Unusual presentation of more common disease/injury

Mai infection simulating metastatic breast cancer

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Summary

We represent a case of an asymptomatic female who was found to have a mass in the right breast which confirmed an invasive ductal carcinoma by core biopsy. After 3 months of completion of chemo-radiotherapy, the patient remained totally asymptomatic. However, positron emission tomography scan showed four hypermetabolic lesions in the left lung thought to be consistent with metastatic disease. Standard uptake value ranged between 3.86 and 6; the results were consistent with metastatic breast cancer, so wedge resection was performed. Caseating granulomatous inflammation with necrosis was reported. Ultimately culture revealed *Mycobacterium avium* intracellular infection. The lesions resolved completely after a course of antibiotics.

BACKGROUND

Mycobacterium avium-intracellular complex (MAC) is the most common non-tuberculous mycobacterial (NTM) cause of systemic disease in humans. MAC is widely disseminated in the environment but the incidence of disease in immunocompetent hosts is very low. HIV infection, underlying lung disease and immunodeficiency predispose patients to MAC infection that is primarily pulmonary. However, MAC has been associated with osteomyelitis, tenosynovitis and disseminated disease involving lymph nodes, central nervous system, liver, spleen, gastrointestinal tract and bone marrow. In people with HIV infection, atypical MAC has become a major opportunistic infection in the advanced stage of the disease.

NTM diseases presenting as solitary pulmonary nodules (NTM-SPN) are rare, usually asymptomatic and may be misdiagnosed as cancer (either primary or metastatic), especially if they are multiple with high standard uptake value (SUV) on fluorodeoxyglucose-positron emission tomography (FDG-PET) scan, and in patients who were previously diagnosed with primary cancer as in our case.

This case report highlights the importance of clinical awareness of the NTM diseases as a cause of hypermetabolic pulmonary nodules in patients with cancer. Increased FDG uptake could be a misleading factor, as it might be increased in both situations. Hence, diagnostic evaluation should be considered in the initial work-up such as fine needle aspiration and CT-guided biopsies with cultures prior to the surgical intervention of these equivocal pulmonary nodules. Antibiotics should be promptly started to avoid morbidity and mortality of MAC infection.

CASE PRESENTATION

A 45-year-old white woman was found to have a mass in the upper outer quadrant of her right breast on routine examination. The patient denied pain or discharge from the breast, changes in her weight, appetite and menstrual cycles. A review of systems was unremarkable. On examination,

she was a middle-aged white woman in no acute distress with BP 103/68 mm Hg, RR 18/min, pulse 85/min and temperature 36.2°C. Breast examination revealed no erythema, puckering or discharge. Her nipples were everted and the nipple-areola complex was properly positioned. In the upper quadrant area of her right breast, there was a firm mass, about 4×4 cm, irregular, non-tender, non-fluctuant and freely mobile. No other swellings were noted in either breast. Axillary lymph nodes were not palpable bilaterally. The remainder of the examination was unremarkable.

INVESTIGATIONS

Mammography showed microcalcifications and core biopsy confirmed an invasive ductal carcinoma. Sentinel lymph node biopsy and lumpectomy were performed. Pathology was consistent with invasive ductal adenocarcinoma. Three of 14 right axillary lymph nodes were positive for metastatic adenocarcinoma. Tumour staging was T2, N1, M0 breast cancer, oestrogen receptor positive, progesterone receptor (PR) positive and Her-2 negative by fluorescent in situ hybridisation. She received initial chemotherapy with doxorubicin hydrochloride and cyclophosphamide. Adjuvant radiotherapy was administered 3–4 weeks after completion of her chemotherapy. After 3 months of completion of chemo-radiotherapy, a routine follow-up and imaging revealed new pulmonary lesions that were followed by F-18 FDG and PET scan (figure 1).

