

Pictorial Essay

Extraosseous Multiple Myeloma: Imaging Features

Lia A. Mouloupoulos,¹ Christine A. J. Granfield,¹ Meletios A. Dimopoulos,² E. Edmund Kim,¹ Raymond Alexanian,² and Herman I. Libshitz¹

Multiple myeloma is a disseminated malignant neoplasm usually derived from a single clone of plasma cells. Patients with myeloma have diverse signs such as anemia, hypercalcemia, uremia, pathologic fractures, and recurrent infections. Extraosseous manifestations are found in less than 5% of patients with multiple myeloma. They can arise in any tissue, and their presence has been associated with more aggressive disease. The purpose of this essay is to illustrate the imaging findings of extraosseous myeloma and heighten awareness of this unusual manifestation of multiple myeloma.

Subjects and Methods

During the past 5 years, we reviewed the imaging studies of 15 patients with extraosseous myeloma. Patients with extraosseous myeloma in contiguity with bony involvement were excluded. Ten patients were men, and five were women (age range, 20–75 years; mean age, 49 years). More than one site of extraosseous involvement was present in 12 of 15 patients, including lymph nodes (eight patients), skin and perirenal space (four patients), liver and meninges (three patients), breast and pleura (two patients), and spleen, pancreas, neck, diaphragm, testes, lung, and omentum (one patient each). Extraskelatal tumor was proved by the presence of diffuse infiltration of monoclonal plasma cells in a tissue specimen in 22 of 33 sites of extraosseous involvement. In 11 cases without histologic confirmation, changes in tumor size in relation to treatment for myeloma and lack of secondary disease were considered sufficient evidence of extraskelatal myelomatosis. All but three patients had received multiple courses of chemotherapy and were studied when their disease was resistant, progressive, or both.

Discussion

Extraosseous manifestations are usually associated with a more aggressive form of multiple myeloma that is characterized by increasing anaplasia of plasma cells, fever unrelated to infection, elevated serum levels of lactate dehydrogenase, pancytopenia, and a decreased serum level of paraprotein [1, 2]. This form of the disease has been termed "aggressive" (anaplastic, undifferentiated) myeloma and is associated with rapid progression, resistance to treatment, and a median survival of 1.5 months [1]. Aggressive myeloma is encountered in younger patients with a mean age of 50 years; the average age of patients at diagnosis of multiple myeloma is 60 years.

Clinicopathologic studies have identified extraosseous sites of involvement in two thirds of patients with multiple myeloma, with gross disease seen in 8–17% of these patients. Direct spread from osseous disease was more frequently encountered. Liver, spleen, and lymph nodes were the most frequent distant sites of involvement in one autopsy series [3]. In clinical series, lymph nodes, skin, lung, and CNS have been cited most often as distant sites of extraosseous manifestations.

Reticuloendothelial System

Lymph nodes were the most frequently involved extraosseous tissue in our series (Figs. 1–3). Their CT appear-

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¹Department of Diagnostic Radiology, Box 57, The University of Texas M. D. Anderson Cancer Center, 1515 Holcombe Blvd., Houston, TX 77030. Address correspondence to L. A. Mouloupoulos.

²Department of Medical Oncology, The University of Texas M. D. Anderson Cancer Center, 1515 Holcombe Blvd., Houston, TX 77030.

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ance is similar to that of lymphoma, with multiple nodal groups involved. In autopsy series, gross involvement of the lymph nodes has been reported in 5% of patients with extraosseous myeloma [1, 3].

An enlarged spleen is an uncommon finding in patients with myeloma; in only 0.6% of patients will the spleen extend below the costal margin by more than 5 cm [1]. Fewer than half the cases of enlarged spleen show tumor infiltration at autopsy [3]. In our case, no focal lesions were detected on CT scans, sonograms, MR images, or angiograms (Fig. 1).

