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Spinal Epidural Granulocytic Sarcoma Preceding Acute Myelogenous Leukemia

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A rare case of spinal epidural granulocytic sarcoma (GS) preceding acute myelogenous leukemia is described. A 10-year-old boy presented with lower leg weakness. The initial diagnosis was a histiocytic lymphoma, and he was treated accordingly. No evidence of bone marrow involvement was found at that time. The correct diagnosis of epidural GS was made possible in retrospect by using immunoperoxidase staining for lysozyme fourteen months later when the patient showed the full-blown features of leukemia. This rare tumor should be considered in the differential diagnosis of an epidural mass with cord compression in patients with or even without acute leukemia, because early diagnosis followed by appropriate combined chemotherapy and radiation may obviate surgical intervention and eventually prevent leukemic transformation.

Key Words: *Granulocytic sarcoma, Spinal epidural, Aleukemic patient*

INTRODUCTION

Granulocytic sarcoma (GS) is a tumor of the myeloid precursors in extramedullary sites. Most cases of GS occur in the course of leukemia, and this tumor is reported in 0.7-9.0 per cent of patients with acute or chronic myelogenous leukemia (Krause, 1979; Neiman et al, 1981; Swirsky et al, 1984). Rarely, however, GS may present before leukemia becomes evident in blood or bone marrow (Neiman et al, 1981; Meis et al, 1986; Yoon et al, 1987). It is generally thought that such cases will invariably progress to acute myelogenous leukemia (AML) if left untreated.

Presentation as an epidural GS and cord compression in aleukemic patients is extremely rare, so that only six such cases have been described so far in the literature (Ragins and Tinsley, 1950; Mason et al, 1973; McCarty et al, 1980; Chan et al, 1986; Ripp et al, 1989; Doshi et al, 1991). We report here a patient presenting with acute paraparesis due to a spinal epidural GS, who developed AML 14 months later.

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CASE REPORT

A 10-year-old boy who had been healthy developed gradual weakness in both legs for one week. Physical examination on admission revealed paraparesis of the lower extremities, hypesthesia below the T5 level of sensory dermatome, increased deep tendon reflexes in the lower extremities, and the loss of sphincter tone. Computerized tomography (CT) and myelography of the spine showed an isodense epidural mass with anterior displacement of the spinal cord along with complete spinal block (Fig. 1 and Fig. 2). Emergency thoracic laminectomies were performed, and the tumor mass was totally removed. The tumor was 2×2cm, gray to green, soft and friable, but not encapsulated. Histologically, there were sheets of immature cells separated by fibrous septa, and the cells had round or oval nuclei with scanty cytoplasm. The diagnosis of non-Hodgkin's lymphoma of diffuse histiocytic type was made (Fig. 3). White cell count was 7,400/μl with normal differentials; platelets 309,000/μl; hemoglobin 11.2g/dl. Bone marrow smears and biopsy at that time revealed normal findings. Cerebrospinal fluid examination showed normal cytology and chemistry. Serum neuron specific enolase, urinary excretion of vanillylmandelic and homovanillic acids were within

