The Ochsner Journal 15:457–467, 2015

Asymptomatic Multiple Myeloma Presenting as a Nodular Hepatic Lesion: A Case Report and Review of the Literature

Hans Huang, MD,[1,*] Fateh Bazerbachi, MD,[1,*] Hector Mesa, MD,[2] Pankaj Gupta, MD[3]

[1]Department of Medicine, University of Minnesota, Minneapolis, MN [2]Department of Pathology and Laboratory Medicine, Minneapolis VA Health Care System, Minneapolis, MN [3]Division of Hematology/Oncology, Minneapolis VA Health Care System, Minneapolis, MN

*These authors contributed equally to this work.

Background: Plasma cell myeloma is the most common primary bone malignancy in adults. However, liver involvement in the form of an initial and asymptomatic nodular plasmacytoma is exceedingly rare.

Case Report: A 64-year-old male was found to have a right hepatic lobe nodule on a routine abdominal ultrasound prior to bariatric surgery. Liver biopsy revealed a plasma cell neoplasm that, given the location of the lesion, was favored to represent a lymphoma with prominent plasmacytic differentiation. Positron emission tomography (PET) demonstrated a hypermetabolic hepatic mass and identified multiple destructive bony lesions. Biopsy of a clavicular lesion revealed sheets of plasma cells and confirmed the diagnosis of multiple myeloma. The patient underwent 6 cycles of chemotherapy with cyclophosphamide, bortezomib, and dexamethasone before transitioning to lenalidomide and dexamethasone because of early disease progression. Although the patient had International Staging System I (low-risk) disease, his disease demonstrated an aggressive clinical course and resistance to multiple lines of therapy.

Conclusion: Extramedullary nodular hepatic plasmacytoma is exceedingly rare. Nevertheless, extramedullary plasmacytomas should be included in the differential diagnosis of patients with indistinct hepatic lesions visualized on computed tomography scan, especially if PET scans show associated bony lesions. In general, extramedullary plasmacytomas are a poor prognostic sign and a harbinger of an aggressive clinical course in the context of multiple myeloma.

Keywords: *Hypercalcemia, liver neoplasms, multiple myeloma, neoplasms–plasma cell, plasmacytoma*

Address correspondence to Pankaj Gupta, MD, Division of Hematology/Oncology, Minneapolis VA Health Care System, 1 Veterans Drive, 111E, Minneapolis, MN 55417. Tel: (612) 467-4135. Email: pankaj.gupta@va.gov

INTRODUCTION

Multiple myeloma (MM) is a malignant proliferation of clonal plasma cells, characterized by infiltration of bone marrow and overproduction of monoclonal immunoglobulins (Igs) and/or free light chains.[1] The incidence of extramedullary disease with newly diagnosed MM is variable, ranging from 7%-18%.[2] Extramedullary plasmacytomas arise most commonly from direct extension of primary bone tumors, but rarely they may also result from hematogenous spread involving distant organs. Plasmacytoma involvement of the gastrointestinal system—more specifically, presentation as an asymptomatic nodular hepatic lesion—is exceedingly rare.[3] We report the case of a patient with an incidental nodular hepatic lesion who was ultimately diagnosed with MM.

CASE REPORT

A 64-year-old male with a medical history significant for obesity and remote gastric stapling underwent preoperative workup for bariatric surgery revision. Routine ultrasound revealed an incidental 2.2 cm solid right hepatic lobe lesion, barely visible on contrast-enhanced computed tomography (CT) scan (Figure, A). The patient reported right shoulder pain, fatigue, and intentional weight loss, and his physical examination was unremarkable. Laboratory workup at this time was significant for mild hypercalcemia (10.3 mg/dL). An ultrasound-guided biopsy of the hepatic lesion performed 1 week later showed a plasma cell neoplasm. Although a lymphoid component was not identified by morphology or immunohistochemistry, given the location of the lesion and the lack of other identifiable lesions on CT scan, it was considered a primary hepatic lymphoma with plasmacytic differentiation (Figure, B-D).

A subsequent positron emission tomography (PET) scan showed a hypermetabolic hepatic mass and destructive bony lesions in the clavicle, manubrium, right third rib, pelvis, and sacrum (Figure, E and F). Biopsy of the clavicular lesion revealed confluent sheets of plasma cells