Involvement of the liver occurs as diffuse sinusoidal plasma cell infiltration and less frequently as tumor nodules [3]. In three cases in this series, involvement of the liver was manifested by hypovascular lesions indistinguishable from metastatic disease (Figs. 1 and 4).

Skin

The skin is a frequent site of extraosseous myelomatosis, which may be manifested by subcutaneous masses with a purplish hue with or without purpura [1] (Fig. 5).

Genitourinary System

Renal disease in multiple myeloma has several causes, and only rarely is plasma cell infiltration implicated [1]. Perinephric nodules or masses, as seen in four of our patients, are an unusual extraosseous manifestation of myeloma that to the best of our knowledge has not been previously reported (Figs. 2 and 6). Similar findings may be seen in patients with metastatic melanoma and less often in patients with other malignant disease.

Testicular involvement in multiple myeloma is extremely uncommon, even in autopsy series. In one of our patients, involvement of both testes was proved by fine-needle aspiration. MR imaging showed enlarged testes with abnormal heterogeneous signal intensity.

Meninges

CNS involvement independent of bone lesions occurs in less than 1% of patients with multiple myeloma. Thirty-seven cases of diffuse infiltration of the leptomeninges by plasma

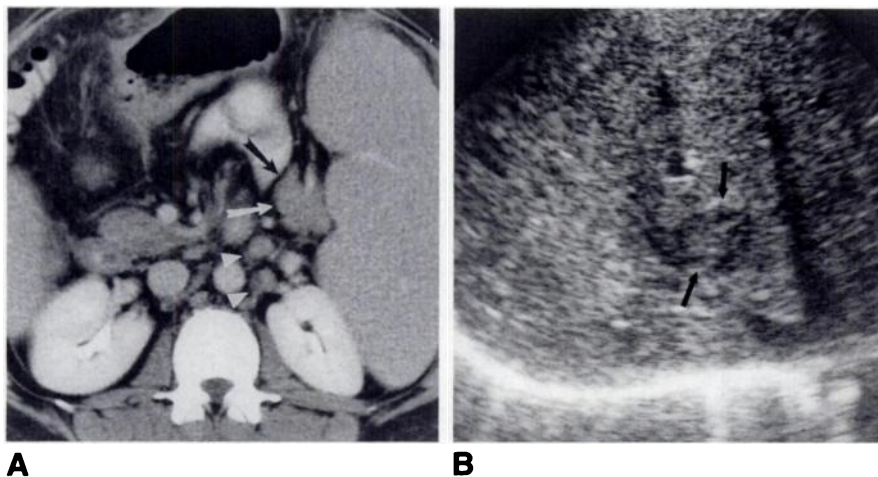


Fig. 1.—47-year-old woman with multiple myeloma manifested by splenomegaly, liver involvement, and lymphadenopathy. She died 11 months after diagnosis. Biopsy was not performed.

A, CT scan of abdomen shows enlarged spleen and retroperitoneal (arrowheads) and splenic hilar (arrows) lymph nodes.

B, Transverse sonogram of liver shows a well-defined "target" lesion (arrows).

