



Effective Treatment of Thymic Carcinoma with Operation and Combination Chemotherapy Against Acute Monocyte Leukemia: Case Report and Review of the Literature

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Footnote

Effective Treatment of Thymic Carcinoma with Operation and Combination Chemotherapy Against Acute Monocyte Leukemia: Case Report and Review of the Literature

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Thymic carcinoma associated with acute monocyte leukemia (AMoL) and a history of choriocarcinoma was diagnosed in a 58-year-old female. We found no other such case in a literature search. She was first treated with DCMP therapy: daunorubicin, cytosine arabinoside, 6MP-riboside, and prednisolone against AMoL. After induction chemotherapy, complete AMoL remission was attained. Chest CT scan after chemotherapy revealed regression of the mediastinal tumor. Resection of the tumor included the left upper lobe of the lung, phrenic nerve and pericardium. Pathological diagnosis showed poorly or moderately differentiated squamous cell carcinoma. Although the patient died of pneumonia during chemotherapy for relapsed AMoL, chest X-ray and CT revealed no recurrence of the mediastinal tumor after the original operation. Judging from this case and other successful cases of chemotherapy, we feel that intensive chemotherapy may be a beneficial strategy against thymic carcinoma.

Key words: thymic carcinoma - acute monocyte leukemia - chemotherapy

INTRODUCTION

Thymic carcinomas are relatively rare tumors, with distinct pathological and clinical characteristics. These tumors are obviously histologically malignant and usually not associated with any paraneoplastic syndromes. The clinical course of patients with thymic carcinoma tends to be aggressive, and conventional chemotherapy for thymic carcinoma often results in minimal or no response. We describe a patient with thymic carcinoma associated with acute monocyte leukemia (AMoL) and a history of choriocarcinoma in whom tumor regression was achieved with combination chemotherapy for AMoL.

CASE REPORT

A 58-year-old female was admitted to Showa University Fujigaoka Hospital because of purpura of the lower extremities, general arthralgia and general fatigue in April 1991. She had delivered three children about 30 years previously and had no episodes of artificial or spontaneous abortion. In August 1986, at another hospital, she underwent extended hysterectomy and adjuvant chemotherapy (etoposide 800 mg/cycle, three cycles preoperatively and one cycle postoperatively) for choriocarcinoma. Nine months prior to this admission, an abnormal shadow was pointed out on a routine chest X-ray film, but she had no further examination. Physical examination on admission revealed purpura of the upper and lower extremities, swelling of the gums and tonsils, but no symptoms showing the complication of myasthenia gravis. Hematological tests revealed leucocytosis: WBC count 68 700/ μ l (blasts 11.5%, myelocytes 0.5%, bands 2.0%, segments 16.0%, monocytes 65.5%, lymphocytes 4.0%, atypical lymphocytes 0.5%), Hb 7.1 g/dl (reticulocytes 12%) and a platelet count of 9.1×10^4 / μ l. Further laboratory examination revealed elevated serum lactic dehydrogenase (589 U/l), vitamin B₁₂ (2010 pg/ml) and ferritin (650.0 ng/ml). Human chorionic gonadotropin and [alpha]-fetoprotein levels were normal. A bone marrow aspiration revealed hypercellular bone marrow with a decreased number of erythroblasts and megakaryocytes and an increased number of monoblasts that were positive for staining by [alpha]-naphthyl butyrate esterase and negative for staining by naphthol ASD chloroacetate esterase (Fig. 1). Chest X-ray upon admission revealed a mediastinal mass and an elevated left diaphragm (Fig. 2). Computed tomography (CT) of the chest showed a left anterior mediastinal mass (Fig. 3). Based on these findings, the patient was diagnosed with a mediastinal tumor accompanied by AMoL. First, in June 1991, the patient was treated with DCMP therapy: daunorubicin (DNR) (25 mg/m², days 1, 2, 3, 4, 6 and 8), cytosine arabinoside (Ara-C) (100 mg/m², days 1-9), 6MP-riboside (6-MP) (70 mg/m², days 1-9) and prednisolone (PSL) (20 mg/m², days 1-9), followed by five courses of consolidation chemotherapy [1, DCMP; 2, ID-Ara-C:adriacine (ADR), vincristine (VCR), Ara-C, PSL; 3, DCMP; 4, ID-Ara-C; 5, A-triple V: Ara-C, VP-16, VCR, vinblastine (VBL)]. After induction chemotherapy, a hematological examination and bone marrow findings had improved to normal, and complete remission was attained. Chest CT scan after chemotherapy in November 1991 revealed regression of the mediastinal tumor (Fig. 3). An invasive thymic tumor was suspected and surgery was undertaken in January 1992. The tumor (50 × 45 × 45 mm), located mainly in the anterior mediastinum, was strongly adhered to the adjacent tissues. Resection of the tumor included the left upper lobe of the lung, the phrenic nerve and pericardium. The histological finding was that the tumor cells have large, vesicular nuclei and prominent nucleoli, but keratinization was unclear (Fig. 4). The results of immunohistochemical finding of anti-TdT was negative. From these findings, we diagnosed poorly or moderately differentiated squamous cell carcinoma of the thymus.

