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Acute liver failure as an initial presentation of multiple myeloma

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ABSTRACT

Multiple myeloma (MM) is a clonal plasma cell neoplasm primarily involving the bone marrow and typically presenting with end-organ damage, including renal impairment, lytic bone lesions, anemia, and hypercalcemia. Extramedullary disease at diagnosis is uncommon, and acute liver failure as an initial manifestation is exceptionally rare; consequently, only a limited number of cases have been reported. We describe a 44-year-old woman with no relevant past medical history who was admitted to the intensive care unit with acute liver failure. After an extensive diagnostic work-up, MM with hepatic involvement was identified, and treatment was initiated promptly. Recognition of this unusual presentation is critical given its adverse prognosis, and reporting additional cases may help improve awareness and facilitate earlier diagnosis and management.

Keywords: Multiple myeloma; Monoclonal gammopathy; Acute liver failure; Jaundice; Anemia.

INTRODUCTION

Multiple myeloma (MM) is a clonal plasma cell neoplasm that primarily involves the bone marrow and classically presents with myeloma-defining events, including hypercalcemia, renal impairment, anemia, and lytic bone disease.[1] In advanced or biologically aggressive disease, malignant plasma cells may lose dependence on the marrow microenvironment and disseminate to extramedullary sites.[2-5]

Clinically apparent hepatic involvement is uncommon in MM, despite autopsy series reporting liver infiltration in a substantial proportion of patients.[2,6,7] When symptomatic, hepatic infiltration is associated with rapid deterioration and poor outcomes.[2,3] Acute liver failure as the initial presentation of MM is exceptionally rare; most cases of hepatic failure in MM are attributed to AL amyloidosis, whereas massive parenchymal plasma cell infiltration can produce severe non-obstructive cholestasis and abrupt organ failure.[2,3,6]

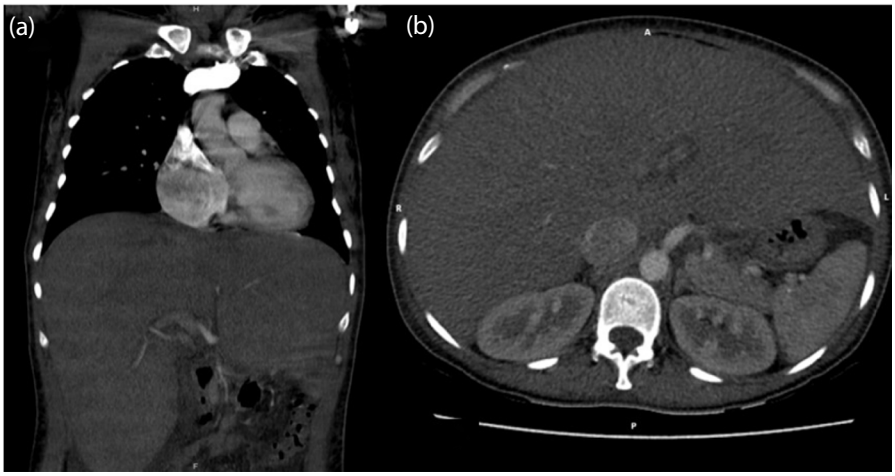
Because imaging findings may be nonspecific and the differential diagnosis is broad, liver biopsy, preferably transjugular in the setting of coagulopathy, remains critical to establish the diagnosis.[2,3,6] We report a case of MM presenting with acute liver failure due to diffuse hepatic plasma cell infiltration and discuss key diagnostic and therapeutic considerations.

Case report

A 44-year-old woman with no relevant past medical history presented with a 1-month history of epistaxis, spontaneous bruising, and gingival bleeding. She also reported progressive fatigue, lower-limb swelling, and abdominal distension over the preceding 3 months, with marked worsening during the week prior to admission.

On admission, vital signs were as follows: temperature 36 °C, blood pressure 120/80 mmHg, heart rate 100 beats/min, respiratory rate 18 breaths/min, and oxygen saturation 94% on room air. Physical examination revealed generalized jaundice and multiple ecchymoses over the legs and trunk. On neurologic examination, she was temporally disoriented but oriented to person and place; no focal deficits were noted, and limb strength was preserved. The liver was markedly enlarged and palpable approximately 15 cm below the right costal margin. Bilateral lower-extremity edema was present.