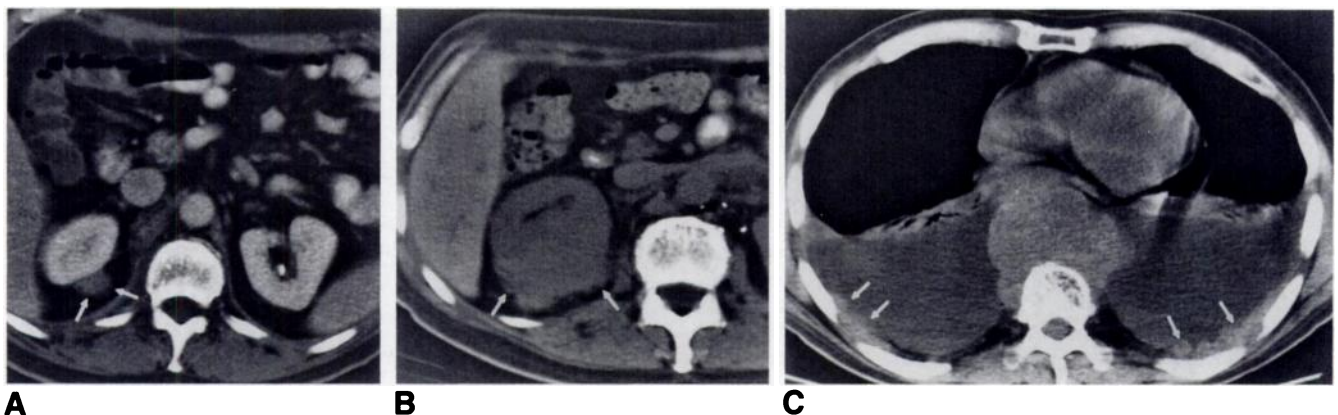


Fig. 2.—51-year-old man with myeloma and extraosseous involvement. Biopsy of right renal mass and aspiration of pleural fluid confirmed presence of myelomatosis.

A, Contrast-enhanced CT scan of abdomen shows small right-sided perirenal nodule (arrows).

B, Unenhanced CT scan of abdomen obtained 7 months later shows large mass (arrows) in perirenal space indistinguishable from right kidney.

C, CT scan of chest obtained at same time as **B** shows extensive adenopathy in posterior part of mediastinum, bilateral pleural effusions, and nodular pleural thickening (arrows).

Fig. 3.—43-year-old woman with myeloma who had jaundice 3 years after diagnosis. Biopsy of peripancreatic nodes showed abnormal plasma cells.

A, CT scan of abdomen shows extensive peripancreatic adenopathy encasing hepatic artery (*long arrow*) and portal vein (*short arrow*). Retrocrural nodes are present (*arrowhead*).

B, CT scan at a lower level than **A** shows retroperitoneal adenopathy.

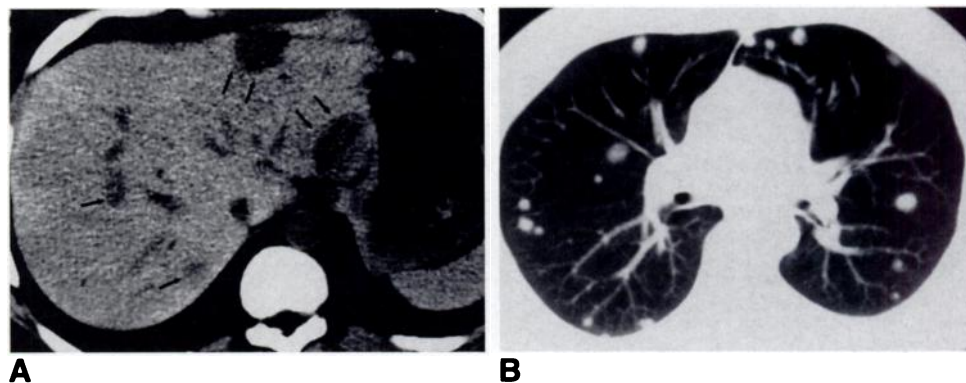
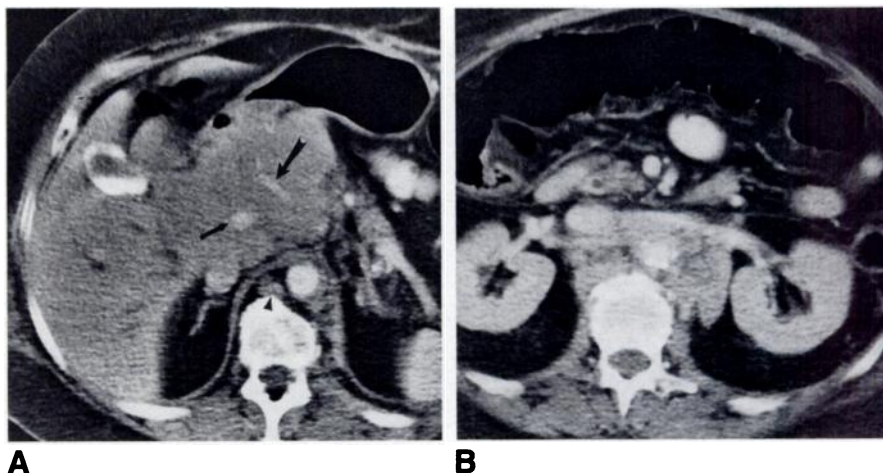
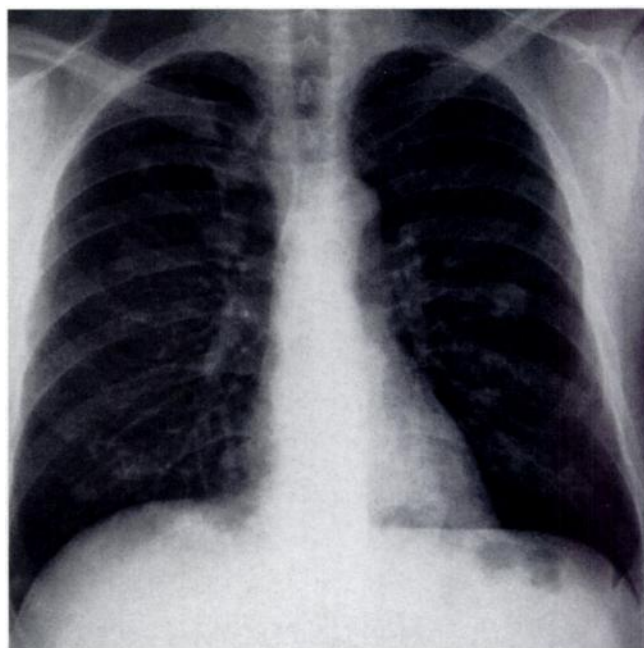


