ACUTE MYELOID LEUKEMIA FOLLOWED BY HEPATIC LEIOMYOSARCOMA. A CASE REPORT

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SUMMARY

The unique occurrence of a primary leiomyosarcoma of the liver in a 59-year-old woman who had been successfully treated for an acute myeloid leukemia is reported and used as a basis for a review of the literature on similar cases. It is concluded that there is not enough evidence to claim that patients aggressively treated for acute leukemia are at an increased risk of developing therapy-related secondary solid cancers.

RESUMO

Leucemia mieloide aguda seguida de leiomiossarcoma hepático

Descreve-se um caso de leiomiossarcoma primitivo do fígado numa mulher de 59 anos com uma leucemia mieloide aguda em fase de remissão induzida por quimioterapia. Discutem-se, tomando em consideração os casos referidos na literatura, as diferentes possibilidades etiopatogénicas. Conclui-se não haver, pelo menos por ora, evidência suficiente para afirmar um aumento significativo do risco de desenvolvimento de tumores «sólidos» como consequência do tratamento de leucemias agudas.

INTRODUCTION

The occurrence of acute myeloid leukemia (AML) in patients with several types of solid cancers treated with cytotoxic drugs or ionizing radiation is well established. However, the opposite is rare. Indeed, only a few cases of secondary solid neoplasms occurring in patients with acute leukemia (AL) intensively treated with chemotherapy and/or radiotherapy have been reported so far.

The relatively poor survival of patients with AML probably contributes to such rarity of secondary neoplasms but the same reasoning does not apply to children with acute lymphoblastic leukemia (ALL) who have nowadays 5-year-survival rate above 50%.

It seems unquestionable that more cases of AL followed by solid tumors have to be reported before we may evaluate whether or not patients aggressively treated for acute leukemia are at an increased risk of developing therapy-related secondary solid cancers.

This report aims to contribute to the enlargement of the aforementioned short list of such cases. It describes the unique occurrence of a primary leiomyosarcoma of the liver, which is by itself an exceedingly rare tumor, in a 59-year-old woman who had been «successfully» treated for an AML.

CASE REPORT

O.Z.L.V., a previously healthy 58-year-old white woman was admitted in November 82 with asthenia and paleness. The physical examination showed an acutely ill patient without enlarged lymph nodes, hepatomegaly or splenomegaly; there were no signs of hemorrhagic diathesis and no pains in the bones. The hemoglobin was 8.7 g/dl, total white cell count 1.7 x 10^9/1 and platelets 100 x 10^9/1. Twenty percent of the white cells were leukemic blast cells. The morphology of the blasts (98%) of the bone marrow together with the positivity obtained with Sudan black and NASDA led to the diagnosis of M4 type of the FAB classification of acute myeloid leukemia.

The remaining laboratory tests, including liver function tests were normal.

After the first cycle of cytarabine and thioguanine the patient refused further treatment. The clinical situation deteriorated, and was further complicated by pulmonary tuberculosis. Massive blood transfusions were given. In February 83 she was treated with «low dose» cytosine arabinoside (ARA-C) which was given in subcutaneous injections (10 mg/m^2/12h) for 15 days. One month later the patient was in complete remission without any symptom of the disease, normal peripheral counts and less than 5% blast cells in the bone marrow.

She remained in good health until May when she was readmitted complaining of abdominal pain and jaundice. On examination there was abdominal swelling and painful hepatomegaly. Hemoglobin was 11.6 g/dl, total white cell count 13.0 x 10^9/1 (without leukemic blast cells) and platelets 200 x 10^9/1. Laboratory data concerning liver function tests were reported as follows: Direct bilirubin 47 mg/1, SGOT-102 I.U./1 (normal range 0 to 39) SGPT 40 I.U./1 (normal range 1 to 25), LDH 295 I.U./1 (normal range 71 to 207) and alkaline phosphatase 73 I.U./1 (normal range 4 to 13). A technetium — 99 liver-spleen scan showed hepatomegaly with a large area of decreased uptake in the right lobe of the liver. An abdominal C.A.T. scan confirmed the presence of a voluminous, partly necrotic tumor in the right lobe of the liver and the absence of other discernible tumoral masses within the abdomen.

