MIGUEL MARTIN
EDUARDO DIAZ-RUBIO
ANTONIO CASADO
JUAN JOSÉ VALVERDE
DANIEL GARCIA URRA*
JOSE ANTONIO LÓPEZ-MARTIN
ALVARO RODRIGUEZ-LESCURE

Servicio de Oncologia Medica
and Servicio de Neurologia*
Hospital Universitario San Carlos
Madrid
Spain

October 1993

Correspondence to: Dr. M. Martin. Servicio de Oncologia Medica. Hospital Universitario San Carlos. Ciudad Universitaria s/n. E-28040 Madrid, Spain.

REFERENCES

1. Mattson W, Von Eyben F, Turesson I, Wahlby S. Prednimustine (NSC-134087) treatment of lymphocytic and lymphocytic-histiocytic lymphomas. Cancer 1978; 41: 112–6.
2. Kaplan RS, Wiernek PH. Neurotoxicity of antitumor agents. In: Perry MC, Yarbro JW, eds. Toxicity of chemotherapy. Orlando: Grune and Stratton Inc., 1984: 365–431.
3. Karch FE, Lasagna L. Toward the operational identification of adverse drug reactions. Clin Pharmacol Ther 1977; 21: 247–54.
4. Williams SA, Makker SP, Grupe WE. Seizures—A significant side-effect of chlorambucil therapy in children. J Pediatr 1978; 93: 516–8.
5. LaDelta I, Bayer N, Myers R, Hoffstein V. Chlorambucil-induced myoclonic seizures in an adult (letter). J Clin Oncol 1985; 3: 1691–2.
6. Gaver RC, Deeb G, Pittman KA, Isdell BF, Mittelman A, Smyth RD. Disposition of orally administered ^{14}C-prednimustine in cancer patients. Cancer Chemother Pharmacol 1983; 11: 139–42.

SIMULTANEOUS PULMONARY CARCINOMA IN TWINS—A CASE REPORT AND REVIEW OF THE LITERATURE

The biological mechanisms responsible for the malignant transformation of a cell and the development of malignant tumours remain largely unknown, even if some progress has been made owing to recent advances in cell and molecular genetics. Concerning risk factors for development of different tumours, epidemiological studies have given considerable knowledge. For lung cancer, smoking is thus known to be the predominant risk factor, explaining approximately 80% of the cases. However, lung cancer also occurs in non-smokers, and the occurrence in pairs of twins strongly suggests that the disease may also be caused by genetically determined changes. Having participated in the treatment of one twin of a pair of female non-smokers with lung cancer, we reviewed the literature on simultaneous cancer, particularly lung cancer, in twins but found only five reported such pairs with lung cancer (1–5). Here we present brief case reports on two twins, one of whom was treated by us, and comment on some possible factors involved.

Case 1. Previous to her lung cancer, this patient (BG), who was born in 1923, was in good health. She was a housewife but occasionally assisted her husband in his company. She had never smoked. In the summer 1983 she developed respiratory tract symptoms, and observed during one period blood in sputum. During the autumn she developed multiple small adenopathies in the right supraclavicular fossa and mild pain in the back and one hip. Left-sided parenchymal changes seen on chest x-rays during the summer were found to have progressed, giving reason to suspect cancer. She deteriorated and was admitted with severe back pain in November 1983. On admission she had lymph node metastases on the right side of the neck, which were extirpated and yielded a diagnosis of poorly differentiated large cell carcinoma with solid growth. Bronchoscopy confirmed left-sided lung cancer, and x-rays showed metastases in the spinal column. She received four courses of cisplatin and etoposide from December 1983 to March 1984, but subsequently manifested progression with pleural effusion and increase of the spinal metastases. In May and June 1984, the patient was given radiotherapy to the lumbar and lower thoracic spine, and in June 1984 she got a course of etoposide. Her condition subsequently deteriorated, however, and she died on July 19, 1984, with disseminated lung cancer. No autopsy was performed.