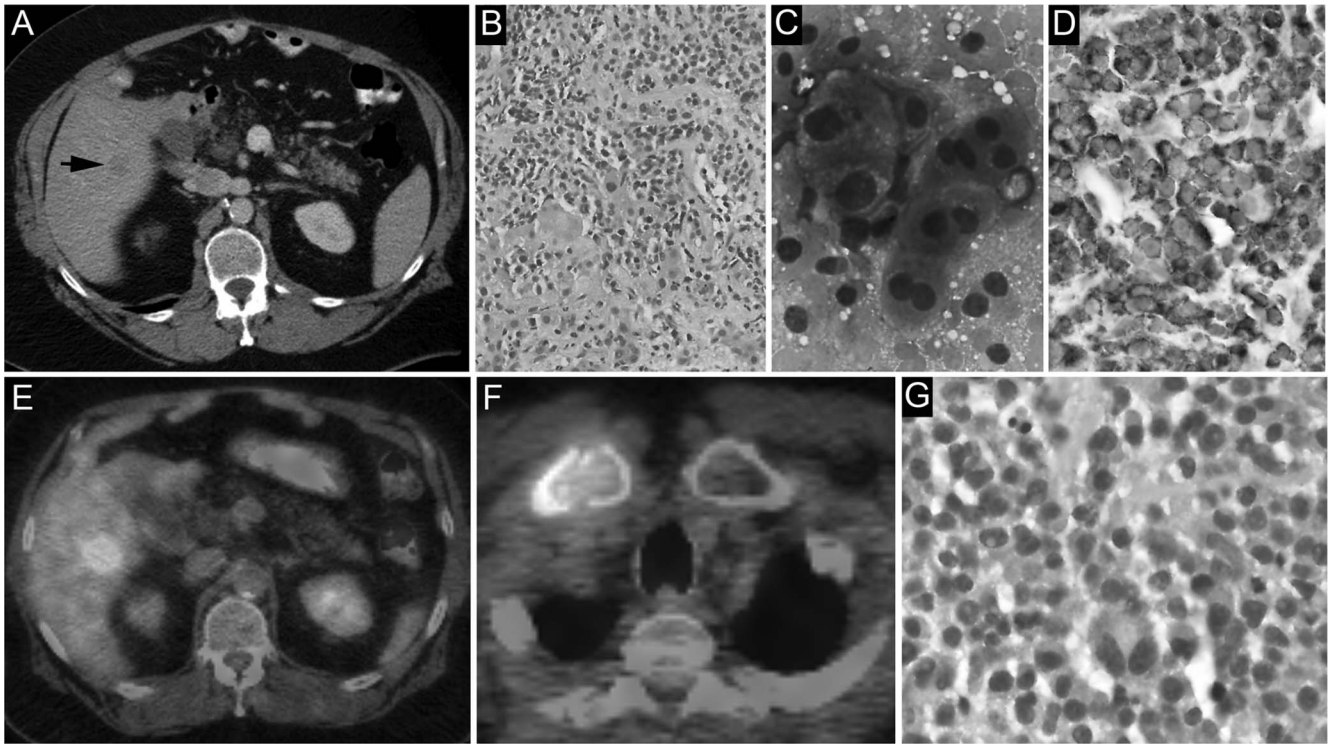

Figure. A: The lesion is barely visible on contrast-enhanced computed tomography scan (arrow). B: Core sections of an ultrasound-guided liver biopsy show confluent expansile sheets of plasma cells (hematoxylin and eosin [H&E] stain, ×20). C: Touch imprints of the liver biopsy reveal discohesive plasmacytoid cells and naked nuclei (Diff-Quik stain, ×100). D: Chromogenic in situ hybridization analysis demonstrates cytoplasmic kappa light chain restriction (immunohistochemical stain, ×40). E: Metabolically active lesions in the right hepatic lobe can be seen on positron emission tomography. F: Metabolically active lesions in the right clavicle can be seen on positron emission tomography. G: Core sections of right clavicular bone marrow biopsy show sheets of plasma cells (H&E stain, ×40).

(Figure, G). Tissue immunohistochemistry and the concurrent flow cytometry study showed kappa-restricted plasma cells without associated clonal lymphoid populations. A myeloma fluorescence in situ hybridization panel revealed an isolated translocation (11;14). Serum and urine protein electrophoresis did not detect a monoclonal protein. Ig quantification showed IgM <16.9 mg/dL (normal 40-230 mg/dL), IgG 769.0 mg/dL (normal 700-1,600 mg/dL), and IgA 94.3 mg/dL (normal 70-400 mg/dL). Serum free light chain assay revealed increased kappa light chains (1,030.5 mg/L, normal 3.3-19.4 mg/L) and an increased kappa/lambda light chain ratio (112.01, normal 0.26-1.65). Additional laboratory investigations were significant for anemia (hemoglobin 11.7 g/dL), preserved renal function (creatinine 0.7 mg/dL), and increased β2 microglobulin (3 mg/L, normal 1.09-2.53 mg/L). Alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase, lactate dehydrogenase, and albumin were all within normal limits. The patient was therefore diagnosed with kappa light chain MM with extramedullary involvement of the liver. The International Staging System (ISS) prognostic stage was I (usually indicative of low-risk/good prognosis disease).

Systemic chemotherapy was initiated with cyclophosphamide, bortezomib, and dexamethasone (CyBorD regimen).[4] The patient completed 6 cycles, initially showing a partial response followed by early disease progression evidenced by new lesions on PET scan and marked rise in the kappa light chain level.