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By light microscopy the neoplasia was mostly composed of interlacing bundles of spindle-shaped cells with prominent nuclear abnormalities and moderate mitotic index (about 5 mitotic figures per 10 HPF). This hemangiopericytic pattern could also be found in limited areas of the tumor. Hematein-eosin. 240×

Figure 1: A - By light microscopy the neoplasia was mostly composed of interlacing bundles of spindle-shaped cells with prominent nuclear abnormalities and moderate mitotic index (about 5 mitotic figures per 10 HPF). B - This hemangiopericytic pattern could also be found in limited areas of the tumor. Hematein-eosin. 240×

By electron microscopy the cytoplasm of most of the neoplastic cells displayed abundant bundles of thin filaments with dense zones — «myofilaments». Uranyl acetate and lead citrate. 8,800×

Figure 2: By electron microscopy the cytoplasm of most of the neoplastic cells displayed abundant bundles of thin filaments with dense zones — «myofilaments». Uranyl acetate and lead citrate. 8,800×

COMMENTS

The presentation of this hepatic leiomyosarcoma fits most of the cases reported so far in the literature with regard to age and sex of the patients and clinico-laboratory features (for a thorough review of thirteen cases on record see O’Leary et al.).

The histological diagnosis of leiomyosarcoma was confirmed by ultrastructural study which revealed the presence of abundant myofilaments in the neoplastic cells. This finding is in agreement with those of Bloustein in a similar case and shows that leiomyosarcomas of the liver differ from leiomyosarcomas of the digestive tract which do not generally display cytoplasmic myofilaments.

The tumor was considered non-resectable and the patient died one month after the diagnosis from hepatic coma. This dreadful prognosis confirms previous reports and reinforces the assumption that the morbidity of these tumors depends on local invasiveness rather than on their metastatic potential.

The material obtained by two percutaneous liver biopsies revealed a spindle cell sarcoma (Fig. 1) which was further classified as a leiomyosarcoma by electron microscopy study (Fig. 2). The tumor was considered inoperable and the patient died in June 1984 of hepatic coma. No autopsy was done.

It is tempting to relate the occurrence of the sarcoma with the previous chemotherapy for the AML. This hypothesis faces, however, two major drawbacks.

First, it has never been definitely proved that patients treated with chemotherapy and/or radiotherapy for ALL are at increased risk of developing a secondary solid tumor. The same conclusion applies — even on a more solid bases — to patients treated for AML who usually experience shorter survivals than those with ALL.

Second, the diagnosis of the hepatic sarcoma was made 8 months after the beginning of the chemotherapy. Taking into consideration the huge dimensions of the tumor at the time of diagnosis, such interval is probably too short to sustain the etiological role of the chemotherapy.

The literature does not also provide any evidence to support the hypothesis that the occurrence of both neoplasms is more than coincidental. In fact, a renal leiomyosarcoma in a 12-year-old boy treated for ALL is the only secondary leiomyosarcoma.
on record. Most of the other sarcomas reported in association with leukemia are malignant fibrous histiocytomas or belong to the group of pediatric sarcomas and have preceded rather than followed the leukemias.

Most of the cases of hepatic leiomyosarcomas tend to occur, like their soft tissue counterparts, in middle aged and elderly women. Since AML often occurs in this group of patients, the association found in our case cannot be considered, even from a purely statistical point of view, totally unexpected.

Taking all this together it seems logical to conclude that there is not enough evidence to consider our case more than an anecdotal coincidence. However, the evaluation of a larger series of cases appears to be necessary before one can rule definitely out the possibility of the sarcoma being induced by the treatment for the AML.

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REFERENCES


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