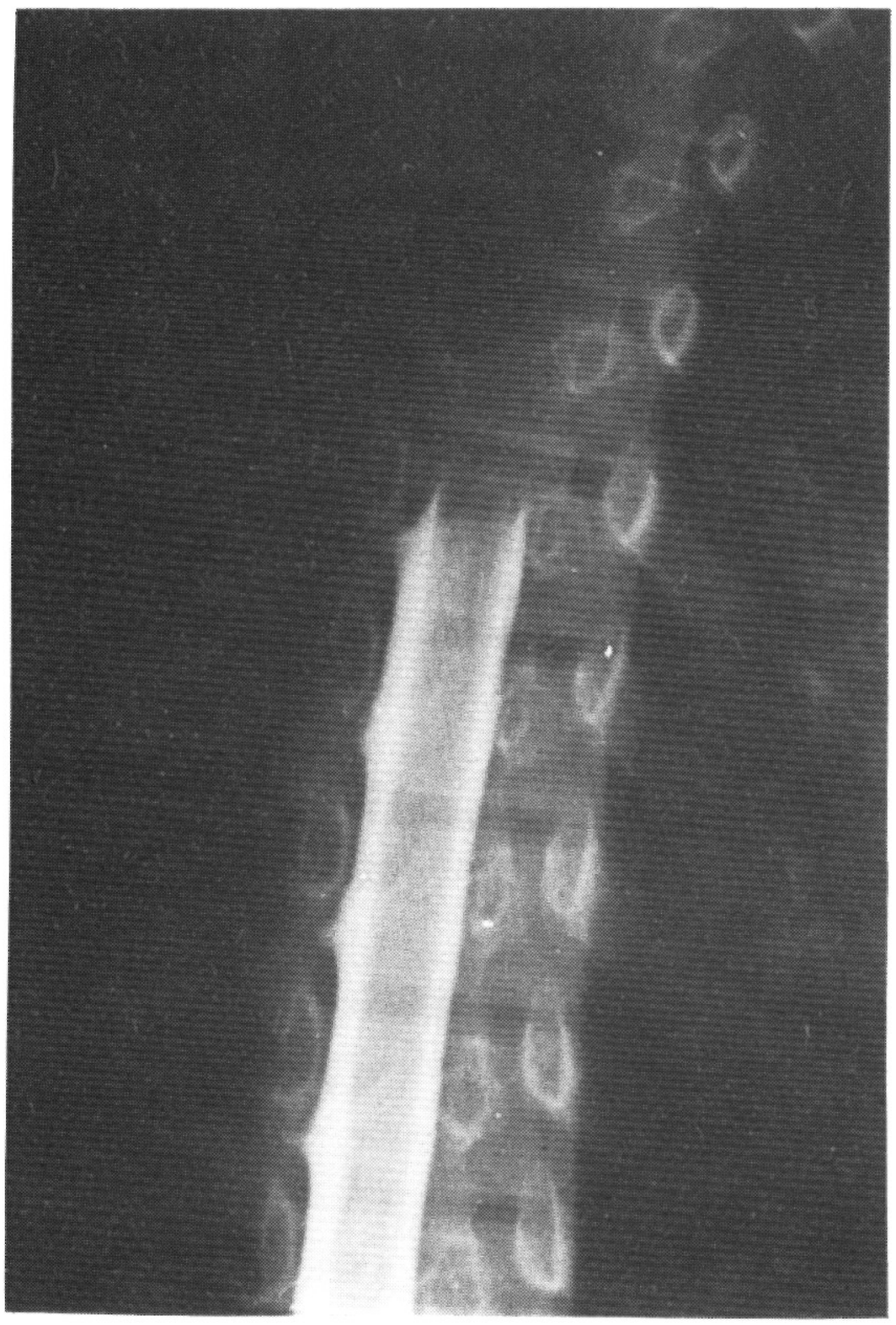

Fig. 1 Myelogram demonstrating a complete block at T5 due to an extradural mass.

normal range.

On physical examination immediately after surgery, the weakness was decreased in both legs. Two weeks after surgery, however, weakness in both legs began to aggravate and facial nerve palsy was noted on the right side. Brain CT showed no abnormality accountable for the Bell's facial palsy.

He was started on radiotherapy of 3,000 cGy to the thoracic spines, intrathecal methotrexate, and systemic cyclic chemotherapy consisting of vincristine, adriamycin, cytoxan, solumedrol, and prednisolone.

