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GRANULOCYTIC SARCOMA IN NONLEUKEMIC CHILDREN: REPORT OF TWO NEW CASES SUCCESSFULLY TREATED BY LOCAL RADIATION THERAPY AND SYSTEMIC CHEMOTHERAPY

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ABSTRACT

Granulocytic sarcoma (GS) is a rare tumor composed of immature myeloid cells. Exceedingly rare in childhood, it has more commonly been described in association with acute myeloid leukemia. Occasional nonleukemic patients generally go on to develop overt leukemia in a mean period of 10.5 months from diagnosis of GS. We report here two new cases of GS diagnosed in nonleukemic children. They were successfully treated with local radiation therapy and conventional systemic chemotherapy. The need to suspect more often this all too frequently misdiagnosed disease is emphasized. The role of optimally delivered radiation therapy in achieving and maintaining local control of the tumor is discussed.

Key words: granulocytic sarcoma, children, acute leukemia, radiotherapy

Granulocytic sarcoma (GS) is a rare, localized tumor mass composed of immature myeloid cells. Most often it involves the skin, lymph nodes, soft tissue and bone.[1] Its association with acute myeloid leukemia is well known, having been reported concurrently with onset, during remission or at relapse. GS has also been described as an isolated lesion in nonleukemic patients; however, the majority of these subjects develop acute leukemia within a mean interval of 10.5 months from diagnosis.[1,2] Patients who remain leukemia free have a better prognosis,[3] but correct treatment is delayed in most cases because of a high rate of initial misdiagnosis, most frequently as large cell lymphoma.[3-5]

We report here two cases of GS diagnosed in nonleukemic children; the first was localized in the orbit and the second in the skin. Despite a long delay in diagnosis in both cases, we did not observe progression to acute leukemia. The role of therapy is emphasized and discussed.

Case reports

Case #1

The patient, a 12-year-old female, was admitted to the Orbital and Oculoplastic Services, University Federico II of Naples, in February 1991 because of right exophthalmos. At that time histological examination of the tissue obtained by an excisional biopsy led to a diagnosis of *pseudotumor.* She remained well until August 1991 when reappearance of the exophthalmos was noticed. In November 1991 the girl was admitted to the Department of Pediatrics of the same University. On admission her general condition was good. Physical examination was normal apart from the above mentioned exophthalmos.

A CT scan of the orbit showed contrast-enhancing tissue involving the superior and medial parts of the orbit and displacing the eyeball downwards and anteriorly (Figure 1a). A

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repeat biopsy of the mass revealed diffuse proliferation of small and medium-sized malignant cells, with a high nucleus/cytoplasm ratio, round nuclei with finely granular chromatin and inconspicuous nucleoli; the cytoplasm was eosinophilic (Figure 2). Antilysozyme stain showed strong and diffuse positivity in the majority of tumor cells. Other special stains, such as antimyoglobin, S100, vimentin, desmin, were all negative.

A complete evaluation, including CT scans of the head and abdomen, radionuclide 99mTc bone scan, multiple bone marrow biopsies and chest x-ray, was negative. On the basis of the above clinical and histopathologic data a diagnosis of granulocytic sarcoma was made.

From December 1991 to January 1992, the child received radiation therapy to the primary tumor. The total dose of radiation was 3,800 cGy, delivered in 200 cGy fractions five times per week. The radiation field included the tumor volume with a safety margin of 2 cm in all directions. An anterior cobalt 60 teletherapy field was used until 2,000 cGy were reached. The remaining dose was then administered with a 7×5 cm lateral field.

In January 1992, the patient was started on systemic chemotherapy, consisting of two courses of daunorubicin (days 1-3) and cytosine arabinoside (days 1-7) followed by a consolidation phase that included four courses of daunorubicin, cytosine arabinoside and 6-thioguanine (days 1-5). In July 1992, a complete work-up documented the remission of the disease, with the disappearance of the primitive mass (Figure 1b). At the present time, 53 months after the onset of the disease and 38 months after the end of therapy, the patient is well and free of detectable disease.

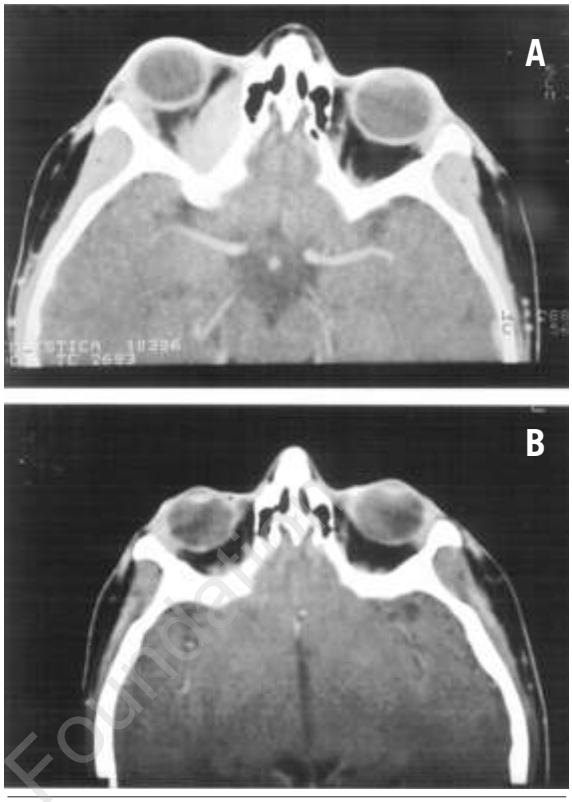

Figure 1. Case one: a) CT scan of the head at diagnosis showing the orbital mass; b) repeat CT scan five months after completion of radiotherapy documenting complete disappearance of the primitive lesion.