Case 2. PG, the twin sister of BG (case 1) had also been generally healthy before her cancer. She had never smoked, and her alcohol consumption was negligible. She ran her own textile shop. Upon learning of her sister's cancer, she consulted a physician although she was asymptomatic. Chest x-rays showed a $3 \times 3 \times 5$ cm apical right-sided lung tumour that was operated on December 21, 1983, with resection of the right upper lobe and wedge resection of the apical segment of the right lower lobe. Histology showed a $4.5 \times 4 \times 4$ cm tumour, classified at retrospective review as a well-to-moderately differentiated bronchioalveolar carcinoma, with hilar lymph node metastases. It was staged as T2 N1 M0. The patient was given postoperative radiotherapy to the mediastinum, a total dose of 60 Gy. She was recurrence-free until February 1992, when chest x-rays showed newly developed parenchymal changes in her left lung, which fine-needle aspiration cytology showed to be adenocarcinoma. She was operated (September 7, 1992) with lobectomy of the left upper lobe, histologic examination showed a 2.3×1.8 cm tumour assessed as being a well-differentiated bronchioalveolar large-cell carcinoma. The postoperative course was smooth, and she was discharged on September 14, 1992. Subsequent comparison of slides from 1983 to 1992 showed a similar picture of well-to-moderately differentiated adenocarcinoma of bronchioalveolar type.

Discussion. According to information obtained at history taking the two reported sisters were monozygotic twins, with the same blood group (A+). However, no other objective evidence of monozygosity was available. Both twins were non-smokers, and, as far as could be ascertained, none of them had been exposed to any other known environmental risk factors for lung cancer. They did not know of any other cancer in the family. In several respects they differed from other reported cases of lung cancer in twins (1–5). All these twin pairs were male, and as far as information was available the patients were smokers; both twins in one pair had been exposed to asbestos. Histological diagnosis was available for both twins in four pairs, and in these it was mutually consistent (anaplastic bronchial cancer in one pair, bronchio-alveolar carcinoma in one pair, and squamous cell carcinoma in two pairs). In the fifth pair, histological diagnosis (squamous cell carcinoma) was available for only one twin. In our twin pair the lung cancers were, according to retrospective review, definitely of different types. In case 1 it was a poorly differentiated large-cell carcinoma whereas in case 2 it was an adenocarcinoma of bronchio-alveolar type. The tumours in the right and left lungs of case 2, developing with an interval of 9 years, had quite similar histology. Bronchioalveolar carcinoma is a rather unusual form of lung cancer. Its occurrence is correlated to smoking (6), but similar to other adenocarcinomas this association is much less pronounced than

for squamous cell or small cell cancer, and a significant proportion of bronchio-alveolar carcinoma patients are non-smokers.

The twin pair described by us was probably, even if not definitely proved, monozygotic. The possibility of genetic predisposition is further suggested by the fact that none of the twins were smokers or had been exposed to other known environmental risk factors. Identification of hereditary causes of different cancers has rapidly become a very active field in biochemical and in toxicological research and by molecular biological methods it has become possible to identify various genes and gene alterations associated with specific types of cancer. Genes, possibly associated with lung cancer, include oncogenes of the myc and ras families, the neu, myb, raf and bcl-1 genes, the epidermal growth factor (EGF) receptor gene, and platelet-derived growth factor gene (7). Recently, anti-oncogenes have been found to be associated with lung cancer. They include the retinoblastoma (rb) (8) and p53 genes (9). Cytogenetic studies have also indicated that a deletion of the short arm of chromosome 3 (3p) occurs more frequently in small cell lung cancers (10). No studies of this type were, however, performed in the now reported twin pair.

ACKNOWLEDGEMENT

Special thanks are due to Dr. Pawel Mikulowski of the Dept. of Clinical Pathology, Malmö General Hospital, for his invaluable help with the retroactive review of slides and his experienced opinion.

MÅNS AGRUP* Department of Oncology
LARS EKBERG* and Radiotherapy*
MARIA ALBERTSSON* Malmö General Hospital
JANERIC SEIDEGÅRD** Malmö
Department of Molecular Ecogenetics**
The Wallenberg Laboratory
and Astra Draco AB,
Lund
Sweden

October 1993

Correspondence to: Dr Måns Agrup, Department of Oncology, University Hospital, S-581 85 Linköping, Sweden.