He had been in good condition without any neurologic dysfunction for fourteen months until fever and pallor developed. The liver was palpated 5cm below the right costal margin. White cell count was 9,600/μl, the majority being the blasts (Fig. 4). Platelets were 45,000/μl; hemoglobin 6.7g/dl. The finding of the bone marrow examination was consistent with AML. Some of the blasts showed Auer rods. They were positive for myeloperoxidase reaction and Sudan black B stain, and also for CD13 and CD33. Further pathological review of the previous epidural mass was performed. Immunoperoxidase staining for lysozme revealed positivity on the formalin-fixed paraffin-embedded specimens, rendering a revised diagnosis of GS (Fig. 5). Naphthol-ASD-chloroacetate esterase (CAE) staining, however, was negative on these sections.

Subsequently, systemic chemotherapy with aclacinomycin, ara-C, and prednisolone was started. During severe myelosuppression, pain and tenderness developed in the right lower quadrant due to typhlitis with abscess formation. Surgical resection of the involved bowel and pus drainage were done successfully. He achieved complete remission, but only for a short duration. Three months later, during the severely myelosuppressed period of reinduction therapy, he unfortunately succumbed to intracranial hemorrhage. Autopsy was not granted.

DISCUSSION

Known also as chloroma by the green hue the enzyme myeloperoxidase gives off, GS is an unusual tumor of immature granulocytes. GS is reported to occur in three clinical settings: (1) in association with known AML, (2) in association with myelodysplastic disorders with leukemic transformation or chronic myelogenous leukemia with impending blast crisis, and (3) as a harbinger of AML in aleukemic patients. (Neiman et al, 1981; Meis et al, 1986). GS is reported in up to 10 per cent of patients with AML.

Common sites of occurrence are the orbits, paranasal sinuses, periosteum, bones and skin, with rare involvement of the central nervous system (Neiman et al, 1981; Freedy and Miller, 1991). The spinal involvement of GS usually manifests as an epidural mass with signs of cord compression (Petursson and Boggs, 1981; Swirsky et al, 1984; Pui et al, 1985). However, a few cases of intramedullary involvement have been reported (Petursson and Boggs, 1981; Ang and Virapongse, 1990; Kook et al, 1992). Spinal epidural GS was found in only two patients in a study of 1,000 cases of AML (Swirsky et al, 1984), and also in two among 323 cases of AML (Neiman et al, 1981).

GS preceding the evidence of leukemia in peripheral blood or bone marrow is reported to occur in 0.6% of AML (Krause, 1979). Reports of sixteen (Meis et al, 1986) and fifteen patients (Neiman et al, 1981) are the largest series describing GS in aleukemic patients. Not only for its rarity, but also for its similarity to lymphoma pathologically and radiologically, the correct diagnosis of GS was made initially only in 25-54% of cases in the absence of leukemic evidence (Neiman et al,

