group of the European Organization for Research and Treatment of Cancer. Blood 1997;90:354–71.
[4] Stansfeld AG, Diebold J, Noel H, Kapanci Y, Rilke F, Kelenyi G, et al. Updated Kiel classification for lymphomas. Lancet 1998;1:292–3 (letter).
[5] Willemze R, Meijer CJLM, Scheffer E. Diffuse large cell lymphomas of follicle center cell origin presenting in the skin: A clinicopathologic and immunologic study of 16 patients. Am J Pathol 1987;126:325–33.
[6] Vermeer MH, Geelen FAMJ, van Haselen CW. Primary cutaneous large B-cell lymphomas of the legs: A distinct type of cutaneous B-cell lymphoma with an intermediate prognosis. Arch Dermatol 1996;132:1304–8.
[7] Grange F, Hedelin G, Joly P, Beylot-Barry M, D'Incan M, Delaunay M, et al. Prognostic factors in primary cutaneous lymphomas other than mycosis fungoides and the Sézary syndrome. Blood 1999;93:3637–42.
[8] Jaffe ES, Harris NL, Stein H, Vardiman W, et al. editors. World Health Organization classification of tumors: Pathology and genetics of tumours of hematopoietic and lymphoid tissues. Lyon, France: IARC Press; 2001.
[9] Willemze R, Jaffe ES, Burg G, Cerroni L, Berti E, Swerdlow SH, et al. WHO-EORTC classification for cutaneous lymphomas. Review article. Blood 2005;105:3768–85.
[10] Grange F, Bekkenk MW, Wechsler J, Meijer CJLM, Cerroni L, Bernengo M, et al. Prognostic factors in primary cutaneous large B-cell lymphomas: A European multicenter study. J Clin Oncol 2001;19:3602–10.
[11] Kodama K, Massone C, Chott A, Metze D, Kerl H, Cerroni L. Primary cutaneous large B-cell lymphomas: Clinicopathologic features, classification, and prognostic factors in a large series of patients. Blood 2005;106:2491–7.
[12] Chang Y, Moore PS. Kaposi's Sarcoma (KS) – associated herpesvirus and its role in KS. Infect Agents Dis 1996;5: 215–22.
[13] Said JW, Tasaka T, Takeuchi S, Asou H, de Vos S, Cesarman E, et al. Primary effusion lymphoma in women: Report of two cases of Kaposi's sarcoma herpes virus-associated effusion-based lymphoma in human immunodeficiency virus-negative women. Blood 1996;88:3124–8.
[14] Geelen FAMJ, Vermeer MH, Meijer CJLM, Van der Putte SCJ, Kerkhof E, Kluin PM, et al. Bcl-2 expression in primary cutaneous large B-cell lymphoma is site-related. J Clin Oncol 1998;16:2080–5.
[15] Hoefnagel JJ, Vermeer MH, Janssen PM, Fleuren GJ, Meijer CJ, Willemze R. Bcl-2, Bcl-6 and CD10 expression in cutaneous B-cell lymphoma: Further support for a follicle centre cell origin and differential diagnostic significance. Br J Dermatol 2003;149:1183–91.
[16] Hoefnagel JJ, Dijkman R, Basso K, Jansen PM, Hallermann C, Willemze R, et al. Distinct types of primary cutaneous large B-cell lymphoma identified by gene expression profiling. Blood 2005;105:3671–8.
[17] Mao X, Lillington D, Child FJ, Russell-Jones R, Young B, Whittaker S. Comparative genomic hybridization analysis of primary cutaneous B-cell lymphomas: Identification of common genomic alterations in disease pathogenesis. Genes Chromosomes Cancer 2002;35:144–55.
[18] Hallermann C, Kaune KM, Gesk S, Martin-Subero JI. Molecular cytogenetic analysis of chromosomal breakpoints in the IGH, MYC, BCL6 and MALT1 gene loci in primary cutaneous B-cell lymphomas. J Invest Dermatol 2004;123: 213–9.

