CASE REPORT

Multidisciplinary approach to fetal adenocarcinoma of the lung: A case report

Raffaele Giusti¹, Daniela Iacono¹, Paris Ida¹, Luigi Ruco² & Paolo Marchetti¹

¹ Medical Oncology, S. Andrea Hospital, Sapienza University II Faculty, Rome, Italy

² Pathology, Department of Clinical and Molecular Medicine, S. Andrea Hospital, Sapienza University II Faculty, Rome, Italy

Keywords

Fetal adenocarcinoma; lung cancer; pulmonary blastoma.

Correspondence

Raffaele Giusti, Oncology Unit, S. Andrea Hospital, "Sapienza" University of Rome, Rome 00189, Italy.

Tel: +39 0633775699

Fax: +39 0633776663

Email: raffaelegiusti@yahoo.it

Received: 22 August 2012;

accepted 10 December 2012.

doi: 10.1111/1759-7714.12022

Abstract

This paper reports a case of high-grade fetal lung adenocarcinoma with particularly aggressive clinical and biological features in a 57-year-old man. Our patient first underwent neoadjuvant chemotherapy followed by surgery, and was then treated with adjuvant chemotherapy. Next, he had radiotherapy on the mediastinal region and prophylactic whole brain radiation therapy (WBRT). Following radiotherapy treatment, the patient started maintenance therapy with a somatostatin analogue. After 58 months of follow-up he is asymptomatic and disease free.

Case report

In July 2007, a 57-year-old man, a former smoker of more than 40 pack-years, came to our attention with the following symptoms: dry cough, persistent fever, and marked fatigue, for about three months. Clinical tests were performed and revealed a 6.2 cm × 5.3 cm × 7.4 cm pulmonary lesion at the left lower lobe, with irregular and spiculated margins and inhomogeneous contrast enhancement. The mass appeared to be in close contact with the parietal pleura on the lateral side of the thoracic aorta, close to the lower lobe bronchus and adherent to the ipsilateral inferior pulmonary vein (Fig. 1).

The patient underwent computed tomography (CT)-guided lung needle biopsy and two distinct tissue fragments were obtained (Fig. 2). The first showed cytokeratin-positive small round cells with high proliferative activity (Fig. 2b); the second fragment was consistent with a diagnosis of adenocarcinoma (Fig. 2a,c). A tentative diagnosis of combined small cell lung carcinoma was made. However, this diagnosis was not consistent with the lack of expression of the tumoral neuroendocrine markers CD56, chromogranin, and synaptophysin. Because of the inconsistent histology, the patient was treated with Cisplatin 75 mg/mq plus Docetaxel 75 mg/mq

day 1 q21 schedule for three cycles of therapy from September 2007 to December 2007. The CT scan after the first three cycles of treatment showed a partial response (PR) of more than 50% (Fig. 3) and the treatment was continued for three additional cycles until February 2008. However, the CT performed at the end of the sixth cycle showed a local progression of the disease (PD).

In March 2008 the patient underwent a right lower lobectomy and station 9 lymph node sampling. Pathological evaluation revealed the presence of a 7.5 cm diameter primary tumor of the lung with histological features consistent with a diagnosis of poorly differentiated (high grade) fetal adenocarcinoma. In some areas, the tumor showed glandular elements with endometrioid morphology and intraluminal squamoid morules (Fig. 4). In other areas, the tumor was poorly differentiated and presented cytokeratin+/CD56-small round cells. Extensive areas of necrosis and a high proliferative activity were also present. Visceral pleura, lymph nodes and surgical resection margins were free of tumor infiltration (ypT2 ypN0, Stage IIB tumor node metastasis [TNM] 7th Edition).

After performing a post-surgery baseline CT scan in April 2008, the patient received four cycles of treatment from May to August 2008 of CBDCA AUC 5 d1-Vinorelbine 25 mg/mq

Figure 1 August 2007 computed tomography (CT) scan (cm 6.2 × 5.3 × 7.4).

days 1, 8 q21 schedule. The patient then had clinical follow-up checks carried out every two months, and presented negative evidence of disease.

On May 2009, the patient was treated with complementary mediastinal radiotherapy (50 Gy in 25 fractions of 2 Gy each) and prophylactic whole brain radiotherapy (WBRT), with a total dose of 24 Gy in eight 3Gy fractions.

From May 2009 the patient started maintenance therapy with a somatostatin analogue (Lanreotide acetate 90 mg d1 q28 i.m.).

Currently, the patient receives clinical and radiologic exams every three months, which remain negative for recurrence. Disease free survival (DFS) as of October 2012 is 58 months.