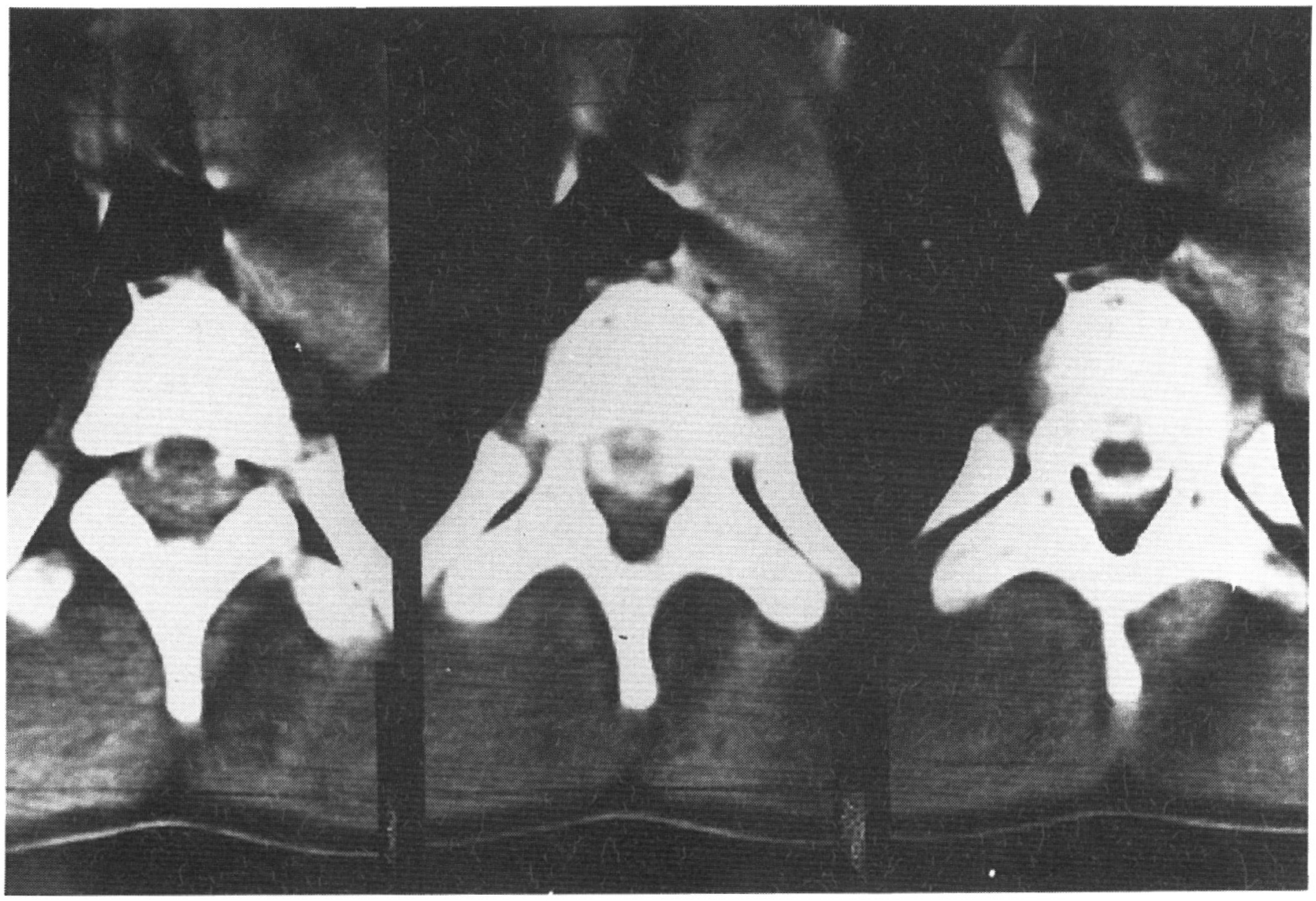

Fig. 2 Myelographic CT showing anterior displacement of the spinal cord and obstruction of the contrast medium-filled subarachnoid space by a posterior epidural soft tissue mass.

1981; Meis et al, 1986; Fellbaum and Hansmann, 1990). Often, the first indication of misdiagnosis was the lack of response to treatment (Adam et al, 1991).

To our knowledge, presentation with an epidural mass in aleukemic patients has been reported in only six cases (Ragins and Tinsley, 1950; Mason et al, 1973; McCarty et al, 1980; Chan et al, 1986; Ripp et al, 1989; Doshi et al, 1991). Because of its rarity, GS is not routinely considered to be the cause in progressive paraparesis secondary to an epidural spinal cord mass. Rather, it is misdiagnosed as malignant lymphoma, especially of high grade malignancy (Pomeranz et al, 1985; Ripp et al, 1989). Similarly, in this report correct diagnosis was possible in retrospect only after the patient showed the full-blown features of leukemia fourteen months later.

The most frequent initial symptom of paraspinal GS is back pain or radicular pain. Weakness and/or paralysis of one or more extremities was noted in more than 80%. The thoracic level was the most commonly affected site of cord involvement (Petursson and Boggs, 1981).