Secondary acute lymphoblastic leukaemia following oxaliplatin for adjuvant chemotherapy in colon cancer

FEDERICA MERLIN[1], TIZIANA PROCHILO[1], BASEM KILDANI[1], ALESSANDRA TUCCI[2], SAMANTHA FERRARI[2], GIUSEPPE ROSSI[2], PAOLO D'ADDA[3] & GIORDANO DOMENICO BERETTA[1]

[1]*U.O. Oncologia Medica, Ospedale Sant'Orsola-Fatebenefratelli, Brescia, Italy,* [2]*U.O. Ematologia, Spedali Civili, Brescia, Italy and* [3]*U.O. Medicina Generale, Ospedale Sant'Orsola-Fatebenefratelli, Brescia, Italy*

To the Editor

A highly increased risk of myelodysplasia and acute leukaemia is well established in patients previously treated for other malignancies with alkylating agents or topoisomerase II inhibitors [1]. Recently, new chemotherapeutic agents have been introduced in the clinical practice and their late complications have not yet been described.

Oxaliplatin has resulted in a significant progress in the treatment of colorectal cancer both in the advanced disease and in the adjuvant setting [2–4]. Late toxicity and particularly secondary cancer are a very important topic in adjuvant setting where

Correspondence: Giordano Domenico Beretta, U.O. Oncologia Medica, Ospedale Sant'Orsola, FBF, via Vittorio Emanuele II, 25122 Brescia, Italy. Tel: +39 30 2971226, +39 30 2971224. Fax: +39 30 2971223. E-mail: gdberetta@fatebenefratelli.it

(Received 14 June 2007; accepted 6 July 2007)

ISSN 0284-186X print/ISSN 1651-226X online © 2008 Taylor & Francis
DOI: 10.1080/02841860701558864

potentially cured patients may receive a toxic regimen. We report a case of a patient with possible treatment-related acute leukaemia after adjuvant chemotherapy with oxaliplatin.

In October 2005, a 65-year-old woman underwent resection of sigma for an adenocarcinoma (pT4 N0/3 M0, G2). From November 2005 to May 2006, the patient received 12 cycles of infused 5-fluorouracil, leucovorin, and oxaliplatin (the FOLFOX-4 regimen). She tolerated it well except for minimal peripheral neuropathy and mild leucopoenia. During follow-up she remains in remission and a computer tomography scan didn't show any lesion consistent with recurrence. In November 2006, she developed fatigue, nightly sweatiness and quotidian mild fever. The platelet count was $283 \cdot 10^9$/l and the white cell count $17.9 \cdot 10^9$/l with 7.6% blasts; she has a mild anaemia (haemoglobin level was 10.5 g/dl). Peripheral blood examination established the diagnosis of acute lymphoblastic leukaemia-associated antigen (CALLA) positive (80% blasts). After 2 days, she rapidly developed a heavy headache. A computed tomography scan of brain showed a wide haemorrhage in the temporal hemisphere. The platelet count changed to $145 \cdot 10^9$/l and the white cell count $21.4 \cdot 10^9$/l with 72% blasts and the haemoglobin level was 7.5 g/dl. The clinical conditions of patient rapidly aggravated. The bleeding in brain increased and she went into an irreversible coma. Death occurred rapidly before any specific treatment was started. It was not possible to have a cytogenetic and karyotype analyses.