Initial laboratory evaluation showed a white blood cell count of 5,000/mm^3, hemoglobin 8 g/dL, and platelet count 58,000/mm^3. Liver function tests demonstrated predominantly direct hyperbilirubinemia (total bilirubin 8 mg/dL, direct bilirubin 6 mg/dL), with mild transaminase elevation (AST 56 U/L, ALT 31 U/L) and elevated gamma-glutamyl transferase (GGT 98 U/L). The alkaline phosphatase (ALP) level was within the normal range (44 U/L). Coagulation studies were abnormal, with a prothrombin time of 19 seconds, an activated partial thromboplastin time of 60 seconds, and an international normalized ratio of 1.6. Thoracoabdominal computed tomography revealed marked hepatomegaly (liver span 23 cm) without focal lesions (Fig. 1).



Source: Elaborated by the authors.

Figure 1. Coronal section of chest and abdominal computed tomography scan. a) Hepatomegaly is evidenced without evidence of focal damage. b) Enlarged liver, regular contours, homogeneous parenchyma, with no evidence of lesions.

The patient was admitted to the intensive care unit with a diagnosis of acute liver failure. An extensive etiologic workup was performed and was negative, including serologies for hepatitis A, B, and C viruses, cytomegalovirus, and Epstein-Barr virus, as well as autoimmune and thrombophilia testing (rheumatoid factor, antinuclear antibodies, anti-ENA, anti-dsDNA, anti-mitochondrial, anti-LKM-1, anti-smooth muscle, anticardiolipin, and anti-β2-glycoprotein I antibodies).

Given elevated serum total protein levels, serum protein electrophoresis was obtained and revealed a prominent monoclonal spike in the gamma region (M-spike 9.10 g/dL) (Fig. 2). Serum immunofixation identified an IgG kappa monoclonal protein (Fig. 3).

Bone marrow aspiration demonstrated approximately 60% plasma cell infiltration (Fig. 4), and monoclonality was confirmed by flow cytometry. Fluorescence *in situ* hybridization performed on sorted plasma cells was negative for high-risk cytogenetic abnormalities, including deletion 17p, chromosome 1 abnormalities, and translocations t(4;14), t(14;16), and t(14;20). A transjugular liver biopsy subsequently demonstrated plasma cell infiltration of the hepatic parenchyma. Congo red staining was negative in both bone marrow and liver tissue (Figs. 5 and 6). These findings confirmed the diagnosis of MM with primary hepatic involvement presenting as acute liver failure.

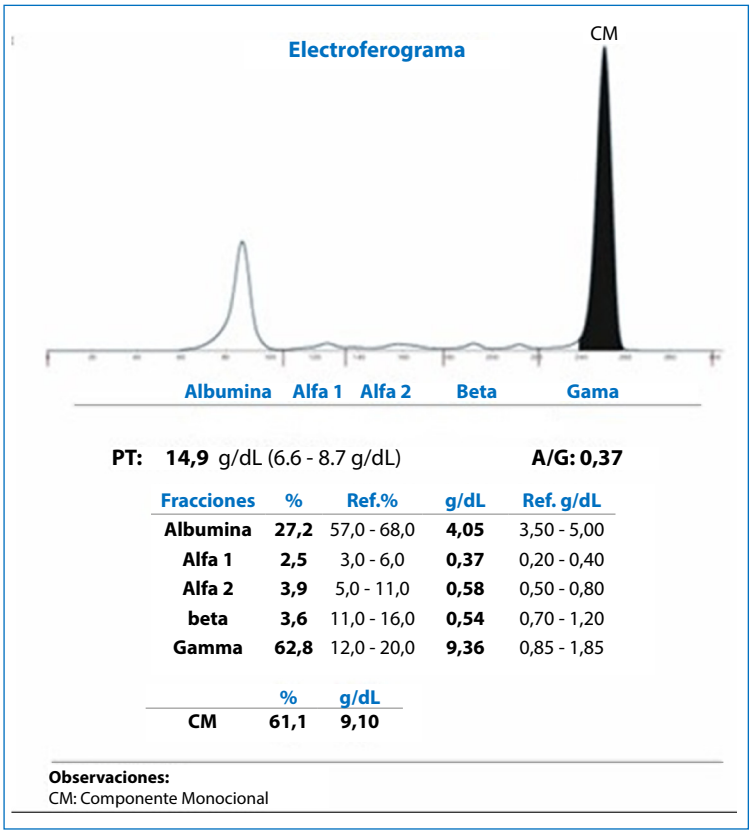


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Figure 2. