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CASE REPORT

Oral treatment with Itraconazole of aspergilloma in cavitary lung cancer

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ABSTRACT: We report a case of aspergilloma in a necrotic small cell lung cancer, where poor pulmonary function and performance status of the patient precluded surgical treatment. High dose Itraconazole, a new oral anti-mycotic drug, was given for 13 months. During this treatment there was a decrease of the fungus ball size and no haemoptysis. Moreover control of the aspergilloma allowed chemotherapeutic treatment of the underlying bronchocarcinoma.

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Aspergillus fumigatus classically grows in cavitated pulmonary lesions, most often in inactive tuberculous lesions, sarcoidosis lesions, lung abscess, bronchiectasis, necrotic lung cancer and cystic fibrosis.

Notwithstanding the primary disease, its occurrence is a potentially fatal complication due to the risk of life threatening bleeding [1]. The only effective treatment is surgical removal by lobectomy or pneumectomy [1, 2]. However, surgery is often impossible because the extent of the primary lung disease results in poor pulmonary function or general condition of the patient. The only effective drug against *Aspergillus* species was amphotericin, which has acute toxic effects, such as hypersensitivity reactions, haematological abnormalities and disturbance of renal function.

Itraconazole is a new triazoles [3, 4] which has shown pronounced antifungal activity *in vitro* against a wide range of fungi including *Candida, Pityrosporum, Aspergillus, Cryptococcus, Cladosporium etc.* After oral ingestion, this lipophylic substance is readily absorbed, and catabolized in the liver to inactive metabolites. Itraconazole was first introduced to treat fungal infections in the gynaecological and dermatological sphere and no serious side-effects have been reported. Some case reports suggest that it can also be successfully used in deep-seated mycosis, including aspergillosis.

Case report

A 62 yr old male with a substantial drinking and smoking habit (45 cigarette pack-years) presented with anorexia, weight loss, dyspnoea and left thoracic inspiratory pain for three months. His past history revealed chronic asthmatic bronchitis and a surgical intervention for discus hernia. He was cachectic and hoarse. A left supraclavicular firm lymphadenopathy was palpable.

The chest X-ray (not shown) revealed a left-sided phrenic paralysis and a spherical homogeneous lung condensation in the left upper lobe, with a prominent lymphadenopathy in the aortic pulmonary window. Fibreoptic bronchoscopy showed left vocal cord paralysis and tumour growth in the culmen. Biopsy and pathological examination showed an undifferentiated epithelioma.

Chemotherapy with Platinol® and Vindesine® was started but was interrupted after only one cycle because of a retro-obstructive bronchopneumonia with severe hyponatraemia attributed to a Schwartz-Barter syndrome. A radiological cavitation of the primary lesion developed at this time. The patient recovered under treatment with furosemide, fluid restriction, antibiotics (ampicillin) and demeclocycline hydrochloride.

One month later he was readmitted with a vena cava superior syndrome, for which he received radiotherapy (55 Gy split course) on the mediastinum, the primary lesion and the left supraclavicular region. Chest

X-ray showed concomitant appearance of a characteristic aspergilloma growth in the increasing cavitary lesion (fig. 1). The patient was judged inoperable because of poor pulmonary function testing (forced expiratory volume in one second (FEV_1) 1.87 *l*, carbon monoxide transfer coefficient (Kco) 2.43 (57% N)) and general condition.

Itraconazole at a dose of 100 mg·day^{-1} was initiated, without clear improvement. The dose was increased stepwise to 300 mg·day^{-1} under control of liver biochemistry (transaminases, LDH) and precipitins for *Aspergillus* species. Simultaneously a chemotherapy with carboplatinum and VP 16 was resumed in monthly cycles.