Myelography and CT have been widely used in evaluating various kinds of spinal lesions, although magnetic resonance imaging has gained increasing popularity as the first choice. The myelographic and CT-myelographic findings of spinal GS involvement as seen in our case may well be interpreted as non-specific findings of an isodene intra-or extradural mass impinging on the thecal sac and/or nerve roots. Occasionally complete spinal block may be demonstrated (Eelkema et al, 1989; Freedy and Miller, 1991). Therefore, in differential diagnosis of a paraspinal lesion based on the above techniques, GS should be included in addition to para/intraspinal abscess, hematoma, metastatic lesions, or primary tumor such as a neurofibroma (Freedy and Miller, 1991).

For the pathological diagnosis of GS, light microscopy with standard Romanowsky staining on the formalin-fixed paraffin-embedded section may be inadequate, whereas touch print preparation with Romanowsky may be useful in identification of immature myeloid cells. Although the presence of eosinophilic myelocytes has traditionally been regarded as a useful marker in the recognition of GS (Neiman et al, 1981; Guitart et al, 1990), Naphthol-ASD-CAE staining and im-

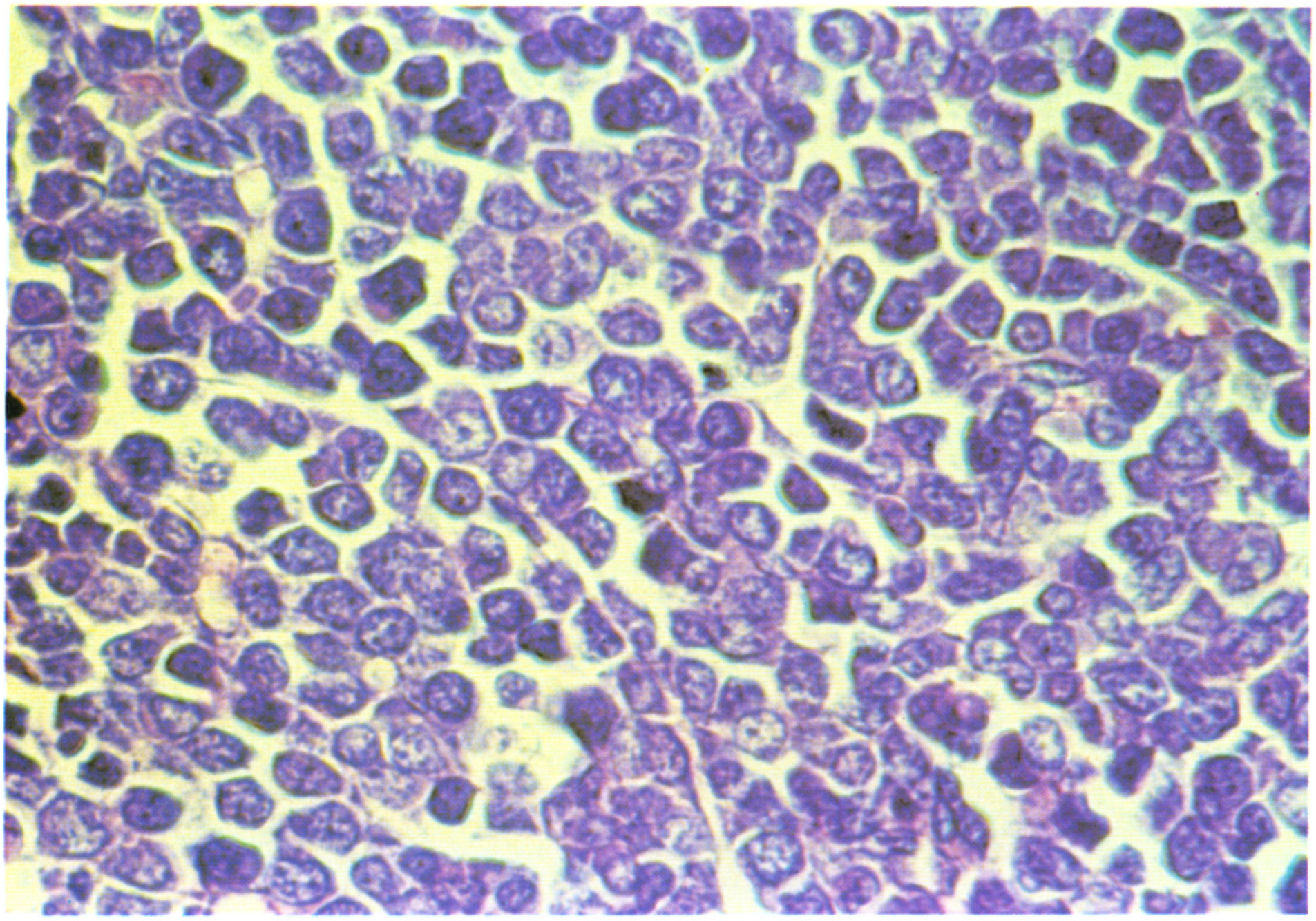

Fig. 3. Light microscopic finding of the epidural mass showing a population of immature cells with round to oval nuclei, fine chromatin and scanty cytoplasm (H&E ×400).