The postoperative course was uneventful. The patient underwent radiation therapy of the mediastinum and left hilum at doses of 4000 cGy delivered over 4 weeks. She was discharged in March 1992. After the first AMoL remission, the patient suffered a relapse six times and was repeatedly admitted for chemotherapy. During these periods, chest X-ray and CT revealed no recurrence of the mediastinal tumor. During her tenth admission, the patient developed pneumonia during chemotherapy and died in October 1996. No autopsy was performed.

Figure 1. Microscopic features of bone marrow aspiration. The blast cells are large with an abundant rim of cytoplasm and the nucleus is round with delicate, lacy chromatin.

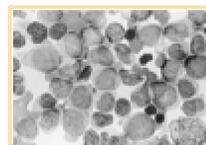


Figure 2. Chest X-ray upon admission demonstrating a mediastinal mass with an elevated left diaphragm.



Figure 3. (a) CT scan of the chest showing a left anterior mediastinal mass. (b) CT scan of the chest after chemotherapy revealing regression of the mediastinal tumor.

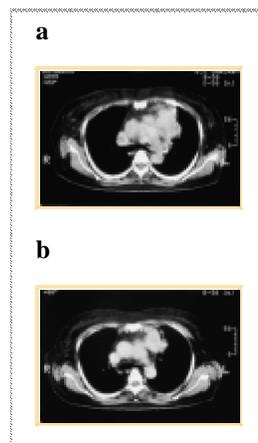


Figure 4. Microscopic features of the resected tumor. The tumor cells have large, vesicular nuclei and prominent nucleoli.



DISCUSSION

Thymic carcinoma is defined as a thymic epithelial tumor with a high degree of histological anaplasia, obvious cell atypia and increased proliferative activity, which closely resembles carcinoma seen in other organs and is unassociated with immature T cells (1). Although thymic carcinomas are distinct neoplasms that differ from thymoma, the classification of thymic carcinoma is controversial. A variety of histopathological subtypes of thymic carcinoma have been reported: squamous cell, spindle cell, lymphoepithelioma like, sarcomatoid, basaloid, small cell, mucoepidermoid, clear cell, mixed and undifferentiated carcinomas (2-7). Although lymphoepithelioma-like and squamous cell carcinomas have been considered different entities, some authors state that lymphoepithelioma-like carcinoma is a form of poorly differentiated squamous cell carcinoma (1,8,9). More recently, Suster and Rosai (10) reported 60 patients with thymic carcinoma and separated them into two prognostic groups based on pathological criteria (low-grade versus high-grade histological type). The present case was poorly or moderately squamous cell carcinoma, and is classified as high-grade histological type using the classification of Suster and Rosai.

Although paraneoplastic syndrome such as myasthenia gravis (MG), pure red cell aplasia (PRCA) and autoimmune diseases are frequently seen in patients with thymoma, they are extremely rare in cases with thymic carcinoma (5,8,9) In the literature, we found two cases accompanied by MG (11,11) and one other case accompanied by PRCA (12). The present case is not associated with MG or PRCA, but is accompanied metachronously by choriocarcinoma and AMoL. We found no such case in other reports on thymic carcinoma.