The most frequently occurring type of chemotherapy related leukaemia is acute myeloid leukaemia while acute lymphoblastic leukaemia (ALL) is rare occurring in about 0.5–1‰ of treated patients [3,4]. Although some cases of secondary ALL with t(4;11)(q21;q23) have been reported in literature [5], the clinical-biological features of these leukaemias are poorly defined [6,7]. Single-agent fluorouracil has demonstrated no carcinogenic potential, either in animals or in humans. Cisplatin and carboplatin have been widely associated with leukaemia, whereas oxaliplatin is associated with acute haematological disease in only two reports. Acute promyelocytic leukaemia in a patient, with metastatic colon adenocarcinoma, treated with 46 cycles of leucovorin plus 5-FU followed by three cycles of irinotecan and three cycles of oxaliplatin was recently published [8]. The second case involved a 56-year-old woman with cecal adenocarcinoma presenting a remission of metastases to ovaries, omentum, after 12 cycles of FOLFOX-4 regimen. Bone marrow biopsy was consistent with therapy-related acute myelogenous leukaemia [9]. Nevertheless, no cases of secondary oxaliplatin-related ALL have been documented.

The occurrence of acute leukaemia in a patient treated with chemotherapy raises the question of whether the disease is aetiologically related to one or more cytotoxic agents [10,11]. Currently, 10 to 20% of all new cases of acute leukaemias and myelodysplastic syndromes diagnosed annually are secondary to therapeutic regimens. They tend to appear with a latency period between 12 to 60 months. In our case, the lack of a chromosome analysis is the weak element but the latency of development and the aggressive clinical course make us suspect a correlation assume with previous chemotherapy. And, as the number of new chemotherapeutic drugs is increasing, clinicians' attention might particularly be drawn to atypical secondary disorders. Delayed toxicity is a complication which must be considered for patients receiving adjuvant therapy, also to identify the true cost-effectiveness of the treatment. We believe that epidemiological surveys with long-term haematological follow-up are needed to monitor carefully their potential for the development of secondary leukaemia.

References

[1] Pedersen-Bjergaard J. Insights into leukemogenesis from therapy-related leukaemia. N Engl J Med 2005;352:1591–4.

[2] de Gramont A, Vignoud J, Tournigand C, Louvet C, Andre T, Varette C, et al. Oxaliplatin with high-dose leucovorin and 5-fluorouracil 48-hour continuous infusion in pretreated metastatic colorectal cancer. Eur J Cancer 1997;33:214–9.

[3] Caglar K, Varan A, Akyuz C, Selek U, Kutluk T, Yalcin B, et al. Second neoplasms in pediatric patients treated for cancer: A center's 30-year experience. J Ped Hematol Oncol 2006; 28:374–8.

[4] Crump M, Tu D, Shepherd L, Levine M, Bramwell V, Pritchard K. Risk of acute leukaemia following epirubicin-based adjuvant chemotherapy: A report from the National Cancer Institute of Canada Clinical trials group. JCO 2003; 21:3066–71.

[5] Ishizawa S, Slovak ML, Popplewell L, Bedell V, Wrede JE, Carter NH, et al. High frequency of pro-B acute lymphoblastic leukaemia in adults with secondary leukaemia with 11q23 abnormalities. Leukaemia 2003;17:1091–5.

[6] Auxenfants E, Morel P, Lai JL, Sartiaux C, Detourmignies L, Bauters F, et al. Secondary acute lymphoblastic leukaemia with t (4;11): Report on two cases and review of the literature. Ann Hematol 1992;65:143–6.

[7] Bigoni R, Cuneo A, Roberti MG, Moretti S, De Angeli C, Dabusti M, et al. Therapy-related adult acute lymphoblastic leukaemia with t(4;11)(q21; q23): MLL rearrangement, p53 mutation and multilineage involvement. Leukaemia 1999; 13:704–7.

[8] Merrouche Y, Mugneret F, Cahn JY. Secondary acute promyelocytic leukaemia following irinotecan and oxaliplatin for advanced colon cancer. Ann Oncol 2006;17:1025–6. Epub 2005 Nov 17.