Fig. 4.—48-year-old man with multiple myeloma who had lytic bone lesions and subsequently had myelomatous involvement of liver, lungs, and mediastinum. Biopsy of hepatic lesions was done, and myelomatosis was confirmed.

A, Unenhanced CT scan shows multiple low-attenuation lesions (*arrows*) in liver.

B and C, CT scan (**B**) and conventional radiograph (**C**) of chest show nodules in both lungs.

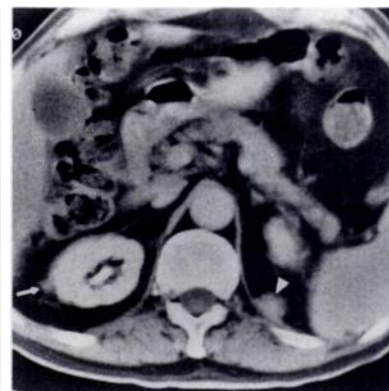


C

cells have been reported [4]. Contrast-enhanced MR imaging is sensitive in depicting leptomeningeal disease, although differentiation from infectious meningitis requires clinical and laboratory correlation (Figs. 7 and 8). An even more rare CNS complication is an extraaxial mass arising from the meninges with CT and MR imaging findings similar to those observed in patients with meningiomas (Fig. 9).

Respiratory System

Involvement of the lung in multiple myeloma is rare and has been reported in clinical series as a mass or infiltrate. In our case, nodules that were indistinguishable from metastases were seen in both lungs (Fig. 4). In two cases, pleural effusions with thickening and nodularity of the pleura were