His chemotherapy regimen was changed to lenalidomide and dexamethasone[5] but was discontinued after 3 cycles because of disease progression. Although the patient had ISS stage I disease, his disease demonstrated an aggressive clinical course, resistant to multiple subsequent lines of therapy. The patient's care was later transferred to an outside facility for ongoing chemotherapy with a plan for autologous stem cell transplant. Despite several cycles of chemotherapy, his disease continued to progress, and he ultimately died after a complicated hospital course for neutropenic fever.

DISCUSSION

MM is the most common primary bone malignancy in adults.[6] Uncontrolled proliferation of clonal plasma cells and overproduction of monoclonal protein lead to organ damage and result in the common clinical manifestations of MM, including hypercalcemia, renal insufficiency, anemia, and bone lesions.[1,2] The incidence of presenting clinical manifestations in patients with MM varies (Table 1). Anemia and bone pain are the 2 most common presenting signs and symptoms.[7,8] Bony lesions commonly involve long bones, ribs, skull, and pelvis, possibly leading to further complications including pathologic fractures. As in our patient, hypercalcemia is a common presenting manifesta-

Table 1. Incidence of Presenting Signs and Symptoms in Patients with Multiple Myeloma[7,8]

Signs and Symptoms	Incidence, %
Anemia	73
Bone pain (generally severe and provoked by movement)	58
Elevated creatinine	48
Fatigue/generalized weakness	32
Hypercalcemia	28
Pathologic fracture	26-34
Weight loss	24
Paresthesias	5
Hepatomegaly	4
Splenomegaly	1
Lymphadenopathy	1
Fever	0.7

tion of MM, and in asymptomatic patients, it may be one of the few subtle abnormalities pointing toward the diagnosis.

Extramedullary spread of MM can be detected at diagnosis but is much more common in the later stages of the disease.[9] Our patient illustrates an atypical initial presentation of MM as an incidentally discovered solitary hepatic mass. The most common mechanism of extramedullary spread is through local growth from focal bone sites into surrounding soft tissue.[2] Alternatively, distant metastasis of malignant plasma cells can spread hematogenously, most commonly to organs of the reticuloendothelial system, but in the terminal stages of the disease any organ may be involved. A study of 64 patients with MM from 1956-1970 reported hepatomegaly in 58%, splenomegaly in 25%, ascites in 14%, and abnormal liver function tests in ~90% of the cases at presentation.[10] Hepatic infiltration by plasma cells was present during autopsy in up to 40% of these patients, most commonly as diffuse sinusoidal infiltrates followed by discrete portal aggregates and masses. Tumors were found in 16% of the cases, but in contrast with our case, the lesions were multiple 1-2 cm nodules distributed throughout the hepatic parenchyma mimicking metastatic disease. These findings would be very unusual today, likely because of much earlier diagnosis and more effective therapies.

More recent studies report much lower frequencies of liver involvement; Perez-Soler et al[11] reviewed 128 patients with MM in a series published in 1985. Histologic study of the liver was available for 21 patients. A diffuse infiltrative pattern of plasma cells was observed in 10 patients, but no cases of nodular liver infiltration were seen. Talamo et al[3] reported 9 cases of nodular liver infiltration in a cohort of 2,584 patients with MM (0.35%) in 2006. These findings underscore the clinical rarity of involvement of the liver in MM patients in present times and the overall rarity of isolated plasmacytomas of the liver that have only been described as case reports.

We performed a literature review and summarized all available studies (n=13) describing MM with nodular hepatic involvement (Tables 2 and 3).[12-24] In the majority of cases (n=8), liver involvement manifested with abdominal pain and/or other gastrointestinal symptoms. Six cases demonstrated abnormalities in liver function tests, with alkaline phosphatase most commonly elevated. Liver function tests were not reported for 3 cases. Distribution of the monoclonal protein was varied: IgG kappa (n=4), IgA kappa (n=3), IgA lambda (n=1), lambda light chain (n=3), and kappa light chain (n=2). Ultrasound and CT were the usual imaging modalities utilized for detection of the hepatic lesions. Only 2 patients had solitary nodular liver lesions, while the remaining patients presented with multiple lesions. Hepatic plasmacytomas were frequently (n=6) described as hypoechoic on ultrasound or hypoattenuating on CT. In all but 1 case, diagnosis of hepatic involvement was based on histologic analysis of tissue samples. Identification of bony lytic lesions was typically achieved using skeletal surveys. PET scan was used in 1 case, similar to our case. In 4 cases, nodular hepatic plasmacytomas presented during a period of relapse after initial diagnosis of MM. In all other cases, hepatic involvement was discovered at the time of MM diagnosis. Finally, the documented clinical course varied among cases and included complete remission (n=2), initial clinical improvement without further follow-up reported (n=3), aggressive course with relapsing disease (n=3), and death (n=3). In 2 cases, the clinical course and response to treatment were not reported.

