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CASE REPORT PEER REVIEWED | OPEN ACCESS

Synchronous pulmonary Cryptococcus and carcinoid tumor in Cushing's syndrome: A diagnostic challenge

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ABSTRACT

The simultaneous occurrence of a pulmonary carcinoid tumor and pulmonary *Cryptococcus* is very rare. A 25-year-old male presented with typical symptoms of Cushing's syndrome. Investigations revealed synchronous lung lesions in the right upper lobe and left lower lobe. The right upper lobe lesion was strongly PET-positive and the left lower lobe lesion was mildly PET-positive. A right upper lobectomy was performed with histological analysis confirming pulmonary cryptococcosis. A delayed left lower lobectomy was performed with histological analysis confirming a typical carcinoid tumor

Keywords: Cushing's syndrome, Pulmonary Cryptococcosis, Carcinoid tumor, PET-positive lesion

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INTRODUCTION

Pulmonary carcinoid tumors are neuroendocrine tumors constituting 1–2% of all pulmonary neoplasms. Presenting symptoms include hemoptysis, cough, fever, recurrent chest infections and localized wheeze. Wherever possible, surgical excision is the treatment of choice. Clinical outcomes are dependent on the type of tumor and staging. Prognosis for typical carcinoid tumors is generally favorable.

Pulmonary Cryptococcus usually occurs in immunocompromised patients but may also occur in non-immunocompromised patients with chronic lung disease. Typical symptoms include fever, malaise and dyspnoea. Advances in antifungal therapy over the last two decades has had an impact in the management of this condition, however, surgery still has a significant role to play in the management of fungal infections of the lung.

Coexistence of a carcinoid tumor and pulmonary cryptococcal infection is very rare. This is the first recorded case of a patient treated with surgical excision of a carcinoid tumor and synchronous cryptococcal infection of the contralateral lung.

CASE REPORT

A 21-year-old male presented with typical symptoms of Cushing's syndrome including weight gain, thin bruised skin and severe fatigue. Serum ACTH was elevated with normal cortisol levels. Diagnostic computed tomography scan revealed a right upper lobe nodule and a left lower lobe nodule. Both lesions took up octreotide suggesting a neuro-endocrine origin (Figure 1). Subsequent PET

scan showed the 20 mm right upper lobe nodule to be markedly FDG avid (SUV max 11.5). The 11 mm nodule in the left lower lobe was moderately FDG avid (SUV max 2.0) (Figure 1). Treatment options were discussed at a multidisciplinary team meeting. The consensus of opinion was that a right upper lobectomy and a wedge resection the left lower lobe nodule should be performed as a staged procedure. Histological analysis of the right upper lobe lesion following VATS lobectomy demonstrated a granulomatous fungal infection consistent with *Cryptococcus* (Figure 2). A six-month course of fluconazole therapy was commenced in accordance with our hospital protocol for fungal infections of the lung.

As there was no resolution of symptoms a left lower VATS lobectomy was performed after 18 months. Histological analysis confirmed a typical carcinoid tumor staged at T1a N0 MX R0 (Figure 2). There was full resolution of the patient's symptoms following resection of the carcinoid tumor.

DISCUSSION

Carcinoid tumors arise from the Kulchitsky cells of bronchial mucosa. These cells release serotonin and ACTH. Carcinoid syndrome appears when these bioactive amines are realised in the blood stream. Harpole Jr et al. reported in their single institution case series that patients with bronchogenic tumors are usually asymptomatic [1]. Four grades of neuroendocrine tumors are described (i) Typical carcinoid tumor, (ii) Atypical carcinoid tumor (iii) Large cell neuroendocrine carcinoma and (iv) Small cell neuroendocrine carcinoma [2]. Carcinoid tumors are classified as malignant tumors. Computed tomography scan has been used to localize the tumors. PET scanning is not suitable for distinguishing this disease from other lung inflammatory conditions or malignancy due to its low metabolic activity [3]. Somatostatin receptor scintigraphy, also known as octreotide scanning is reported to have more specificity and sensitivity than PET scans due to the presence of somatostatin receptors in the tumor cells [4]. The left lower lobe lesion in our patient was a carcinoid tumor with (SUV<2) that was octreotide positive. Histology confirmed a typical carcinoid tumor. The prognosis of carcinoid tumors is related to its histological type and staging. More recently molecular targeted agents have shown promising outcomes but these warrant randomised controlled trials before their use can be justified over conventional treatment strategies.

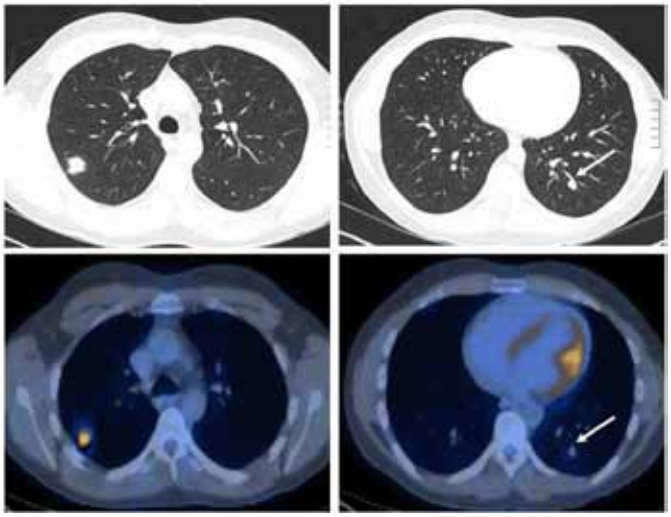

Figure 1: Computed tomography scan showing right upper lobe and left lower lobe lesion. Positron emission tomography (PET) scan reveals PET positive lesion in right upper lobe lesion.