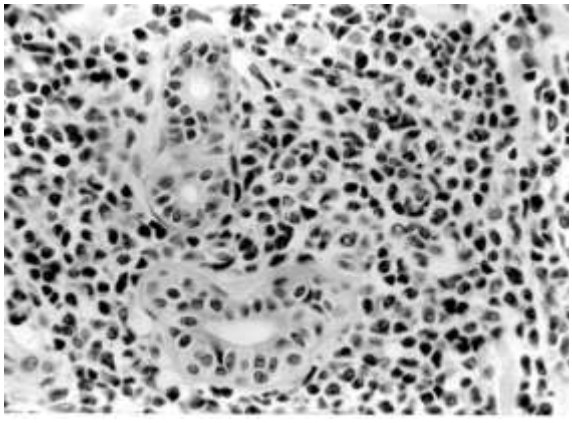

Figure 2. Granulocytic sarcoma involving the orbit. Notice the high nucleus/cytoplasm ratio and the round nuclear shape of blastic cells. (H&E; 100×).

Case #2

The patient, an 11-year-old female, presented in April 1993 with a mass in her right parietal scalp. It had first appeared right after a direct trauma and then progressively enlarged over the following two years. During this period neither a diagnostic evaluation nor a therapeutic approach was made. In January 1995 the girl was referred to our Department because of the appearance of a preauricular tumefaction. At admission her general condition was good. Physical examination showed a painful, tender, firm mass, measuring 7×3 cm in diameter,

localized in the right fronto-parietal region. A firm but painless lymph node 1 cm in diameter was also evident in the right preauricular area. No other signs or symptoms of systemic disease were present. An excisional biopsy of the primitive mass and a fine needle aspiration of the preauricular swelling were performed. The tissue specimens showed histological and cytological features consistent with a diagnosis of GS.

Therefore the child underwent a complete work-up for systemic disease that proved to be negative. Fifteen days after admission the patient was started on radiation therapy to the scalp. The total dose of radiation was 3,000 cGy, delivered in 200 cGy fractions five times per week.

At the end of the radiotherapy, complete regression of the above mentioned masses in the parietal scalp and in the preauricular region was documented. Between March and August 1995 the girl received two courses of induction therapy (daunorubicin days 1-3 and cytosine arabinoside days 1-7) and four consolidation courses of daunorubicin, cytosine arabinoside and 6-thioguanine.

At the present time, 30 months after the onset of disease and two months after the end of therapy, the child is well and free of detectable disease.

Discussion

Granulocytic sarcoma has seldom been reported in children.[1,3,4,6-10] Moreover, in the majority of cases it has been diagnosed at presentation or during the course of acute myeloid leukemia. Almost always the association of GS with overt leukemia implies a dismal prognosis. GS presenting as an isolated mass is a rare condition, most notably in childhood.[3,7,9] However, most of these patients develop systemic disease and eventually die of it.[3] One possible explanation for this behavior could be a delay in diagnosis or even misdiagnosis due to the equivocal histological features of the disease. In fact, in H&E stained histologic sections the lesions are similar to large cell lymphoma and are frequently misdiagnosed as such.[3-5]

Our two cases, with their great delay in diagnosis, testify to these diagnostic difficulties.

Most of the nonleukemic patients affected by GS have been aggressively treated with chemotherapy or radiotherapy or both; however, the regimens employed have been quite heterogenous. Many patients have received more than one chemotherapeutic schedule and some have been treated for lymphoma for at least part of their therapy. More importantly, only a few patients received radiation therapy for local control of the primary tumor, and the total doses and timing of treatments varied widely from patient to patient.

We treated our two patients with the current protocol for acute myeloid leukemia, preceded by immediate radiotherapy to the primary lesion at doses among the highest utilized by other authors.[3,8,11] As a matter of fact, both these patients are in complete remission 56 and 30 months after disease onset and, although the follow-up of the second patient is too brief for definitive conclusions, the first patient could be considered cured. Nevertheless, we cannot exclude the possibility that for our patients, as well as for the ones reported in the literature[7] who did not develop acute leukemia, correct treatment might only be a factor of good prognosis together with favorable biological behavior of the tumor itself.

Addendum

Since this paper was submitted for publication the second patient has experienced an unexpected disease course. In October 1995, three months after the end of therapy, we documented overt acute lymphoblastic leukemia. The immunophenotype of blast cells was: $CD10^+$ (73%), $CD19^+$ (94%), $CD34^+$ (79%), HLA-DR^+ (98%), $CD24^+$ (96%), $CD33^+$ (45%).

Cytogenetic analysis, performed on bone marrow blast cells, did not reveal any abnormalities. Moreover, we verified and confirmed the initial diagnosis of GS. The child then received induction chemotherapy consisting of association of vincristine, prednisone, L-asparaginase and cyclophosphamide instead of anthracyclines, whose maximum tolerated doses had been reached. In November 1995, we

documented complete clinical and hematological remission. At the present time the patient is in good clinical condition and free of detectable disease.

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