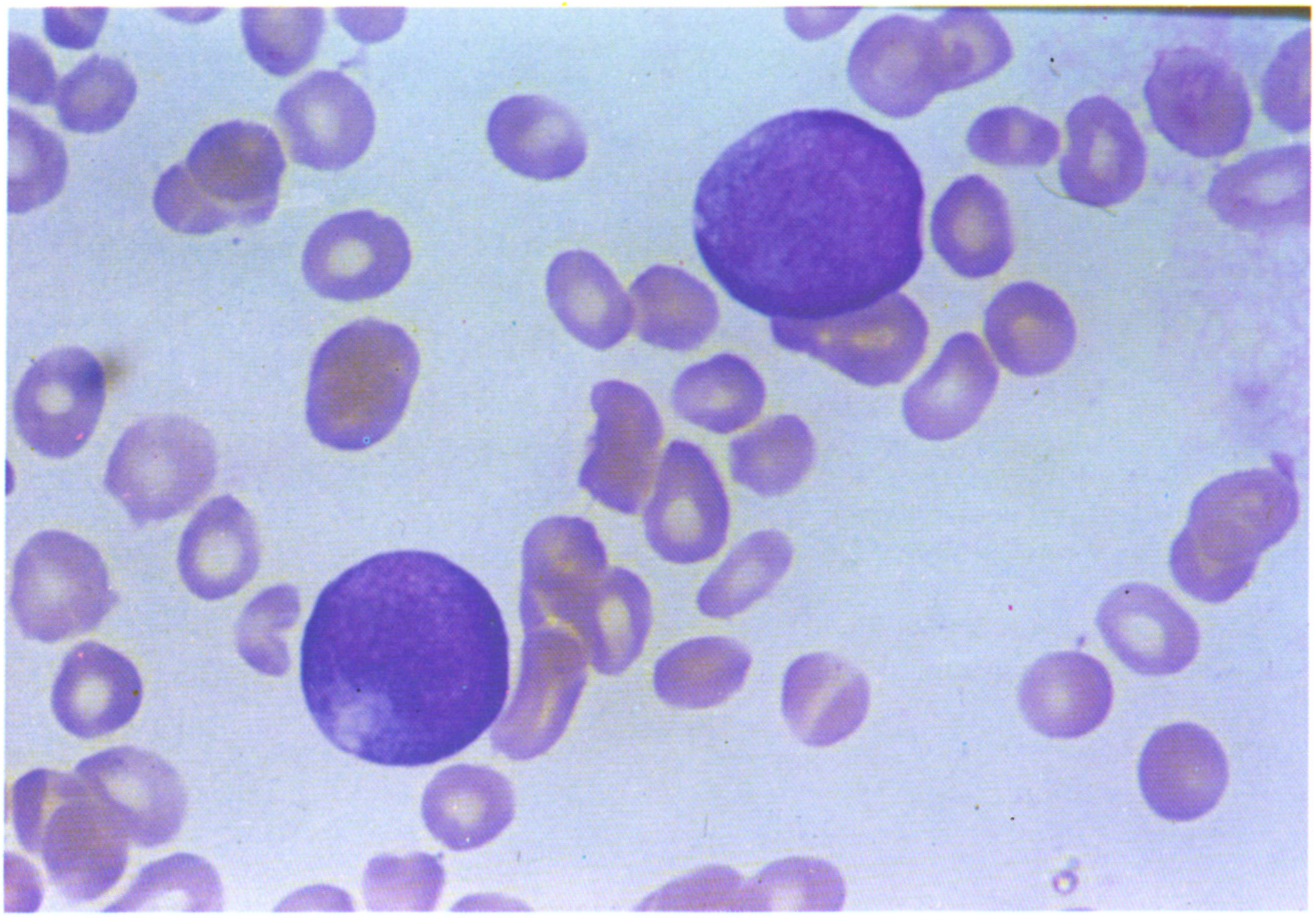

Fig. 4. Peripheral blood smear fourteen months after the initial diagnosis of epidural mass disclosing myeloblasts having nucleoli and a few azurophilic granules (Wright ×1000).