REFERENCES

1. Chenebault J. Tumeurs bronchiques droites comparables et presque contemporaines chez deux frères jumeaux. Maroc Med 1966; 45: 625–6.
2. Joishy SK, Cooper RA, Rowley PT. Alveolar cell carcinoma in identical twins. Ann Intern Med 1977; 87: 447–50.
3. Charpin D, Vervloet D, Poirier R, Charpin J, Laval P. Manifestations thoraciques de l'amiante et génétique. A propos de deux paires de jumeaux univitellins. Rev Fr Mal Resp 1981; 9: 55–9.
4. Orbuch SJ, Perazzo DL, Porta J, Garrido C. Carcinome epidermoide de pulmon en gemelos univitelinos. Medicina (Buenos Aires) 1983; 43: 16–20.
5. Nores JM, Dalayeun J, Chebat J, Dieudonné P, Nenna AD. Concurrent anaplastic bronchial cancer in identical twin brothers. Respiration 1989; 55: 56–9.
6. Morabia A, Wynder EL. Relation of bronchioloalveolar carcinoma to tobacco. BMJ 1992; 304: 541–3.
7. Gazdar AF. Molecular markers for the diagnosis and prognosis of lung cancer. Cancer 1992; 69 (Suppl.): 1592–9.
8. Harbour JW, Sali SL, Whang-Peng J, Gazdar AF, Minna JD, Kaye FJ. Abnormalities in structure and expression of the human retinoblastoma gene in SCLC. Science 1988; 241: 353–7.
9. Takahashi T, Nau MM, Chiba I, et al. A frequent target for genetic abnormalities in lung cancer. Science 1989; 246: 491–4.
10. Whang-Peng J, Kao-Shan CS, Lee EC, et al. A specific chromosome defect associated with human small cell lung cancer. Science 1982; 215: 181–5.

L5 SCIATICA AS FIRST SYMPTOM OF A GRANULOCYTIC SARCOMA

Granulocytic sarcoma (chloroma) consists of immature cells from the myeloid series. It usually arises as part of a known hematological disorder, although in some cases it appears as an isolated mass. We know of few cases where it presents with lumbar radiculopathy as the first symptom (1–3). We now report such a case.

Case report. A 62-year-old man was examined in January 1992 due to a 7-month history of progressive low back pain and left leg pain with L5 distribution, subjective loss of strength in the leg, and weight loss of 6 kg during a 6-month-period. Since 4 months he also had left scapular pain which increased with movement of the left arm. Physical examination showed hepatomegaly, supraclavicular adenopathies, lumbar pain following dorsal and lumbar movements, and a special tenderness of the fourth and fifth vertebrae when pressure was applied. Straight leg raising on the left side was positive. The routine laboratory tests showed ESR 29, LDH 737 U/l (normal 230–460) and hypergammaglobulinemia. X-rays of chest and shoulders, ^{99m}Tc bone scan and barium examination of the gastrointestinal tract were unremarkable. Lumbar x-rays revealed an erosion in the left transverse process of L5. Lumbar CT scan showed a mass in the left transverse process of L5 which surrounded the posterior vertebral musculature on the left side and infiltrated the left lateral recess of L5 and the left lumbosacral conjunction foramen. Thoracic-abdominal CT scan showed moderately enlarged spleen and enlarged lymph nodes in the retroperitoneal space. Histological examination of a supraclavicular lymph node showed granulocytic sarcoma (Figure). Immunohistochemical staining for lysozyme was positive. Granulocytic alkaline phosphatase was 80 (normal 15–45). Karyotype study and bone marrow aspiration smears were normal. Biopsy of the iliac crest showed a moderate predominance of the myeloid series, with abundant band cells and mature forms. Radiotherapy with ^{60}Co beam (30 Gy divided into 10 sessions) against L4-S1 was administered with an excellent analgesic response. However, the shoulder pain increased and spread to the neck and left arm during the initial radiotherapy and a painful mass with 6 cm diameter was palpated in the left paravertebral area. A CT scan showed a left-sided paravertebral mass at the level T1–T2 with extension into the epidural space and the shoulder, and bilateral supraclavicular enlarged lymph nodes. A biopsy confirmed the previous diagnosis. New bone marrow and cytogenetic studies were normal. Radiotherapy (18 Gy in 6 sessions) was applied to the upper back region. Chemotherapy with cytarabine, etoposide, and daunorubicin was started but resulted in pronounced pancytopenia and Candida albicans sepsis. The patient died of a septic shock in April 1992.

Discussion. Granulocytic sarcoma is a rare tumor that has been related to myeloproliferative disorders (4, 5). It can also occur as an isolated event preceding an acute myeloid leukemia or the recurrence of a treated leukemia (4, 6, 7). In a review of 950 cases