Conventional skeletal radiography has traditionally been used to identify bone disease in patients with MM.[25] Skeletal radiography is still widely used today in clinical practice and is generally the recommended first-line imaging modality in the diagnosis and staging of MM.[26] However, with the introduction and widespread availability of newer imaging methods, including CT, magnetic resonance imaging (MRI), 18F-fluorodeoxyglucose PET with CT (PET-CT), the diagnostic criteria and staging of MM have been substantially updated. Compared to skeletal radiography, these newer imaging techniques provide increased sensitivity for the detection of bony lytic lesions.[25] CT and MRI are generally performed to (1) further evaluate lytic lesions that are ambiguous or equivocal on plain radiography, (2) assess the nature and extent of soft tissue disease, (3) evaluate suspected spinal cord compression (MRI preferred), and (4) differentiate between malignant and benign vertebral compression fractures.[27] PET-CT or MRI is routinely performed in patients with a suspected diagnosis of smoldering (asymptomatic) MM or solitary plasmacytoma,[25,28,29] as these diagnostic modalities can detect abnormal infiltrative processes of the bone marrow in the absence of bone lesions. These diagnostic modalities are also important in the diagnosis of MM relapse because the lytic bone lesions frequently persist after successful therapy.

The presence of extramedullary disease is often associated with light chain–secreting MM and a higher number of immature or plasmablastic plasma cells,[30] but most of the cases we reviewed (8/13) had paraproteins with complete Igs. Studies comparing baseline characteristics between patients with and without extramedullary disease at diagnosis showed that nonsecretory disease and lambda chain expression were more common in extramedullary MM.[9,31]

Table 2. Summary of Case Reports Describing Multiple Myeloma with Nodular Hepatic Involvement: Patient Characteristics

Author (year)	Age/Sex	Clinical Manifestations	Laboratory Findings[a]	Monoclonal Component
Thiruvengadam et al (1990)[12]	59/M	• Weight loss, abdominal distension, RUQ pain • Hepatomegaly	Hgb: 8.7 ↓ Ca: 14.4 ↑ Cr: 5.3 ↑ LFTs: ALP ↑	Lambda light chain
Nguyen et al (1992)[13]	67/M	• Weight loss, fatigue, back pain, RUQ pain • No organomegaly	Hgb: 10.3 ↓ Ca: 14.4 ↑ Cr: 3.8 ↑ LFTs: normal	Kappa light chain
Caturelli et al (1993)[14]	57/M	• Hx of MM, nausea, vomiting, bone pain • Hepatomegaly	Hgb: 8.6 ↓ Ca: NR Cr: 3 ↑ LFTs: normal	IgG kappa
Curtis et al (1995)[15]	61/M	• Weight loss, low back pain • Hepatomegaly	Hgb: 7.8 ↓ Ca: normal Cr: normal LFTs: ALP ↑	IgA kappa
Kelekis et al (1997)[16]	32/M	• Weight loss, malaise, vomiting, nausea, diarrhea, back pain • Exam NR	Hgb: severe anemia Ca: 11.8 ↑ Cr: 7.9 ↑ LFTs: NR	Lambda light chain
Chemlal et al (1999)[17]	68/F	• Mild right-sided peripheral edema • Exam unremarkable	Hgb: normal Ca: normal Cr: normal LFTs: normal	IgG kappa
Fernandez-Flores et al (2003)[18]	68/M	• Hx of MM, anorexia, general pain • Exam NR	Laboratory data NR	IgG kappa
Arebi et al (2004)[19]	66/M	• Pale stools, dark urine, weight loss • Jaundice	Hgb: 5.3 ↓ Ca: 10.4 ↑ Cr: 1.42 ↑ LFTs: TB ↑ ALP ↑	IgA lambda
del Giglio et al (2005)[20]	58/F	• Hx of MM, profound weakness • Exam NR	Laboratory data NR	IgA kappa
Invernizzi et al (2007)[21]	83/F	• Weight loss, abdominal pain, weakness • Pallor, hepatomegaly, gross epigastric mass	Hgb: moderate anemia Ca: normal Cr: normal LFTs: GGT ↑	IgG kappa

Table 2. Continued

Author (year)	Age/Sex	Clinical Manifestations	Laboratory Findings[a]	Monoclonal Component
Wu et al (2009)[22]	62/F	• Low back pain • Lumbar spine tenderness	Hgb: 10.2 ↓ Ca: NR Cr: NR LFTs: normal	IgA kappa
Dhakal and Chandra (2013)[23]	47/M	• Hx of MM, abdominal pain, nausea, fever • Jaundice	Hgb: NR Ca: NR Cr: NR LFTs: TB ↑ ALP ↑	NR
Pal et al (2014)[24]	63/F	• RUQ pain, fatigue, weight loss • Pallor, jaundice, bilateral pitting pedal edema, tender hepatomegaly	Hgb: 7.6 ↓ Ca: 9.9 Cr: 2.5 ↑ LFTs: TB ↑ ALP ↑	Lambda light chain
Huang et al (2015) (current case)	64/M	• Right shoulder pain, weight loss • Exam unremarkable	Hgb: 11.7 ↓ Ca: 10.3 ↑ Cr: 0.7 LFTs: normal	Kappa light chain

F, female; Hx, history; Ig, immunoglobulin; M, male; MM, multiple myeloma; NR, not reported; RUQ, right upper quadrant.
[a]Laboratory findings include the following: hemoglobin (Hgb), g/dL; calcium (Ca), mg/dL; creatinine (Cr), mg/dL; and liver function tests (LFTs) that include alkaline phosphatase (ALP), alanine aminotransferase, aspartate aminotransferase, gamma-glutamyl transferase (GGT), and total bilirubin (TB). ↑, value elevated above normal range; ↓, value decreased below normal range. Unless documented, all other liver function tests were within normal limits.

Nonsecretory multiple myeloma (NSMM) is a rare subtype of MM defined by the absence of monoclonal Igs on serum and urine electrophoresis.[32] However, in the majority of patients with presumed NSMM, monoclonal free light chains can now be detected with newer sensitive automated serum assays,[33] similar to our case, indicating that these presumed NSMM cases likely represent light chain–only myelomas in which the abnormal protein was not detected in 24-hour urine protein electrophoresis, possibly because of technical reasons. Nevertheless, the secretion of an incomplete Ig may imply additional abnormalities and possible mutations in the genes involved in their synthesis compared to regular MM. These additional abnormalities and genetic mutations are likely related to the reported higher incidence of extramedullary disease at diagnosis in light chain MM. A shift in secretion from intact Igs to free light chains (ie, light chain escape) has been associated with progression of MM in the form of extramedullary metastasis.[30] Furthermore, patients with incomplete Ig synthesis or light chain–secreting MM may have a higher incidence of renal failure, anemia, bone disease, amyloidosis, and extramedullary plasmacytomas.[34] This in turn may translate into a more aggressive disease course with worse outcomes, as in our case. In our patient, confirmatory diagnosis of MM after the discovery of an extramedullary plasmacytoma was crucial and held significant prognostic implications. Most extramedullary plasmacytomas that are not associated with bone marrow disease represent marginal zone lymphomas with extensive plasmacytic differentiation and usually pursue an indolent clinical course limited to solitary lesions.[35] Conversely, extramedullary plasmacytomas in the context of MM are indicative of advanced disease and portend a poor prognosis.[9] In our case, PET imaging proved to be a highly sensitive technique that identified occult bony lesions and ultimately helped confirm the diagnosis of MM by identifying a bone lesion amenable to biopsy.

The presence of extramedullary involvement in MM at any time during the course of disease has been associated with shorter progression-free survival and shorter overall survival.[9] Moreover, a series of 24 patients with MM and extramedullary gastrointestinal involvement showed a strong association with adverse biological features and short remission periods.[3]

Stem cell transplantation (SCT) after primary induction chemotherapy remains an important component in the treatment of newly diagnosed MM.[36] Forms of SCT include autologous, tandem, or allogeneic SCT. The standard approach involves early or delayed autologous SCT. However, alternative approaches such as allogeneic SCT may be considered in highly select patients or clinical trials.[36] Early treatment with high-dose therapy or autologous SCT has been shown to provide similar overall survival and progression-free survival irrespective of the presence or

Table 3. Summary of Case Reports Describing Multiple Myeloma with Nodular Hepatic Involvement: Imaging, Pathology, and Treatment

Author (Year)	Radiologic Findings	Basis of Diagnosis	Number of Lytic Bone Lesions	Bone Marrow Cytogenics/ Histologic Analysis	Treatment Course	Response to Treatment
Thiruvengadam et al (1990)[12]	Multiple hypoechoic lesions throughout the liver (US, CT)	Percutaneous fine needle liver biopsy, plasma cells	≥3	NR	• Initiated 1 cycle of CTX with melphalan (plus steroids) • Radiation therapy	• Partial shrinkage of liver lesions but progressive clinical deterioration • Death 1.5 months after diagnosis
Nguyen et al (1992)[13]	8 × 9 cm heterogeneous lesion occupying lateral segment of left hepatic lobe (US, CT, MRI)	US-guided fine needle liver biopsy, atypical plasma cells	≥1	Large sheets of plasma cells	• Completed 1 cycle of CTX with melphalan (plus prednisone) • Radiation therapy	• Clinical improvement • No further follow-up reported
[a]Caturelli et al (1993)[14]	Hepatomegaly with multiple hypoechoic nodular lesions of varying sizes throughout the liver (US)	US-guided fine needle liver biopsy, atypical plasma cells stained positive for IgG-κ	≥3	NR	• Completed 2 cycles of CTX with high-dose cyclophosphamide (plus dexamethasone) after diagnosis of hepatic plasmacytoma • Subsequent relapse → local radiation therapy and CTX with vincristine, mitoxantrone (plus dexamethasone)	• Initial response with clinical improvement before relapse • Death 4 months after last cycle of CTX
Curtis et al (1995)[15]	Hepatomegaly with multiple rounded hypoechoic lesions throughout the liver (US)	US-guided fine needle liver biopsy, plasma cells stained positive for kappa light chains	None	Presence of plasma and plasmacytoid cells	• Completed 1 cycle of CTX with adriamycin/ carmustine and cyclophosphamide/ melphalan	• Clinical improvement with reduction in number and size of liver lesions • No further follow-up reported

Table 3. Continued

Author (Year)	Radiologic Findings	Basis of Diagnosis	Number of Lytic Bone Lesions	Bone Marrow Cytogenics/ Histologic Analysis	Treatment Course	Response to Treatment
Kelekis et al (1997)[16]	Multiple focal lesions, 1-2 cm and 2-5 mm in diameter, throughout the liver (US, CT, MRI)	No liver biopsy reported	≥3	Presence of immature plasmablasts	NR	NR
Chemlal et al (1999)[17]	Several hypoechoic nodular hepatic lesions of varying sizes throughout the liver (CT)	Laparoscopy, plasma cells stained positive for IgG-κ	≥3	Presence of plasma cells, strongly positive for kappa light chains	• Completed 3 cycles of CTX with melphalan (plus prednisone)	• Disease remained stable • Liver nodules unchanged on US
[a]Fernandez-Flores et al (2003)[18]	Several nodular hepatic lesions, largest 24.5 mm in diameter (CT)	US-guided fine needle liver biopsy, plasma cells stained positive for kappa light chains	≥3	NR	• Initial diagnosis of MM → 8 cycles of CTX with melphalan (plus prednisone) • No report of treatment plan after diagnosis of new hepatic plasmacytoma	• Initial clinical improvement after 8 cycles of CTX before relapse
Arebi et al (2004)[19]	3 small hypoattenuated lesions in the liver (CT)	Liver biopsy, plasma cells	NR	Presence of immature plasmablasts	• Patient refused treatment	• Patient died several days after refusal of treatment
[a]del Giglio et al (2005)[20]	Multiple nodular hepatic lesions throughout the liver (CT)	CT-guided liver biopsy, plasma cells stained positive for kappa light chains	NR	NR	• Initial diagnosis of MM → HDT followed by autologous transplant • Relapse → thalidomide, achieved complete remission • Relapse (hepatic plasmacytoma) → bortezomib	• Significant improvement in hepatic lesions • Relapsed again, plan to pursue allogeneic BMT

Table 3. Continued

Author (Year)	Radiologic Findings	Basis of Diagnosis	Number of Lytic Bone Lesions	Bone Marrow Cytogenics/ Histologic Analysis	Treatment Course	Response to Treatment
Invernizzi et al (2007)[21]	Several hypoechoic nodular hepatic lesions of varying sizes, largest 6 cm in diameter (US)	US-guided fine needle liver biopsy, plasma cells stained positive for kappa light chains	None	Presence of atypical plasma cells	• Initiated CTX with bortezomib (plus dexamethasone)	• Good clinical improvement • No further follow-up reported
Wu et al (2009)[22]	Multiple nodular lesions involving the liver (CT)	US-guided fine needle liver biopsy, plasma cells stained positive for kappa light chains	≥3[b]	Presence of immature plasmablasts	• Initiated CTX with bortezomib, vincristine, doxorubicin (plus dexamethasone)	• Achieved complete remission
[a]Dhakal and Chandra (2013)[23]	6 hepatic lesions, largest 16.4 × 11.2 cm, intrahepatic biliary duct dilatation because of compression of CBD by porta hepatis lesion (MRI)	CT-guided liver biopsy, plasma cells	NR	NR	• Initial diagnosis of MM → CTX with bortezomib, cyclophosphamide (plus dexamethasone) • Plan to initiate alternative CTX after diagnosis of new hepatic plasmacytoma	NR
Pal et al (2014)[24]	Hepatomegaly with a hypoechoic solid lesion 2.7 × 2.6 cm in the right hepatic lobe (US, CT)	US-guided fine needle liver biopsy, plasma cells	≥3	Presence of atypical plasma cells	• Completed 4 cycles of induction CTX with thalidomide (plus dexamethasone) • Completed 4 cycles of consolidation with the same CTX regimen	• Complete remission following induction therapy

Table 3. Continued

Author (Year)	Radiologic Findings	Basis of Diagnosis	Number of Lytic Bone Lesions	Bone Marrow Cytogenics/ Histologic Analysis	Treatment Course	Response to Treatment
Huang et al (2015) (current case)	2.2 cm solid lesion involving the right hepatic lobe (US, CT)	US-guided liver biopsy, plasma cells with kappa light chain expression	≥3[b]	Presence of translocation (11;14)	• Completed 6 cycles of CTX with cyclophosphamide, bortezomib (plus dexamethasone) • Subsequent relapse → CTX changed to lenalidomide (plus dexamethasone)	• Initial partial response followed by disease progression and death

BMT, bone marrow transplant; CBD, common bile duct; CT, computed tomography; CTX, chemotherapy; HDT, high-dose therapy; Ig, immunoglobulin; MRI, magnetic resonance imaging; MM, multiple myeloma; NR, not reported; US, ultrasound.
[a]Patients previously diagnosed with multiple myeloma developed nodular hepatic lesions during relapse of disease.
[b]Positron emission tomography was used to identify bony lytic lesions.

absence of extramedullary disease.[9,31] Newer agents, including immunomodulatory drugs (eg, thalidomide, lenalidomide, and pomalidomide) and proteasome inhibitors (eg, bortezomib and carfilzomib), are now used earlier in the treatment of MM, as well as in relapsed disease. However, data are scarce on the efficacy of these drugs in newly diagnosed patients with extramedullary MM. Our patient demonstrated initial treatment response before showing early disease progression despite treatment with an ordinarily highly effective multidrug regimen including cyclophosphamide, bortezomib, and dexamethasone. Our case illustrates the clinical aggressiveness of a light chain MM with extramedullary involvement that progressed despite several lines of multiagent chemotherapy. The patient's progressive disease and rapid decline in functional status prevented SCT and ultimately led to his death.

CONCLUSION

We describe the case of a single hepatic nodule discovered incidentally during routine preoperative ultrasound that unexpectedly proved to represent MM with extramedullary involvement. In our review of the literature, we found only 2 other cases of MM with a solitary liver plasmacytoma at presentation. Although rare, an extramedullary plasmacytoma should be included in the differential diagnosis of radiologically indistinct hepatic lesions, especially in the context of hypercalcemia and concurrent bone lesions. The presence of extramedullary plasmacytoma is indicative of advanced disease and poor prognosis in the setting of MM. Our case also demonstrates that PET scan is a highly sensitive modality for identifying plasmacytomas and occult bony lesions in cases with uncommon presentations.

ACKNOWLEDGMENTS

The authors have no financial or proprietary interest in the subject matter of this article.

REFERENCES

1. Raab MS, Podar K, Breitkreutz I, Richardson PG, Anderson KC. Multiple myeloma. *Lancet*. 2009 Jul 25;374(9686):324-339.
2. Bladé J, Fernández de Larrea C, Rosiñol L, Cibeira MT, Jiménez R, Powles R. Soft-tissue plasmacytomas in multiple myeloma: incidence, mechanisms of extramedullary spread, and treatment approach. *J Clin Oncol*. 2011 Oct 1;29(28):3805-3812.
3. Talamo G, Cavallo F, Zangari M, et al. Clinical and biological features of multiple myeloma involving the gastrointestinal system. *Haematologica*. 2006 Jul;91(7):964-967.
4. Khan ML, Reeder CB, Kumar SK, et al. A comparison of lenalidomide/dexamethasone versus cyclophosphamide/lenalidomide/dexamethasone versus cyclophosphamide/bortezomib/dexamethasone in newly diagnosed multiple myeloma. *Br J Haematol*. 2012 Feb;156(3):326-333.
5. Weber DM, Chen C, Niesvizky R, et al. Lenalidomide plus dexamethasone for relapsed multiple myeloma in North America. *N Engl J Med*. 2007 Nov 22;357(21):2133-2142.
6. Resnick D. Tumors and tumor-like lesions of bone: imaging and pathology of specific lesions. In: Resnick D, ed. *Bone and Joint Imaging*. 2nd ed. Philadelphia, PA: W.B. Saunders; 1996:991-1063.
7. Nau KC, Lewis WD. Multiple myeloma: diagnosis and treatment. *Am Fam Physician*. 2008 Oct 1;78(7):853-859.
8. Kyle RA, Gertz MA, Witzig TE, et al. Review of 1027 patients with newly diagnosed multiple myeloma. *Mayo Clin Proc*. 2003 Jan;78(1):21-33.
9. Varettoni M, Corso A, Pica G, Mangiacavalli S, Pascutto C, Lazzarino M. Incidence, presenting features and outcome of extramedullary disease in multiple myeloma: a longitudinal study on 1003 consecutive patients. *Ann Oncol*. 2010 Feb;21(2):325-330.
10. Thomas FB, Clausen KP, Greenberger NJ. Liver disease in multiple myeloma. *Arch Intern Med*. 1973 Aug;132(2):195-202.
11. Perez-Soler R, Esteban R, Allende E, Tornos Salomo C, Julia A, Guardia J. Liver involvement in multiple myeloma. *Am J Hematol*. 1985 Sep;20(1):25-29.
12. Thiruvengadam R, Penetrante RB, Goolsby HJ, Silk YN, Bernstein ZP. Multiple myeloma presenting as space-occupying lesions of the liver. *Cancer*. 1990 Jun 15;65(12):2784-2786.
13. Nguyen BD, Dash N, Lupetin AR. MR imaging of hepatic plasmacytoma: a case report. *Clin Imaging*. 1992 Apr-Jun;16(2):98-101.
14. Caturelli E, Squillante MM, Castelvetere M, Falcone A, Musto P. Myelomatous nodular lesions of the liver: diagnosis by ultrasound-guided fine-needle biopsy. *J Clin Ultrasound*. 1993 Feb;21(2):133-137.
15. Curtis JM, Pellegrini V, Tappin JA. Case report: multiple myeloma—a rare presentation. *Clin Radiol*. 1995 Jan;50(1):63-64.
16. Kelekis NL, Semelka RC, Warshauer DM, Sallah S. Nodular liver involvement in light chain multiple myeloma: appearance on US and MRI. *Clin Imaging*. 1997 May-Jun;21(3):207-209.
17. Chemlal K, Couvelard A, Grange MJ, et al. Nodular lesions of the liver revealing multiple myeloma. *Leuk Lymphoma*. 1999 Apr;33(3-4):389-392.
18. Fernandez-Flores A, Fortes J, Smucler A, Orduña M, Pol A. Involvement of the liver by multiple myeloma as nodular lesions: a case diagnosed by fine-needle aspiration and immunocytochemistry. *Diagn Cytopathol*. 2003 Nov;29(5):280-282.
19. Arebi N, Patel B, Aqel NM, Pitcher MC. IgA multiple myeloma presenting as non-obstructive jaundice. *Postgrad Med J*. 2004 Aug;80(946):489-490.
20. del Giglio A, Weinschenker P, Manhani AR, Carbonell AL, Mitteldorf CA. Hepatic plasmacytosis as a manifestation of relapse in multiple myeloma treated with thalidomide. *South Med J*. 2005 Feb;98(2):238-240.
21. Invernizzi R, Maffè GC, Travaglino E, Pagani E, Pieresca C. Nodular lesions of the liver in multiple myeloma. *Haematologica*. 2007 Jul;92(7):e81.
22. Wu XN, Zhao XY, Jia JD. Nodular liver lesions involving multiple myeloma: a case report and literature review. *World J Gastroenterol*. 2009 Feb 28;15(8):1014-1017.
23. Dhakal A, Chandra A. A multiple myeloma patient presenting with multiple hepatic masses. *J Med Cases*. 2013 Dec;4(10):673-675.
24. Pal S, Chattopadhyay B, Chatterjee A, Bhattacharya B. Lambda light chain myeloma presenting as nodular hepatic lesion: a clinical rarity. *J Cancer Res Ther*. 2014 Jan-Mar;10(1):191-193.
25. Rajkumar SV, Dimopoulos MA, Palumbo A, et al. International Myeloma Working Group updated criteria for the diagnosis of multiple myeloma. *Lancet Oncol*. 2014 Nov;15(12):e538-e548.
26. Zamagni E, Cavo M. The role of imaging techniques in the management of multiple myeloma. *Br J Haematol*. 2012 Dec;159(5):499-513.

