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Multiple Spinal Granulocytic Sarcomas Simulating Neurofibromatosis

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Granulocytic sarcoma may develop at any time during the course of acute or chronic myelogenous leukemia. Symptomatic because of their invasive nature and mass effect, these tumors may occur in any anatomic site. Granulocytic sarcoma is diagnosed in a minority of patients with myelogenous leukemia, but when present, granulocytic sarcoma commonly affects the CNS. The most common manifestation of granulocytic sarcoma in the spine is spinal cord compression due to an extradural mass. We recently observed an unusual case of cervical radiculopathy with multiple spinal granulocytic sarcomas.

Case Report

A 37-year-old woman with a 12-year history of acute myelogenous leukemia presented with a 3-month history of bilateral upper extremity numbness, weakness, and tingling. Since her initial diagnosis of leukemia, she had received several courses of systemic chemotherapy. For the 12 months preceding hospitalization, she was in clinical remission. Bone-marrow biopsy and peripheral blood count 2 weeks before hospitalization also indicated remission.

Cervical myelography with water-soluble contrast material showed multiple bilateral intra- and extradural filling defects filling the cervical nerve root sleeves (Fig. 1A). An extradural filling defect was also present at T10; the remainder of the myelogram was negative. Postmyelographic CT confirmed the multiple intra- and extradural soft-tissue masses, some of which extended through the neural foramina (Figs. 1B and 1C). Cranial CT, chest and spine films, and dermatologic examination were negative for signs of neurofibromatosis. Examination of the CSF showed 188 WBC/ml, with frequent myeloblasts. Treatment was started with intrathecal methotrexate and radiation therapy. Cervical MR obtained after 10 days of treatment showed multiple masses of intermediate signal intensity (Fig. 1D). After completion of therapy, the patient's symptoms resolved. Posttreatment myelography (Fig. 1E) and CT were normal.

Discussion

Granulocytic sarcoma is a firm, locally invasive mass of myelogenous origin that may complicate acute or chronic myelogenous leukemia [1, 2]. These tumors also have been called chloromas if tinged green or myeloblastoma if unpigmented. The difference in color is attributed to differing concentrations of the enzyme myeloperoxidase and does not denote a difference in cell line [2, 3]. Because the cells of granulocytic sarcoma (predominantly myeloblasts, promyelocytes, and myelocytes) are slightly more immature than the circulating leukemic cells, the masses are regarded as true neoplasms rather than just clumps of leukemic cells [3].

Granulocytic sarcoma has been found in 2–8% [1, 2, 4] of patients with acute myelogenous leukemia (AML), and 3.9–4.5% [1, 2] of patients with chronic myelogenous leukemia (CML). Muss and Moloney [2] estimate that only one-half of granulocytic sarcomas are clinically symptomatic, and the tumor is found more commonly at autopsy than in living patients.

Granulocytic sarcoma may be diagnosed concurrently with myelogenous leukemia [3, 5, 6] or during the course of the disease [7, 8]; less frequently the diagnosis of granulocytic sarcoma precedes peripheral blood or bone-marrow evidence of leukemia by weeks to several months [4, 8–13]. It is not rare for granulocytic sarcoma to be diagnosed in a patient in clinical remission of AML [7]. Younger patients are affected more commonly than older patients [1, 14].

The tumors are found most often in subperiosteal locations with cranium, facial bones, ribs, vertebrae, and proximal long bones most commonly affected [2, 9, 11, 12, 15]. Soft-tissue tumors (ovary, kidney, breast, liver, lung, pleura, heart, pericardium) are common [1, 15], and nearly any anatomic site can be involved [8, 9, 11]. Multiple tumors are common [1]. The most frequent initial symptom is pain [1, 16]. Especially in the relatively closed spaces of the cranium and spine, the mass effect predominates. Acute paraplegia due to an epidural mass and proptosis due to orbital involvement are common initial manifestations of granulocytic sarcoma [17]. The first report of spinal symptoms due to granulocytic sarcoma came from Critchley and Greenfield in 1930 [17]. They reported four cases of acute paraplegia in patients with chloroma due to "cellular infiltration of the spinal meninges." Their report, published before the era of effective chemother-

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apy, is valuable for the detailed gross and microscopic findings. In each of the four cases, spinal epidural masses were present. In one case, the lower thoracic arachnoid and the "septa of the anterior roots" were infiltrated with leukemic cells. Another case showed "the spinal roots were in many places infiltrated by leucoma [sic] masses." In another case, "leukemic infiltration of the meninges and of the sheaths and interstitial connective tissue of the anterior and posterior nerve roots [spread] into the cord via the anterior fissure and the sheaths of the blood vessels."