The patient remained totally asymptomatic with no cough, haemoptysis or chest pain. PET scan showed four hypermetabolic lesions in the left lung thought to be consistent with metastatic disease without evidence of regional lymphadenopathy or local recurrence. SUV ranged between 3.86 and 6. The results were consistent with metastatic breast cancer. Fine needle aspiration and CT-guided biopsies were attempted but samples were insufficient to make a diagnosis, although some atypical cells were seen. Wedge resection was performed and an ill-defined white-yellow mass measuring 1.5 cm in diameter was removed. Caseating granulomatous inflammation

Figure 1 F-18 fluorodeoxyglucose and positron emission tomography scan revealed hypermetabolic lesions in the left lung that were thought to be consistent with metastatic disease based on the elevation of standard uptake value.

with necrosis was reported. Stain for acid-fast bacillus (AFB) was negative. A Grocott's silver stain was negative for fungi. Ultimately, culture revealed *M avium* intracellular infection. Clarithromycin 1000 mg and rifampin 600 mg (3 times/week) were begun and after 4 months, CT scan revealed resolution of previously demonstrated lesions.

DIFFERENTIAL DIAGNOSIS

- Pulmonary nodules due to metastatic breast cancer
- Tuberculous mycobacterial disease
- NTM diseases/MAC.

TREATMENT

Clarithromycin 1000 mg and rifampin 600 mg (3 times/week).

OUTCOME AND FOLLOW-UP

After 4 months of treatment with antibiotics, CT scan revealed resolution of previously demonstrated lesions.

DISCUSSION

Some pulmonary MAC may be radiographically indistinguishable from malignancy, and biopsy with appropriate cultures is necessary for diagnosis. In a study of 17 patients who had a preoperative diagnosis of *Mycobacterium* other than tuberculosis by sputum bacterial cultures, 2 patients were suspected of having lung cancer on CT scan, and video-assisted thoracoscopic resection of the lung was performed. The diagnosis of malignancy was made by an intra-operative frozen section of resected tissue. Hence, it is possible to see MAC infection coexisting with pulmonary malignancy.¹

Kobashi *et al* reported a 56-year-old man with a history of surgical resection of a primary pulmonary adenocarcinoma in the right lung. He was hospitalised because of a rapidly enlarging right middle lobe solitary nodule on CT scan. Resection of the middle lobe was performed. A caseating epitheloid granuloma with AFB with MAC on culture was found.²

A 63-year-old woman was found to have a solitary nodule in her right middle lobe detected during a routine health examination. Pleural indentation was seen on chest CT scan, suggesting malignancy. Video-assisted thoracoscopic surgery (VATS) was performed and caseating epitheloid granulomas with MAC on culture were found.³

A similar case was reported by Suzuki *et al*⁴ in which a solitary pulmonary nodule was resected and MAC was cultured. Pathology showed no cancer.

Nakamura *et al*⁵ reported a case of endobronchial carcinoid tumour combined with pulmonary NTM infection presenting as a nodule. Similarly, Lillo *et al*⁶ found six cases with bronchogenic carcinoma in their review of 44 patients combined with pulmonary isolates of *Mycobacterium kansasii*. Gettler and el-Sadr reported a case of concomitant NTM infection and primary lung cancer. Both lesions presented as solitary nodules that were indistinguishable radiographically.⁷ Kobashi *et al* reported four cases of pulmonary MAC presenting as a solitary pulmonary nodule. In each case, the nodule was first identified either on routine chest x-ray (CXR) or on CXR taken for respiratory symptoms not referable to the nodule.⁸

Pulmonary nodules due to NTM disease (exclusively MAC) can mimic tuberculoma.⁹ Of the 15 patients with SPNs due to MAC, 10 were initially diagnosed with 'tuberculoma' and administered antituberculosis medication.

Hence, MAC pulmonary disease should be considered in the differential diagnosis of SPNs, even when encountered in geographic regions with a high prevalence of pulmonary tuberculosis.¹⁰

It is unclear whether there is any relationship between non-tuberculous mycobacterial infections (NTMI) and carcinoma. Gettler and el-Sadr⁷ reported activation of NTMI by carcinoma secondary to disruption of the granuloma either by cancer cells or by immune response to tumour antigens. Takii *et al*¹¹ found that interleukin 1 or tumour necrosis factor α augmented the cytotoxic effect of mycobacteria on human fibroblasts.

Our patient highlights the presence of a positive FDG-PET in a patient with pulmonary MAC infection. FDG-PET scanning has increasingly been proposed as a method to differentiate between benign and malignant lesions.¹² FDG uptake, however, is not limited to the malignant lesions only; it also occurs in inflammatory cells. Active inflammatory cells exhibit a very robust glycolysis and take up significant amounts of FDG. Nonetheless, this uptake is far less than that of neoplastic tissue.¹² Therefore, inflammation and malignancy may be differentiated on the basis of SUV. A threshold of 2.5 ordinarily differentiates between benign and malignant lesions in patients with a pulmonary nodule. In our patient, the SUV was more than 3.5 and hence supported the presence of a malignant process. This emphasises the importance of VATS in order to obtain tissue confirmation.¹² Schmeekle reported that a 59-year-old woman with a history of both breast and lung cancer developed a new 1.5 cm solitary pulmonary nodule on CT scan. The

nodule had increased 18F-FDG uptake on PET with an SUV of 3.4. A CT-guided biopsy was performed, and MAC was identified.¹³

(18)F-FDG-PET appears to be useful for the evaluation of disease activity and in monitoring response to chemotherapy in patients with MAC. A group of 22 patients with MAC, who presented with small peripheral pulmonary nodules, were evaluated using high-resolution CT (HRCT) and (18)F-FDG-PET, and the findings were compared. Of all the lesions, 87.2% had SUVmax levels ranging from 3 to 7. Further, SUV levels in patients with MAC reflected disease activity as estimated by HRCT. (18) F-FDG uptake was significantly decreased in all 14 patients who received chemotherapy, indicating a positive response to treatment.¹⁴ Literature review revealed that among 53 patients with NTM lung disease, serum CA-125 levels were elevated in 28 (52.8%); moreover, the clinical course of NTM lung disease was correlated with changes in serum CA-125 levels.¹⁵

Since culture results may take up to 4–8 weeks and obtaining antibiotic sensitivities a further 3–4 weeks, it is important to consider mycobacterial infection when histological evidence of granulomatous changes is seen.¹⁶ Azithromycin or clarithromycin are among the most potent monotherapy for MAC bacteraemia, although many blood stream isolates demonstrate increased minimum inhibitory concentrations after 4 months of treatment.¹⁷ Ethambutol has modest activity against MAC and its benefit is in potentiating the effects of other active compounds.¹⁷ The regimens used along with their usual doses and side effects are illustrated in figure 2.

1.2x.6cm LUL, SUV 3.8

Figure 2 Regimens of antibiotic treatment for *Mycobacterium avium*-intracellulare complex used along with their usual doses and side effects.

HIV-negative patients with MAC pulmonary disease should be given a combination of daily clarithromycin or azithromycin, rifampin or rifabutin and ethambutol. Therapy should be continued for 12 months after sputum conversion although the optimal duration of treatment is unknown. Relapses after treatment are common and long-term benefit is seen in only a few patients. Surgical resection is an option for the patient with progressive disease that responds poorly to chemotherapy and the success rate with surgical therapy is good.¹⁸

Learning points

- ▶ *Mycobacterium avium*-intracellulare complex (MAC) is an opportunistic infection associated with malignancy (as in our case), HIV infection, underlying lung disease and immunodeficient patients.
- ▶ MAC is a cause of hypermetabolic pulmonary nodules in patients with cancer.
- ▶ Increased fluorodeoxyglucose uptake could be a misleading factor in diagnosing the cause of pulmonary nodules, as it might be increased in MAC and cancer. Hence, diagnostic evaluation should be considered in the initial work-up such as fine needle aspiration and CT-guided biopsies with cultures prior to the surgical intervention of these equivocal pulmonary nodules.
- ▶ Antibiotics should be promptly started to avoid morbidity and mortality of MAC infection.

competing interest None.

Patient consent Obtained.

REFERENCES

1. Tsunozuka Y, Ishikawa N, Hiranuma C, et al. Mycobacteria other than tuberculosis combined primary lung cancer. *Kyobu Geka* 2004;**57**:119–22.
2. Kobashi Y, Yoshida K, Miyashita N, et al. Pulmonary *Mycobacterium avium* disease with a solitary pulmonary nodule requiring differentiation from recurrence of pulmonary adenocarcinoma. *Intern Med* 2004;**43**:855–60.
3. Kobashi Y, Yoshida K, Miyashita N, et al. A case of pulmonary *Mycobacterium intracellulare* infectious disease with a solitary pulmonary nodule in the peripheral lung field. *Nihon Kokyuki Gakkai Zasshi* 2004;**42**:831–6.
4. Suzuki K, Hashimoto T, Tanaka E, et al. A case of *Mycobacterium avium* disease presenting as a solitary pulmonary nodule and resected under a suspicion of lung cancer. *Kekkaku* 1995;**70**:25–9.
5. Nakamura Y, Okada Y, Endo C, et al. Endobronchial carcinoid tumor combined with pulmonary non-tuberculous mycobacterial infection: report of two cases. *Lung Cancer* 2003;**39**:227–9.
6. Lillo M, Orengo S, Cernoch P, et al. Pulmonary and disseminated infection due to *Mycobacterium kansasii*: a decade of experience. *Rev Infect Dis* 1990;**12**:760–7.
7. Gettler JF, el-Sadr W. *Mycobacterium kansasii* infection following primary pulmonary malignancy. *Chest* 1994;**105**:325–6.
8. Kobashi Y, Fukuda M, Yoshida K, et al. Four cases of pulmonary *Mycobacterium avium* intracellulare complex presenting as a solitary pulmonary nodule and a review of other cases in Japan. *Respirology* 2006;**11**:317–21.
9. Lim J, Lyu J, Choi C, et al. Non-tuberculous mycobacterial diseases presenting as solitary pulmonary nodules. *Int J Tuberc Lung Dis* 2010;**14**:1635–40.
10. Hahn CR, Park HY, Jeon K, et al. Solitary pulmonary nodules caused by *Mycobacterium tuberculosis* and *Mycobacterium avium* complex. *Lung* 2010;**188**:25–31.
11. Takii T, Abe C, Tamura A, et al. Interleukin-1 or tumor necrosis factor- α augmented the cytotoxic effect of mycobacteria on human fibroblasts: application to evaluation of pathogenesis of clinical isolates of *Mycobacterium tuberculosis* and *M. avium* complex. *J Interferon Cytokine Res* 2001;**21**:187–96.
12. Davidoff S, Talwar A, Ali SK, et al. *Mycobacterium avium* complex infection simulating lung cancer in AIDS patient after immune reconstitution with antiretroviral therapy. *Respir Med Extra* 2006;**2**:19–22.
13. Schmeckle KD, Yankelevitz D, Kim JW, et al. Increased uptake of 18F-fluorodeoxyglucose due to *Mycobacterium avium* complex in a solitary pulmonary nodule. *J La State Med Soc* 2008;**160**:150–2.
14. Demura Y, Tsuchida T, Uesaka D, et al. Usefulness of 18F-fluorodeoxyglucose positron emission tomography for diagnosing disease activity and monitoring therapeutic response in patients with pulmonary mycobacteriosis. *Eur J Nucl Med Mol Imaging* 2009;**36**:632–9.
15. Kim SY, Hong Y, Choi C, et al. Elevated serum CA-125 levels in patients with non-tuberculous mycobacterial lung disease. *Respirology* 2010;**15**:357–60.
16. Alagarswamy RK, Halfpenny W, Thiruchelvam JK, et al. Rare presentation of *Mycobacterium avium*-intracellulare infection. *Br J Oral Maxillofac Surg* 2007;**45**:670–2.
17. Young LS. Treatment and prophylaxis of *Mycobacterium avium* complex. *Int J STD AIDS* 1996;**7**(Suppl 1):23–7.
18. Shiraishi Y, Nakajima Y, Katsuragi N, et al. Pneumonectomy for nontuberculous mycobacterial infections. *Ann Thorac Surg* 2004;**78**:399–403.

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