Author’s response to reviews

Title: Case Report: Nocardia infection associated with Ectopic Cushings

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Author’s response to reviews:

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Editor,
BMC Endocrine Disorders
BioMed Central
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Dear Editor,

Enclosed is our revised manuscript entitled “Nocardia infection associated with Ectopic Cushings” for consideration by the BMC Endocrine Disorders. The manuscript has been submitted as a case series.

Cushing’s syndrome is a disease resulting from exposure to excess glucocorticoids. Excess cortisol secretion has a high mortality if left untreated. There are several causes of hypercortisolism. Ectopic Cushings is endogenous ACTH dependant form of Cushing’s associated with markedly raised ACTH and, subsequently, cortisol levels. Elevated cortisol levels lead to an impaired immune response by neutrophils & macrophages and diminished recruitment of these inflammatory cells into the infected site. This sets the stage for the occurrence of bacterial and fungal opportunistic infections. Opportunistic infections in Cushing’s syndrome carry a high mortality and morbidity. A variety of opportunistic infections have been demonstrated in the presence of endogenous cortisol production. Most popular are pneumocystis jirovecci, Cryptococcus neoformans and Nocardia spp. Nocardiosis is a gram positive bacterial infection caused by aerobic actinomycetes in the genus Nocardia.

Our case series highlights the importance of considering Nocardia spp. as a causative agent for the pulmonic manifestations of patients diagnosed with
Cushing’s syndrome, particularly in the Ectopic Cushing’s subset. This series also includes the first case reported in which the signs and symptoms of Cushing’s subsided simply after antibiotic treatment of Nocardia.

To the best of our knowledge, no case to date has been reported in the literature in which treatment of the Nocardia spp. resulted in disappearance of the clinical, biochemical and radiologic manifestations of the Ectopic Cushing’s (as in one of our cases). This included the severe proximal myopathy, refractory hypokalemia, hypercortisolism and the pulmonary lesions that the patient had presented with. We were able to withdraw all therapy, with the patient remaining symptom-free till date (2011-2014).

This suggests that nocardiosis may not only result from hypercortisolism, but can also itself lead to raised cortisol levels, and the manifestations of Cushing’s syndrome. The mechanism by which Nocardia spp can cause Cushing’s syndrome is not clear, and, therefore, needs to be further investigated.

The manuscript has nearly 3000 words, excluding title page, tables, & references. There are three tables and six figures. All authors have read the final manuscript and have no conflict of interest. Thank you for your consideration. We look forward to hearing from you.

The editorial requirement was to re upload the figures so that each part of the figure is one file.

In this connection, the first figure consists of two parts, labeled figure 1a (Case 1) (left of the page) “CT Chest before treatment for nocardia”. To the right of the page is figure 1b: “near doubling of lesion within span of 14 days”.

For the second figure, there is a single CT scan picture of CT chest after treatment of Nocardia case 1- resolution of cavitatory lesion.

For the third figure- there is a single CT scan picture of CT chest before treatment case 3 (consolidation right anterobasal segment and pleural effusion).

For the fourth figure, this consists of two parts: at the top of the page is figure 4a (case 3) chest x ray before treatment (consolidation right anterobasal segment and pleural effusion). Below figure 4a (bottom of page) is figure 4b (case 3) chest x ray after treatment (resolution of right anterobasal segment consolidation and pleural effusion).

Sincerely,

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