Some hematological disorders with thymic tumors have been documented. Peripheral T cell lymphocytosis (13,14) and acute lymphoblastic leukemia (15,16) associated with thymoma and acute myeloid leukemia associated with thymic carcinoma (17) have been reported, but we did not find a case report presenting with AMoL and thymic carcinoma. Regarding lymphocytosis with thymoma, Pedraza (18) assumed that the lymphocytosis represented a 'spill-over effect' from the thymus, because lymphocytosis disappeared after mediastinal irradiation. It is difficult to speculate on the pathogenesis of non-lymphocytic leukemia with thymic tumors. The present patient was treated with high-dose chemotherapy (etoposide) for choriocarcinoma about 5 years before the onset of AMoL. It is known that leukemia has occurred after treatment for other malignancies. Secondary (therapy-related) leukemia is mostly non-lymphocytic leukemia and the interval from the first therapy and the onset of leukemia is usually about 5-6 years (19). Pedersen-Bjergaard et al. (20) reported that the mean cumulative risk of leukemic complications was 4.7% (SE 2.3) 5.7 years after the start of etoposide-containing chemotherapy for germ cell tumors. Thus the role of prior chemotherapy in choriocarcinoma cannot be fully excluded in the present case.

The role of chemotherapy in thymic carcinoma is unclear. In some large series of thymic carcinoma, it has been noted that the response to chemotherapy was unsatisfactory (7,10). Recently, however, a few reports have cited the efficacy of chemotherapy in treating thymic carcinoma (Table 1) (21-26). These reports included both squamous cell carcinoma and poorly or undifferentiated carcinoma.

Successful applications of chemotherapy for thymic carcinoma almost all used a cisplatin-containing regimen, originally used to treat advanced thymoma. In our case, we used daunorubicin, cytosine arabinoside, 6MP-riboside and PSL as induction therapy for AMoL. It is unknown which drug was the key component in this regimen in this case because these drugs, except for PSL, are not typically used for thymic carcinoma or invasive thymoma. Corticosteroids are sometimes used for thymoma and the efficacy of these drugs has been reported (27), but the efficacy of corticosteroids in thymic carcinoma is questionable because thymoma regression after corticosteroid treatment may reflect only the regression of the lymphocytic components, not truly the epithelial components. Although the role of anthracyclines has also remained unclear, cases of partial remission have been reported with doxorubicin (28). Daunorubicin may play a significant chemotherapy role in the present case.

Table 1.

Ref.	Patient age/gender	Histology type	Chemotherapy regimen	Outcome (after diagnosis)
21	19/M	LE	CDDP, ADR, BLM, PSL	Dead 11 months, liver metastases
22	30/F	LE	CDDP, ADR, CPA, PSL	Alive 24 months, NED
23	21/M	PD	CDDP, BLM, VBL	Alive 64 months, NED
24	55/M	?	CDCDP, VP16	Alive 8 months, NED
25	55/F	UD	CDDP, VBL, IFX	Dead 36 months, lung metastases
	35/M	PD SCC	CDDP, ADR, CPA	Unknown
26	14/M	LE	CDDP, VP16, IFX	Alive 12 yr

CDDP, cisplatin; BLM, bleomycin; VBL, vinblastin; CPA, cyclophosphamide; ADR, doxorubicin; CDCDP, carboplatin; PSL, prednisolone; VP16, etoposide; IFX, ifosfamide; LE, lymphoepithelioma like; PD, poorly differentiated; UD, undifferentiated; SCC, squamous cell; NED, no evidence of disease.

The initial treatment for thymic carcinoma is complete surgical excision when possible, the same as for thymoma. Thymic carcinomas, however, commonly invade the surrounding tissue and, in many cases, tumors cannot be completely resected. In our case, remarkable tumor regression was attained after DCMP therapy for AMoL and we removed the whole tumor. Judging from this case and other successful cases of chemotherapy, we feel that intensive chemotherapy may be a beneficial strategy against thymic carcinoma. Further accumulation of clinical experience with this disease is necessary to determine a treatment protocol.

In conclusion, we treated a patient with thymic carcinoma associated with AMoL and choriocarcinoma. Combination chemotherapy for AMoL was effective for tumor regression of thymic carcinoma.

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Abstract

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Abbreviations: AMoL, acute monocyte leukemia; MG, myasthenia gravis; PRCA, pure red cell aplasia; DNR, daunorubicin; Ara-C, cytosine arabinoside; PSL, prednisolone; ADR, adriacin; VCR, vincristine; VBL, vinblastine

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