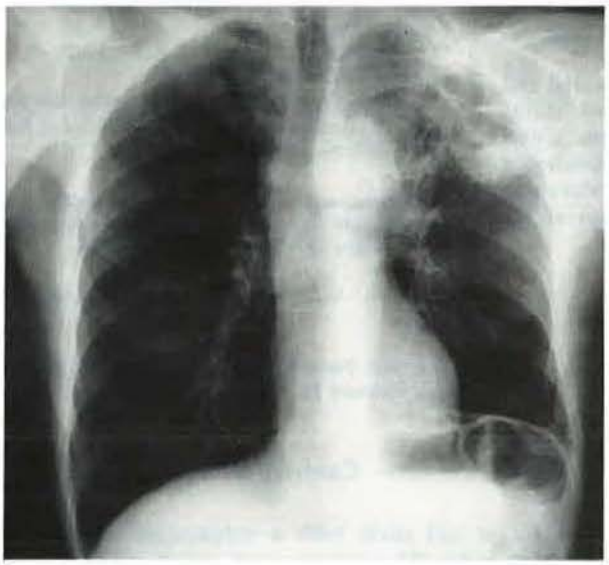

Fig. 1. – Anteroposterior chest X-ray shows a cavitation of the lung lesion in the left upper lobe. On the bottom of this cavitary lesion a fungus ball is growing.

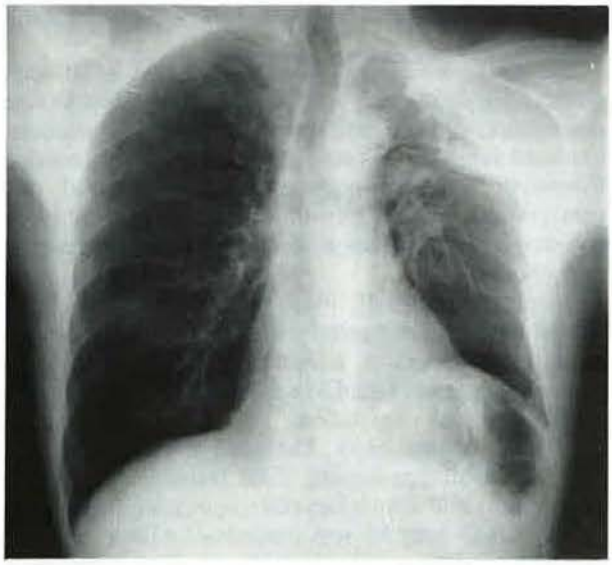

Fig. 2. – Chest X-ray six months later: the fungus ball is diminished in size. Also the cavitary lesion becomes smaller and is surrounded by fibrotic reaction due to previous radiotherapy.

Radiological regression of the aspergilloma after 6 months treatment with itraconazole is shown in figure 2.

Upon lowering the dose of Itraconazole to 100 mg *bid*, haemoptysis developed. This again disappeared at 100 mg *tid* of Itraconazole.

The patient died of septic shock and complications of a hip fracture 15 months after initial diagnosis of lung cancer, with his small cell lung cancer in remission.

Discussion

Aspergilloma is known to occur in cavitated pulmonary lesions [5], but its occurrence in association with necrotic lung cancer is rather rare [6].We report a case of aspergilloma occurring in a necrotic small cell lung cancer (stage T2N3M0). As is mostly the case, the aspergilloma was situated in an upper lobe. Surgical resection is the treatment of choice [1] because of the risk of potential fatal haemoptysis and the possible evolution towards invasive aspergillosis. The likelihood of the latter complication is even greater in the presence of immune deficiency states, was is the case in our patient with cancer, chemotherapy and a drinking history.

This case demonstrates the feasibility of long-term, high dose administration of Itraconazole® to a debilitated patient, without any detectable clinical or biological toxicity. With this long-term treatment, the aspergilloma lesion has gradually improved despite a background of immune deficiency.

Finally, it is shown to be possible to administer a myelosuppressive chemotherapy in the presence of an aspergilloma. This chemotherapy has maintained a situation of remission, induced by radiotherapy.

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Traitement oral à l'itraconazole pour un aspergillome dans un cancer pulmonaire excavé. N. Impens, J. De Greve, K. De Beule, M. Meysman, S. De Beuckelaere, W. Schandevyl.

RÉSUMÉ: Description d'un cas d'aspergillome développé dans un épithélioma bronchique nécrosé. Les épreuves fonctionnelles respiratoires et l'état général du patient interdisant une résection chirurgicale, nous avons administré l'itraconazole, un antimycosique. Nous démontrons que l'itraconazole peut être donné à des doses élevées et pendant une période prolongée. Ce traitement, administré dans le ces particulier pendant 13 mois, semble capable d'induire une réduction du volume de l'aspergillome et de prévenir les hémoptysies, permettant ainsi la poursuite d'une chimiothérapie pour le carcinome bronchique du patient.

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