Discussion

Fetal adenocarcinoma of the lung is a rare type of non-small cell lung cancer (NSCLC) first described by Koss *et al.* in 1991.^{1,2} It was initially described as monophasic or a well-differentiated form of pulmonary blastoma because it is

Figure 2 Needle-biopsy from the lung tumor. Two distinct tissue fragments were obtained. (a) The histology of the first was consistent with a diagnosis of adenocarcinoma with high proliferative activity (C, immunostaining for Ki-67, ×100). (b) The second fragment was made of cytokeratin-positive small round cells with high proliferative activity (immunostaining for Ki-67, ×100). A tentative diagnosis of combined small cell lung carcinoma was made.

Figure 3 December 2007 computed tomography (CT) scan (cm 2.5 × 2.9).

formed only of epithelial-like cells. The World Health Organization (WHO) classification of lung cancer separated fetal adenocarcinoma from pulmonary blastoma. Fetal adenocarcinoma is considered a lung adenocarcinoma form with a good prognosis,^{3,4} whereas biphasic pulmonary blastoma, characterized by malignant mesenchymal tissue and epithelial cells is considered a tumor with a poor prognosis because the typical symptoms (dry cough and hemoptysis) relate to mediastinal mass (about 20% of cases).⁵

Nakatani *et al.* first described a high-grade form of fetal adenocarcinoma in 1998.⁶ Since the first case in 1945, approximately 200 new cases have been reported.⁵

Figure 4 Fetal adenocarcinoma of the lung. The tumor was made up of glandular elements showing endometrioid morphology and exhibiting intraluminal squamoid morules (arrows) (immunostaining for cytokeratin, counterstained with hematoxylin ×200).

Although in many cases surgery is the elective treatment, the general approach to this type of disease is often multidisciplinary with the participation of surgeons and medical and radiation oncologists at different stages. The management of this particular case required a neoadjuvant systemic treatment before surgery and adjuvant chemotherapy with complementary mediastinal and WBRT after surgery.^{7–9}

The most commonly used treatment regimens reported in the literature for fetal adenocarcinomas are platinum-compound in combination with etoposide,⁷ even if other antineoplastic associations are described. However, from an analysis of the recent literature performed by Van Loo *et al.*,¹⁰ the efficacy of adjuvant chemotherapy and radiotherapy has not yet been established.

Our patient was initially treated with neoadjuvant chemotherapy for six cycles and then underwent surgery. Subsequently, the patient received adjuvant chemotherapy, followed by mediastinal radiation therapy and prophylactic WBRT. Therefore, a medical oncologist, radiation oncologist, and thoracic surgeon managed the case.

The patient is currently asymptomatic and disease free after 58 months of follow-up.

Disclosure

No authors report any conflict of interest.

References

- 1 Koss MN, Hochholzer L, O'Leary T. Pulmonary blastomas. *Cancer* 1991; **67**: 2368–81.
- 2 Fujino S, Asada Y, Konishi T, Asakura S, Kato H, Mori A. Well-differentiated fetal adenocarcinoma of lung. *Lung Cancer* 1995; **13**: 311–6.
- 3 Longo M, Levra MG, Capelletto E *et al.* Fetal adenocarcinoma of the lung in a 25-year-old woman. *J Thorac Oncol* 2008; **3**: 441–3.
- 4 Brambilla E, Travis WD, Colby TV, Corrin B, Shimosato Y. The new World Health Organization classification of lung tumors. *Eur Respir J* 2001; **18**: 1059–68.
- 5 Robert J, Pache JC, Seium Y, de Perrot M, Spiliopoulos A. Pulmonary blastoma: report of five cases and identification of clinical features suggestive of the disease. *Eur J Cardiothorac Surg* 2002; **22**: 708–11.
- 6 Nakatani Y, Kitamura H, Inayama Y *et al.* Pulmonary adenocarcinomas of the fetal lung type: a clinicopathologic study indicating differences in histology, epidemiology, and natural history of low-grade and high-grade forms. *Am J Surg Pathol* 1998; **22**: 399–411.
- 7 Zaidi A, Zamvar V, Macbeth F, Gibbs AR, Kulatilake N, Butchart EG. Pulmonary blastoma: medium-term results from a regional center. *Ann Thorac Surg* 2002; **73**: 1572–5.

- 8 Cutler CS, Michel RP, Yassa M, Langleben A. Pulmonary blastoma: case report of a patient with a 7-year remission and review of chemotherapy experience in the world literature. *Cancer* 1998; **82**: 462–7.
- 9 Surmont VF, van Klaveren RJ, Nowak PJ, Zondervan PE, Hoogsteden HC, van Meerbeeck JP. Unexpected response of a pulmonary blastoma on radiotherapy: case report and review of the literature. *Lung Cancer* 2002; **36**: 207–11.
- 10 Van Loo S, Boeykens E, Stappaerts I, Rutsaert R. Classic biphasic pulmonary blastoma: a case report and review of the literature. *Lung Cancer* 2011; **73**: 127–32.