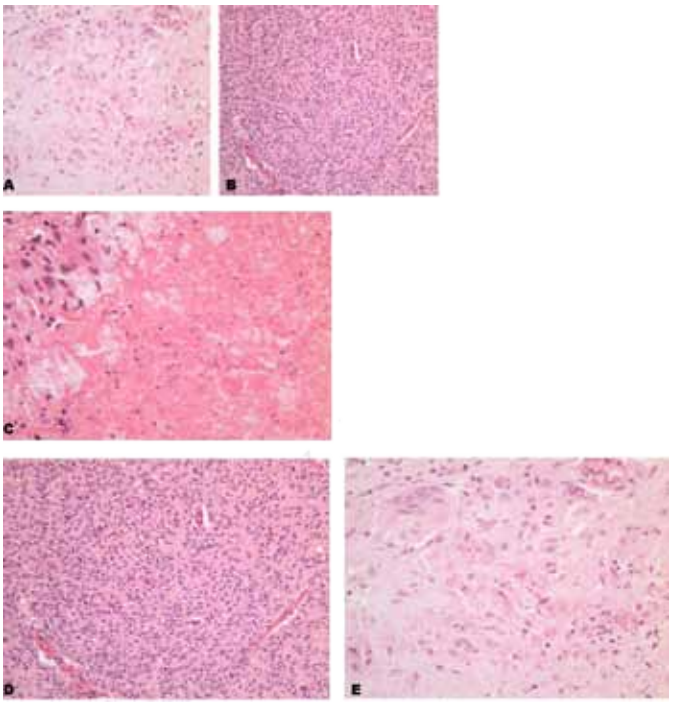

Figure 2: Histological slides of the right upper lobe and left lower lobe lesion. (A) Right upper lobe nodule illustrated necrotizing granulomas (almuci 40x, Mucicarmine stain highlighting cryptococci, high power). (B) Left lower lobe nodule showing typical carcinoid tumor (alc-carcinoid tumor, x20), (C) High resolution of cryptococci (H&E stain, al40x), (D) Mucicarmine stain highlighting Cryptococci (almuci 40x), (E) Neuroendocrine carcinoma (alc-H&E stain).

Two types of Cryptococcus have been isolated: *Cryptococcal neoformans* that infects an immunocompromised host; and *Cryptococcus gattii* that produces infections in an immunocompetent host [5]. Cryptococcal infections can be diagnosed from sputum culture. Recently an antigen test has been used for diagnosis of disseminated cryptococcosis with high specificity and sensitivity. In our case, neither a sputum culture nor antigen test was performed as a fungal infection was not considered in the differential diagnosis. Surgeons are rarely involved in the diagnosis or management of this disease. Surgical intervention may be required to treat

the fibrinopurulent cryptococcal empyema or to rule out carcinoma [6]. In our case, histology of the right upper lobe revealed a fungal infection that was unprecedented and ultimately an incidental finding.

CONCLUSION

The simultaneous occurrence of a pulmonary carcinoid tumor and cryptococcal infection may occur though it is extremely rare. When two lesions are identified on computed tomography scan which are both PET and octreotide scan positive, in presence of Cushing syndrome, the diagnosis can be uncertain. The clinician should be fully aware that two different pathological processes may co-exist.

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Author Contributions

Anupama Barua – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published
Paul Govewalla – Analysis and interpretation of data, Revising it critically for important intellectual content, Final approval of the version to be published
Emanuel Kefaloyannis – Analysis and interpretation of data, Revising it critically for important intellectual content, Final approval of the version to be published
Radhika Ramnath – Analysis and interpretation of data, Revising it critically for important intellectual content, Final approval of the version to be published
Kostas Papagiannopoulos – Analysis and interpretation of data, Revising it critically for important intellectual content, Final approval of the version to be published

Guarantor

The corresponding author is the guarantor of submission.

Conflict of Interest

Authors declare no conflict of interest.

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REFERENCES

1. Harpole DH Jr, Feldman JM, Buchanan S, Young WG, Wolfe WG. Bronchial carcinoid tumors: A retrospective analysis of 126 patients. Ann Thorac Surg 1992 Jul;54(1):50–4.
2. Travis WD, Linnoila RI, Tsokos MG, et al. Neuroendocrine tumors of the lung with proposed criteria for large cell neuroendocrine carcinoma. An ultrastructural, immunohistochemical, and flow cytometric study of 35 cases. Am J Surg Pathol 1991 Jun;15(6):529–53.
3. Daniels CE, Lowe VJ, Aubry MC, Allen MS, Jett JR. The utility of fluorodeoxyglucose positron emission tomography in the evaluation of carcinoid tumors presenting as pulmonarynodules. Chest 2007 Jan;131(1):255–60.
4. Yellin A, Zwas ST, Rozenman J, Simansky DA, Goshen E. Experience with somatostatin receptor scintigraphy in the management of pulmonary carcinoid tumors. Isr Med Assoc J 2005Nov;7(11):712–6.
5. Smith JA, Kauffman CA. Pulmonary fungal infections. Respirology 2012 Aug;17(6):913–26.
6. LoCicero J 3rd, Shaw JP, Lazzaro RS. Surgery for other pulmonary fungal infections, Actinomyces, and Nocardia. Thorac Surg Clin 2012 Aug;22(3):363–74.

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