**Revisor A comentário 1:**

The present manuscript describes a clinical case of a rare complication of adjunctive BCG treatment of bladder cancer. It helps the clinical practice as it points out some precautions that must be remembered in these patients.

These findings are obviously important for the clinical practice although not original. Their rare occurrence throws some importance on multidisciplinary approach.

Both title and abstract are clear and informative about the case findings, correctly aimed on the end of the background section.

The case is thoroughly described and illustrated, mainly with CT scan evolution in time.

The discussion and the conclusions which follow seem adequate to raise the  
awareness on relatively mild symptoms after this therapeutic approach in  
bladder cancer. The reviewer would like the authors to comment in discussion  
section the proposal of some authors (1) of fluoquinolone short prophylactic  
use after each intravesical instillation in these cases.

**Resposta:**

Several studies have been done to demonstrate effective measures in preventing the occurrence of disseminated BCG infection, such as fluoroquinolone short prophylaxis use after each BCG administration. A multicenter, randomized and prospective study [13] presented that ofloxacin reduced the incidence of severe local reactions and the use of antituberculosis treatment. However, no cases of BCG sepsis were reported and the ability of ofloxacin to prevent more severe complications was not evaluated. Fluoroquinolone prophylaxis might reduce the antitumor activity of BCG, but no clear evidence has been found to recommend routine fluoroquinolone prophylaxis. Other study using prulifloxacin reported very comparable findings [14].

[13] M. Colombel, F. Saint, D. Chopin, et al. The effect of ofloxacin on bacillus calmette-guerin induced toxicity in patients with superficial bladder cancer: results of a randomized, prospective, double-blind, placebo controlled, multicenter study. J Urol 176 (2006), pp. 935-939.

[14] R. Damiano, M. De Sio, G. Quarto, et al. Short-term administration of prulifloxacin in patients with nonmuscle-invasive bladder cancer: an effective option for the prevention of bacillus Calmette-Guérin-induced toxicity? BJU Int 2009; 104:633.

**Revisor A comentário 2:**

The reference structure seems correct and comprehensive, Figure are clear  
and legends are correct.

The present case study is relevant to a commonly accepted approach in  
superficial bladder cancer. Therefore he recommends the publication on AMP, eventually adding the recommended comment. The English version could be still improved in syntax structure.

**Resposta:**The authors appreciate the comments and the English version was improved using a qualified English translator.

**Revisor C comentário 1:**

The case report “Subclinical granulomatous pneumonitis due to intravesical  
BCG for bladder cancer” is an interesting case about a known but rare side  
effect of BCG instillation for bladder cancer treatment.

Overall the structure of the case report is well done with a good sequence  
of description. Despite several other cases reported around the world, it is  
still important to keep in mind potential side effects of this treatment in  
order to recognize them soon and treat accordingly.

There are several concerns about this case report that I believe that must  
be clarified:

1. In the “Background” section you state that the patient had  
“subclinical” and “non-specific symptoms”. However the patient had  
low-grade fever for a month with a peak of fever. In my opinion this cannot  
be considered “subclinical” since mycobacterial infections are  
characterized by non-specific symptoms as low-grade fever and night sweats  
for instance.

**Resposta:**The authors recognize that the term “subclinical” can mislead readers, since the patient had already symptoms as low-grade fever. However, globally the symptoms were mild. According to these considerations, the authors decided to alter the term “subclinical” to “mild” when appropriate in order to translate a more correct clinical picture of the patient’s status.

**Revisor C comentário 2:**

2. You state that PCR was performed on BALF. PCR is a wide concept. It must  
be stated which test was used in order to readers know their expected  
sensitivity/specificity and positive/negative predictive values.

**Resposta:**Real-time PCR was performed on BALF.

**Revisor C comentário 3:**

3. The patient was treated with corticosteroids and with a 4-drug regimen:  
isoniazid, rifampin, ethambutol and ciprofloxacin. Ciprofloxacin has  
virtually no effect in mycobacteria (very low) and is never considered as an  
option for mycobacterial infections. To the best of my knowledge no other  
case like this used ciprofloxacin as an option (there is a case report in  
which moxifloxacin was used in other context).

**Resposta:**The authors recognize that the treatment regimen was not successfully explained and agree with the previous comment. The patient was initially medicated by the Urologist with a short-term course of ciprofloxacin, previously to the first consultation in our regional Pulmonology Diagnosis Center. For patients with infection disseminated outside the bladder, such as the present clinical case, multi-drug antibiotic therapy is usually recommended for at least six to nine months, depending upon the severity of symptoms and organ system involved. One common regimen consists of isoniazid and rifampin for six months with a two-month intensive phase including ethambutol; this is based upon the standard recommended therapy for tuberculosis infection. Our patient was medicated with a three-drug regimen (isoniazid, rifampin and ethambutol) for two months and with a two-drug regimen (isoniazid and rifampin) for ten months. No fluoroquinolone was included in the treatment regimen, despite being as option in the literature, for example with levofloxacin or moxifloxacin.

**Revisor C comentário 4:**

4. Treatment duration. The current patient was treated for 12months. The  
usual care is to treat with 6-9 months.

**Resposta:**The authors recognize the usual care treatment, but there is limited evidence to support standard recommendations for the treatment of human disease due to *M. bovis*. The present case was discussed at a multidisciplinary reunion with the presence of a Pulmonologist and Radiologist with experience in respiratory imaging, due to the slow imaging response at nine months of treatment. It was assumed that there was still active imaging disease with some nodule calcification despite the clinical resolution which lead to treatment for 12 months with periodic evaluation with complete imaging resolution of active disease.

**Revisor C comentário 5:**

# 5. The reference 12 does not support your statement that a 4-drug regimen with a quinolone for 6 months is an option for treat this patients. The referred article is about a patient treated with corticosteroids alone.

# Resposta:  The authors agree with the previous comment and the reference that was intended to be added is a systematic review publication:

# 12. Z. Lan, M. Bastos, D. Menzies. Treatment of human disease due to *Mycobacterium bovis*: a systematic review ERS, 48 (2016), pp. 1500–1503.