[9] Carneiro BA, Kaminer L, Eldibany M, Sreekantaiah C, Kaul K, Locker GY. Oxaliplatin-related acute myelogenous leukaemia. Oncologist 2006;11:261–2.
[10] Rund D, Ben-Yehuda D. Therapy-related leukaemia and myelodysplasia: Evolving concepts of pathogenesis and treatment. Hematology 2004;9:179–87.
[11] Takeyama K, Seto M, Uike N, Hamajima N, Ino T, Mikuni C, et al. Therapy-related leukaemia and myelodysplastic syndrome: A large-scale Japanese study of clinical and cytogenetic features as well as prognostic factors. Int J Hematol 2000;71:144–52.

Concurrent mediastinal germ-cell tumour and haematological malignancy: Case report and short review of literature

TONE IKDAHL[1,2], DAG JOSEFSEN[1], ERLING JAKOBSEN[1], JAN DELABIE[3] & SOPHIE D. FOSSÅ[4,5]

[1]*Cancer Clinic, Rikshospitalet-Radiumhospitalet Medical Centre, Oslo, Norway,* [2]*Ullevål Cancer Center, Ullevål University Hospital, Oslo, Norway,* [3]*Department of Pathology, Rikshospitalet-Radiumhospitalet Medical Centre, Oslo, Norway,* [4]*Unit for long term outcome, Department of Clinical Cancer Research, Rikshospitalet-Radiumhospitalet Medical Centre, Oslo, Norway and* [5]*University of Oslo, Oslo, Norway*

Germ-cell tumours (GCTs) account for 2% of human malignancies, but are the most common malignant tumours in males aged 15–35. Approximately 2–5% of the GCTs arise at extragonadal sites, usually in the midline of the body, with the mediastinum and retroperitoneum as the two major sites (54 and 45% of the cases, respectively) [1]. Garnick et al. reported an association between haematological malignancies and mediastinal GCTs in 1983 [2] and several cases have been published since [3–8]. The majority present with a mediastinal GCT and develop the haematological malignancy several months later, with a median interval of 6 months between the two diagnoses [8]. We report three cases in which the haematological malignancies were concurrent with the mediastinal GCTs.

Case 1

A 31-year-old male presented with fatigue, fever, weight loss, night sweating, and diffuse muscular pain. The investigation revealed anaemia, thrombocytopenia, and a mediastinal tumour (Table I). Bone marrow trephine biopsy and aspirate showed acute megakaryoblastic leukaemia (M7) (Figure 1a), whereas a mediastinal biopsy showed a GCT with embryonal carcinoma, endodermal sinus tumour, and mature teratoma components. The serum levels of alpha-fetoprotein (AFP) and human chorion gonadotropin (HCG) were elevated (Table I). An ultrasound scan of the testicles with subsequent biopsies demonstrated bilateral leukemic infiltrates. The patient showed a partial response on cisplatin based chemotherapy and intrathecal chemotherapy (Table I). Five months following diagnosis, however, he developed disease progression with pancytopenia and died due to an acute gastrointestinal bleeding.

Case 2

A 25-year-old male presented with fatigue, fever, cough, and chest pain. The investigation showed anaemia, elevated leukocyte and platelet counts, and a mediastinal tumour (Table I). Bone marrow aspirate and trephine biopsy were compatible with malignant histiocytosis. Fuorescence *in situ* hyridization (FISH) analyses demonstrated the presence of the GCT specific marker isochromosome 12p (i12p). The mediastinal tumour was a GCT with mature and immature teratoma components. AFP and HCG levels were elevated (Table I) and bilateral biopsies from atrophic testicles showed atypic cellular infiltrates, most likely leukemic. The patient received a single course of cisplatin based chemotherapy, but developed septicaemia and an acute respiratory distress syndrome and died less than a month following diagnosis.

Correspondence: Tone Ikdahl, Ullevål Cancer Centre, Ullevål University Hospital, N-0407 Oslo, Norway. E-mail: tone.ikdahl@uus.no

(Received 18 July 2007; accepted 16 August 2007)

ISSN 0284-186X print/ISSN 1651-226X online
DOI: 10.1080/02841860701636272