycosis

La terapia con fluoroquinolonas podría influir en las manifestaciones clínicas de la coccidioidomicosis pulmonar

Dear Editors,

Symptoms of coccidioidomycosis can frequently be mistaken with those of community-acquired pneumonia (CAP) and even be treated initially with antibacterials. Coccidioidal pneumonia is not an infrequent presentation and studies carried out in endemic zones of the United States have shown that 15% of CAP have a positive serology for *Coccidioides*,[5] a reason why the most recent CAP management guidelines recommend thinking about coccidioidomycosis in those cases from endemic areas.[3] There are no definitive studies regarding the possible influence of CAP's empiric therapy in the presentation of an unsuspected coccidioidomycosis. On the other hand, seeing that many cases of coccidioidal pneumonia present a spontaneous resolution of the signs and symptoms, a patient with unsuspected coccidioidomycosis

Table 1
Coccidioidomycosis case-series under fluoroquinolone therapy.

Case Gender (F/M)	Age (years)	Comorbidities	Symptoms presentation	Rx/CT	Initial antimicrobial treatment	Progress	Outcome
Case 1 F	57	DM	1-Month of cough, dyspnea, fever, significant weight loss, other constitutional symptoms	Right lobar pneumonia	3 days of moxifloxacin 400 mg IV o.d. and cefotaxime 1 g IV t.i.d.	Partial improvement in her general symptoms, gas exchange and leukocyte count	After initial antimicrobial withdraw her symptoms were exacerbated.*,† Amphotericin-B therapy was required
Case 2 F	71	DM	3-Weeks of cough, chest pain, fever, fatigue, night sweats	Left lobar pneumonia. Multiple disseminated nodules	7 days of moxifloxacin 400 mg IV o.d.	Gas exchange and leukocyte count improved, periods between fever peaks were more spaced	Amphotericin-B therapy was required†
Case 3 M	42	–	2-Weeks of dyspnea, cough, chest pain, fever, night sweats, malaise	Left lobar pneumonia. Pleural effusion. Multiple disseminated nodules	3 days of ceftriaxone 1 g IM b.i.d. followed by 7 days of moxifloxacin 400 mg orally o.d.	Developed a cutaneous hypersensitivity reaction to ceftriaxone	Symptoms improved significantly but the changes on a control chest X ray persisted.† Itraconazole therapy was required
Case 4 M	34	DM	1-Month of cough, progressive dyspnea, fever, sweating, significant weight loss	Diffuse infiltration. Multiple disseminated nodules	2-Weeks of moxifloxacin 400 mg orally o.d.	Symptoms improved until reaching an asymptomatic state	Antimycotic therapy was not required‡,¶
Case 5 F	73	–	2-Months of symptomatic right sided pleural effusion, fever, night sweats, malaise	Right sided pleural effusion	2-Weeks of ciprofloxacin 500 mg orally b.i.d.	Reach an asymptomatic state without recurrence of pleural effusion	Antimycotic therapy was not required§,¶

DM: diabetes mellitus; F: female; M: male.
* In case 1 it was decided to substitute the initial antimicrobial scheme to one with a wider coverage including staphylococci.
† In cases 1, 2, and 3, a bronchoscopy finally revealed the presence of *Coccidioides* spherules.
‡ In case 4 a polymerase chain reaction (PCR) testing for *Coccidioides* on bronchoscopic biopsy resulted positive.
§ In case 5 a PCR testing for *Coccidioides* on pleural biopsy resulted positive and a serologic testing confirmed high titers of IgM and IgG antibodies to *Coccidioides* antigens.
¶ PCR testing for *M. tuberculosis* was performed in biopsies from cases 4 and 5 and resulted negative.

receiving antibacterials could seem to respond satisfactorily. We herein expose (see Table 1) the experience with the use of empiric antibacterials for CAP in five consecutive cases from our endemic area which were confirmed later on as pulmonary coccidioidomycosis.

The pneumonic presentation of coccidioidomycosis is not infrequent and it has been reported as high as up to 44% of clinical forms among the Hispanic population.[4] Considering this scenario we must not be surprised if many cases are initially treated as CAP.

Because of their wide antibacterial spectrum, fluoroquinolones have been recommended as first line medications during the empiric treatment of CAP in adults, mainly if associated comorbidities exist.[3] All of our patients were exposed to fluoroquinolones. Although lacking of an intrinsic antimycotic activity per se, fluoroquinolones can influence the growth of pathogenic fungi by inhibiting the enzymatic topoisomerase II and topoisomerase IV pathways or, influence their clinical manifestations on inhibiting the production of pro-inflammatory cytokines by the mononuclear cells.[1,2] This latter could also favor the induction of self-limited clinical forms on coccidioidomycosis as occurred in cases 4 and 5.

The co-infection with other microorganisms such as *Mycobacterium tuberculosis* could also explain our results. Those antibacterials with antituberculosis activity such as fluoroquinolones theoretically could alleviate the symptoms caused by the tuberculosis component. However, although our search for *M. tuberculosis* was not exhaustive in some of our cases, the progression of symptomatology after initiating the specific antimycotic treatment conduced convincingly toward its improvement discarding any possibility of comorbidity with tuberculosis.

Spontaneous remission of coccidioidomycosis is a frequent described phenomenon and undoubtedly could explain in part the evolution of our patients. In Valdivia's and colleagues cohort[5] the majority of those patients initially diagnosed as bacterial CAP and who subsequently developed coccidioidomycosis were treated only with one or several cycles of antibacterials and everyone benefited from them. Unfortunately it was not mentioned which antibiotics were used.

The main repercussion an antimicrobial treatment indicated for bacterial CAP that may influence the clinical presentation of coccidioidomycosis would have is the delay in the diagnosis and, consequently, the consumption of unnecessary resources as we observed in case 1. Waiting for more information obtained from blinded trials, the clinician must be alert on how the use of antibacterials in CAP, especially the fluoroquinolones, could influence the clinical manifestations of coccidioidomycosis, contributing to the delay in the correct diagnosis and, consequently, in its treatment.

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