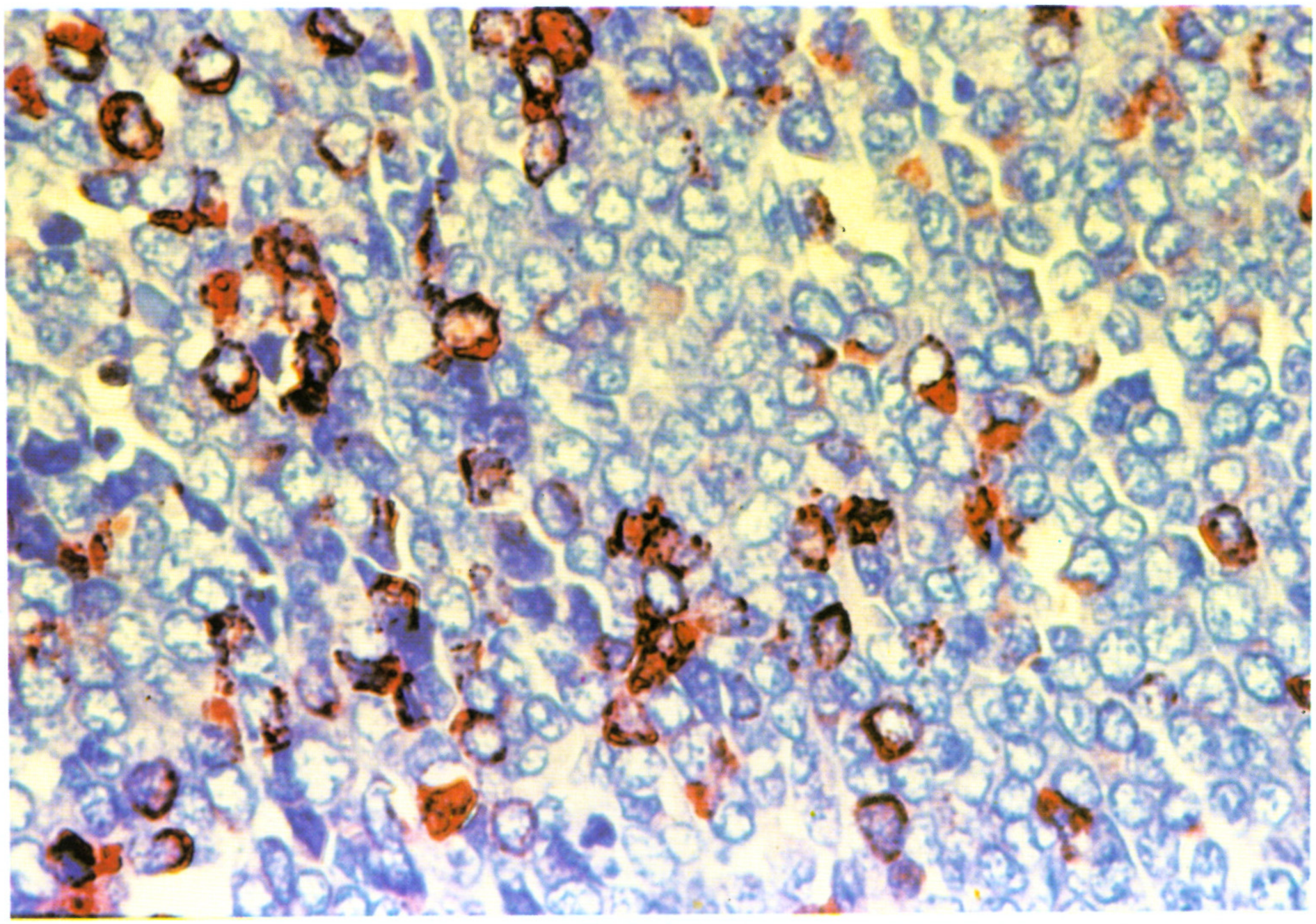

Fig. 5. Immunoperoxidase for lysozyme showing positive reaction in the cytoplasm of immature cells, rendering the diagnosis of granulocytic sarcoma of the previous epidural mass (Immunoperoxidase ×400).

munoperoxidase staining for lysozyme appear to be the most reliable methods (Neiman et al, 1981; Meis et al, 1986; Fellbaum and Hansmann, 1990). Neiman et al (1981) reported that out of 57 cases of GS in which both stainings performed, 56 cases showed positivity in at least one of both special stainings, though 75% were positive for CAE and 89% were positive for lysozyme. In our case, though the epidural mass in formalin-fixed section was negative for CAE, the tumor cells were subsequently shown to be positive for immunoperoxidase for lysozyme. Also, electron microscopic finding of electron-dense specific granules characteristic of granulocytic cells is considered pathognomonic of GS (McCarty et al, 1980; Welchi et al, 1986).

The vast majority of aleukemic patients with GS are known to develop acute leukemia within a matter of months with local therapy alone or with inappropriate chemotherapy. It has been suggested that treatment regimens for AML including systemic chemotherapy and bone marrow transplantation should be given in addition to local irradiation in cases of aleukemic GS to prevent transformation (Petursson and Boggs, 1981; Beck et al, 1984; Meis et al, 1986; Takaue et al, 1987; van Veen et al, 1991).

The optimal management of paraspinal GS in aleukemic patients is still controversial as experience has thus far been limited because of the small number of cases. For the patients with rapidly progressive neurologic signs and with evidence on myelography of spinal block due to epidural GS, emergency laminectomy is recommended (Wodzinsky et al, 1988). However, for the patients with stable neurologic signs without evidence of cord compression, GS may be primarily treated by high dose corticosteroids followed by systemic chemotherapy and radiation considering the high chemo-and/or radiosensitivity of the tumor. (Pui et al, 1985; Wodzinsky et al, 1988; Ripp et al, 1989).

Only by maintaining a high index of suspicion can clinicians and pathologists recognize this tumor in most cases. Therefore, it is advisable for physicians and neurosurgeons to consider epidural GS as a possible etiology for spinal symptoms in leukemic patients, or even in patients free of leukemic evidence, because early diagnosis may allow affected patients to be treated medically, not necessitating surgical intervention, and ultimately give them a greater chance of survival.

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