27. Dimopoulos M, Kyle R, Fermand JP, et al. Consensus recommendations for standard investigative workup: report of the International Myeloma Workshop Consensus Panel 3. *Blood*. 2011 May 5;117(18):4701-4705.
28. Dimopoulos M, Terpos E, Comenzo RL, et al. International myeloma working group consensus statement and guidelines regarding the current role of imaging techniques in the diagnosis and monitoring of multiple myeloma. *Leukemia*. 2009 Sep;23(9):1545-1556.
29. Kato T, Tsukamoto E, Nishioka T, et al. Early detection of bone marrow involvement in extramedullary plasmacytoma by whole-body F-18 FDG positron emission tomography. *Clin Nucl Med*. 2000 Nov;25(11):870-873.
30. Dawson MA, Patil S, Spencer A. Extramedullary relapse of multiple myeloma associated with a shift in secretion from intact immunoglobulin to light chains. *Haematologica*. 2007 Jan;92(1):143-144.
31. Wu P, Davies FE, Boyd K, et al. The impact of extramedullary disease at presentation on the outcome of myeloma. *Leuk Lymphoma*. 2009 Feb;50(2):230-235.
32. Lopes da Silva R, Monteiro A, Veiga J. Non-secretory multiple myeloma relapsing as extramedullary liver plasmacytomas. *J Gastrointesin Liver Dis*. 2011 Mar;20(1):81-83.
33. Drayson M, Tang LX, Drew R, Mead GP, Carr-Smith H, Bradwell AR. Serum free light-chain measurements for identifying and monitoring patients with nonsecretory multiple myeloma. *Blood*. 2001 May 1;97(9):2900-2902.
34. Zhan JJ, Sun WJ, Huang ZX, et al. Light chain multiple myeloma, clinic features, responses to therapy and survival in a long-term study. *World J Surg Oncol*. 2014 Jul 28;12: 234.
35. Fischbach W, Goebeler-Kolve ME, Dragosics B, Greiner A, Stolte M. Long term outcome of patients with gastric marginal zone B cell lymphoma of mucosa associated lymphoid tissue (MALT) following exclusive Helicobacter pylori eradication therapy: experience from a large prospective series. *Gut*. 2004 Jan;53(1): 34-37.
36. Kyle RA, Rajkumar SV. Multiple myeloma. *N Engl J Med*. 2004 Oct 28;351(18):1860-1873. Erratum in: *N Engl J Med*. 2005 Mar 17;352(11):1163.

This article meets the Accreditation Council for Graduate Medical Education and the American Board of Medical Specialties Maintenance of Certification competencies for Patient Care and Medical Knowledge.