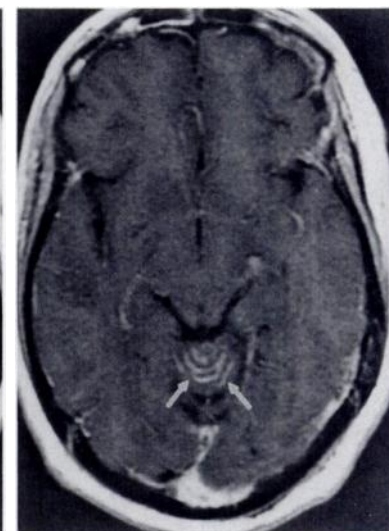
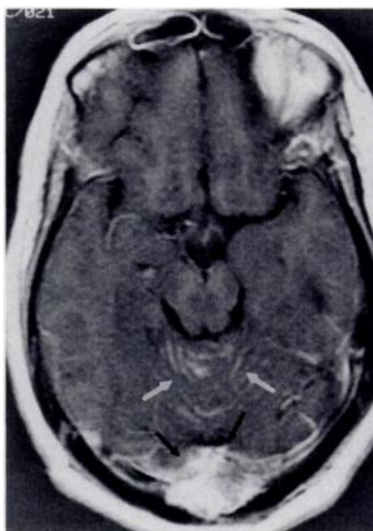
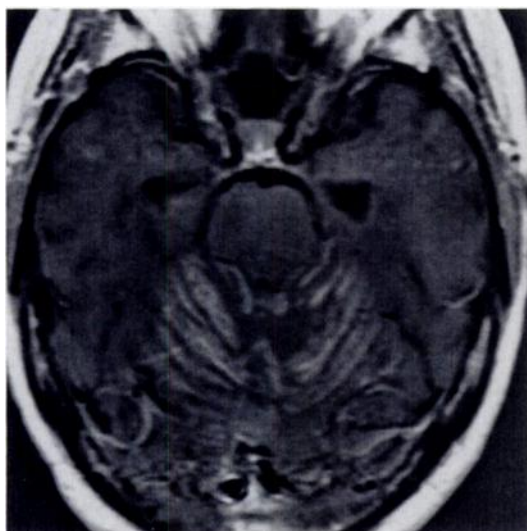
A

B

Fig. 5.—50-year-old man with multiple myeloma who had bone lesions and involvement of subcutaneous tissues and lymph nodes. Biopsy of subcutaneous lesions showed plasmacytosis. CT scan of abdomen shows lytic bone lesions and two gluteal nodules (arrows). Apparent skin thickening on left side is produced by gluteal skin crease (arrowhead).

Fig. 6.—68-year-old man with multiple myeloma who had extraosseous sites of involvement, including lymph nodes, diaphragm, perirenal space, and subcutaneous tissues. He died a year after diagnosis. No biopsy was performed.

A and B, CT scans through abdomen show a mass in left renal hilum (arrowhead in A), bilateral perirenal nodules (arrows), and involvement of left hemidiaphragm (arrowhead in B).



A

B

Fig. 7.—40-year-old man with myeloma and leptomeningeal plasmacytosis. Contrast-enhanced T1-weighted (600/20) MR image shows leptomeningeal enhancement of cerebellar sulci. Cytologic analysis of CSF confirmed plasmacytosis.

Fig. 8.—48-year-old woman with myeloma who had multiple sites of extraosseous involvement, including meninges, lymph nodes, omentum, and subcutaneous tissues. Her condition deteriorated suddenly 9 months after diagnosis.

A and B, Contrast-enhanced contiguous axial T1-weighted (600/20) MR images through upper vermis show abnormal leptomeningeal enhancement (white arrows). Note epidural soft tissue arising from involvement of occipital bone (black arrows). Cytologic analysis of CSF showed plasmacytosis.

Fig. 9.—63-year-old man with myeloma and involvement of meninges, subcutaneous tissue, lymph nodes, and perirenal space.

A, Axial T2-weighted (2000/80) MR image of brain shows heterogeneous, extraaxial parietal mass producing edema in brain parenchyma.

B, Contrast-enhanced axial T1-weighted (600/20) MR image shows marked enhancement of mass and meninges. A meningioma is certainly included in differential diagnosis. At surgery, mass was adherent to undersurface of dura; adjacent brain and bone were intact.