In 1963, Wilhyde et al. [16] described one case and compiled 41 other cases of epidural leukemia (26 myelogenous, eight lymphocytic, seven not specified). The tumors, all verified at surgery, "often involved only the posterior aspect of the epidural space, but anterior involvement, extension through the intervertebral foramina with spinal root infiltration, or complete circling of the cord were not unusual" [16]. The only myelographic description was that of the authors' own case, which showed an extradural mass from T3 to T11 [16]. Several other case reports of acute paraplegia in myelogenous leukemia have shown "epidural masses" or "complete blocks" at myelography [6, 9, 13, 14].

Two recent cases of spinal myeloblastomas have included other myelographic findings. Mirvis et al. [18] described a case of "nodular radiculopathy" in a patient with AML, with symmetric round enlargement of the C8 nerve roots. In a recently published case, McAllister and O'Leary [19] demonstrated lumbar nerve root enlargement and an intradural mass in a patient who had AML, symptoms of cauda equina compression, and myeloblasts in the CSF.

Our case is unique in the myelographic, CT, and MR demonstration of multiple intradural and extradural masses. The initial myelogram was so strongly suggestive of neurofibromatosis that the patient was evaluated for any radiologic or dermatologic manifestations of that disease, but none was found. As in the cases reported by Mirvis et al. [18] and McAllister and O'Leary [19], the excellent response to therapy precluded direct pathologic or histologic examination of the tumors, and the histology must be inferred. In our case, the positive CSF cytology indicates involvement of the subarach-