A



B

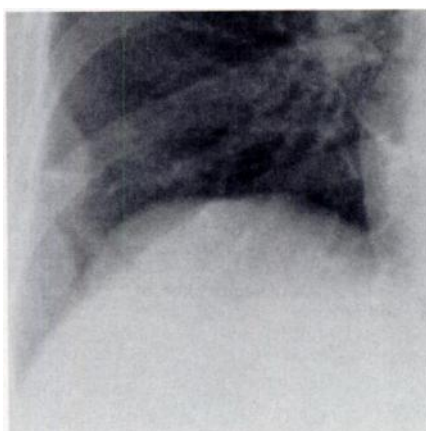


Fig. 10.—Myelomatous involvement of pleura in a 56-year-old woman. Chest radiograph shows nodular thickening of right lateral pleura, which resolved with treatment. No biopsy was performed.

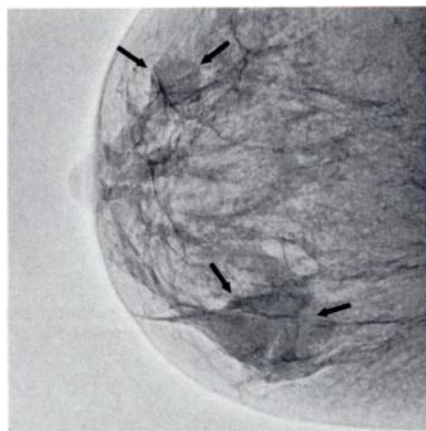


Fig. 11.—41-year-old woman with myeloma and involvement of breast confirmed by biopsy. Lateral xeromammogram of breast shows two well-defined lobulated plasmacytomas (arrows).

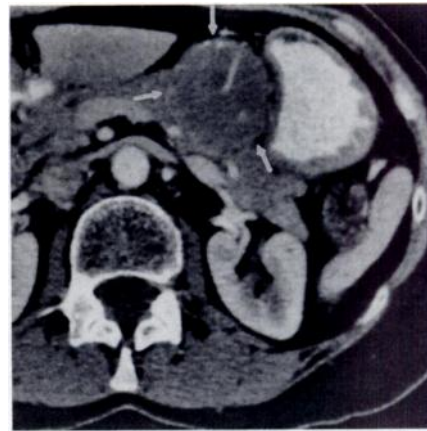


Fig. 12.—65-year-old woman with myeloma manifested by a pancreatic mass. Biopsy of mass showed plasma cell tumor. CT scan of abdomen shows a well-demarcated, hypervascular mass (arrows) arising from body of pancreas.

observed (Figs. 2 and 10). Extensive mediastinal adenopathy was present in one patient (Fig. 2). Involvement of the diaphragm has been reported only in autopsy series. A soft-tissue nodule along the crus of the hemidiaphragm was one of the multiple sites of extraosseous involvement in one of our patients (Fig. 6).

Breast

Few cases of plasmacytoma of the breast have been reported, and most of these were not associated with systemic disease. Breast plasmacytomas are solid, nontender, relatively well defined masses of various sizes, and they cannot be differentiated from other solid benign or malignant lesions on the basis of findings on clinical examination and imaging studies (Fig. 12).

Miscellaneous

Kapadia [3] reported microscopic involvement of the pancreas in two of 60 patients in whom extraosseous myeloma was found at autopsy. One of our patients had a plasma cell

tumor of the pancreas. A well-defined hypervascular mass arising from the body of the pancreas was shown on CT scans, and the diagnosis of an islet cell tumor was initially considered (Fig. 12).

Involvement of the omentum was observed in one patient with end-stage multiple myeloma. The appearance was similar to lymphomatous involvement or peritoneal carcinomatosis.

Radiologists must be aware of these rare manifestations of multiple myeloma so that extensive unnecessary intervention can be avoided when extraosseous sites of disease are encountered.

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