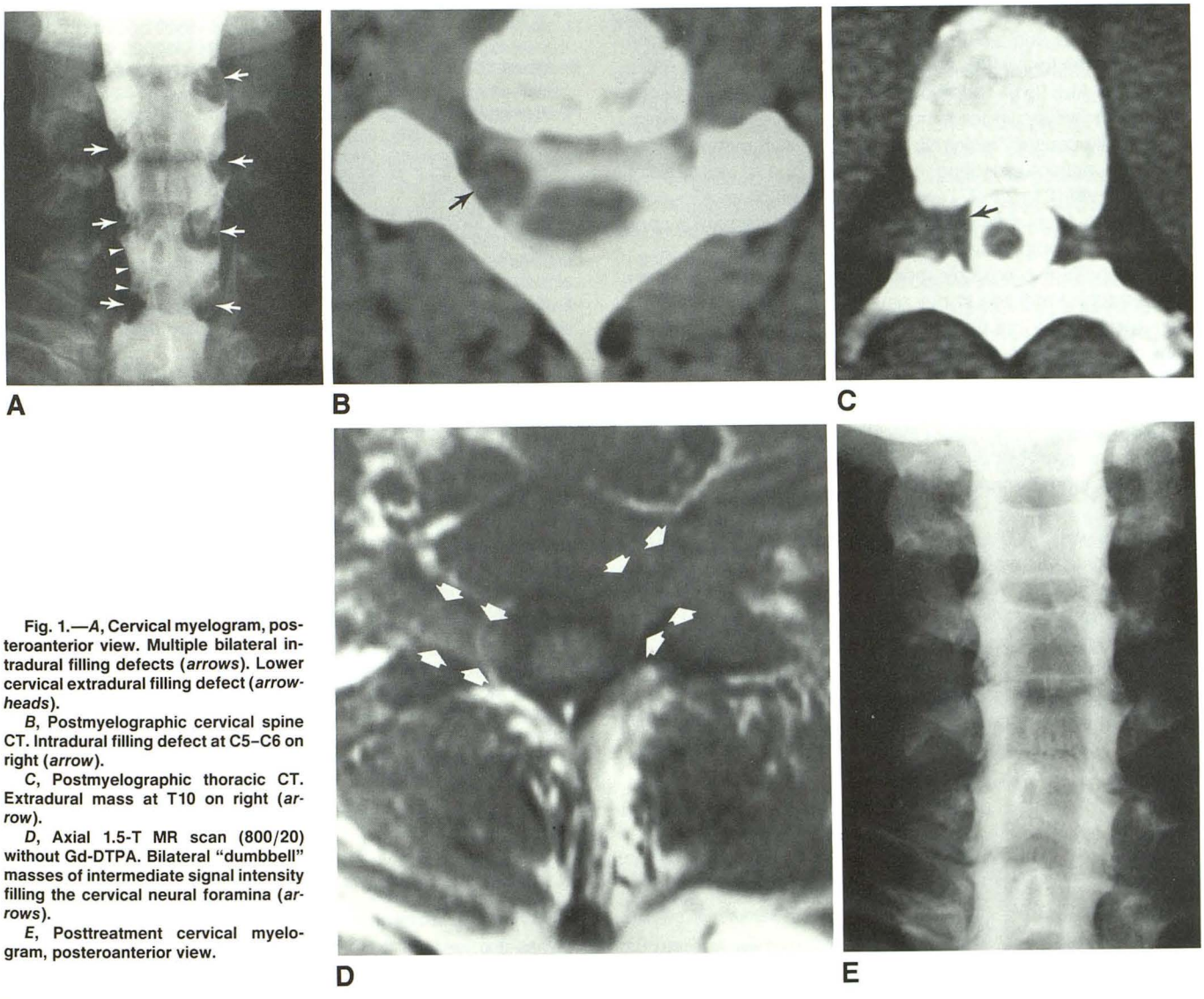

Fig. 1.—*A*, Cervical myelogram, posteroanterior view. Multiple bilateral intradural filling defects (*arrows*). Lower cervical extradural filling defect (*arrowheads*).

***B*, Postmyelographic cervical spine CT. Intradural filling defect at C5–C6 on right (*arrow*).**

***C*, Postmyelographic thoracic CT. Extradural mass at T10 on right (*arrow*).**

***D*, Axial 1.5-T MR scan (800/20) without Gd-DTPA. Bilateral "dumbbell" masses of intermediate signal intensity filling the cervical neural foramina (*arrows*).**

***E*, Posttreatment cervical myelogram, posteroanterior view.**

noid space by leukemia, and the CT and myelographic findings clearly indicated intradural and extradural masses.

Several mechanisms by which leukemia may reach the CNS have been proposed, including independent leukemic transformation of cells with hematopoetic potential in the choroid plexus or leptomeningeal mesenchyme [20, 21], hemorrhage [22], and diapedesis of cells directly through brain or arachnoid capillaries [22]. The most widely accepted theory, with histologic support from both animal and human pathologic material, is that leukemia reaches the CNS via perivenular spread from adjacent periosteum [17, 20, 23–25]. There is a progression from early perivascular cuffing, to dural involvement, to superficial arachnoid infiltration (with or without escape from the perivascular adventitia into the CSF), and finally to deep perivascular arachnoid involvement. Disruption of the pia-glial membrane only follows leukemic infiltration of the Virchow-Robin spaces and is a late manifestation. The studies cited previously have included patients with both acute lymphocytic and myelocytic leukemia and have dealt primarily with the skull and brain [20–26]. No histologic differences in the manner of spread or mechanism of CNS involvement in the types of leukemia has been shown [20, 23]. No differences in the frequency of dural and arachnoid infiltration between acute lymphocytic leukemia (ALL) and AML has been found [20, 26], but perivascular cuffing is more frequent in ALL [26]. The two types of leukemia are distinctly different, however, in their manifestations of CNS leukemia. ALL usually causes "leukemic meningitis" with symptoms of headache, nausea, vomiting, and lethargy due to blockage of arachnoid villi [21, 25–27], whereas AML displays a distinct tendency to form cellular masses and presents with symptoms of local compression [28].

We propose two possible mechanisms to explain the intra- and extradural masses in our patient. Perivenular spread of leukemic cells via the vertebral venous plexus and radicular veins may occur. Alternatively, leukemic cells in the CSF may be trapped by arachnoid granulations of the nerve root sleeve. By either mechanism, once leukemic cells have reached the neural foramen, transdural proliferation could result in "dumbbell" tumors, as in our patient whose multiple cervical tumors resembled neurofibromatosis.

Both the frequency of remission and the length of survival in patients with acute leukemia are increasing [29]. The frequency of CNS involvement in acute leukemia in adults has also increased [28]. A greater awareness of this entity may contribute to earlier diagnosis. Therefore, in a patient with myelogenous leukemia, active or in remission, symptoms of spinal-cord or nerve-root compression should prompt appropriate imaging studies. Spinal involvement with granulocytic sarcoma is most often extradural, but intradural masses or dumbbell-type (combined intra- and extradural) masses may occur.

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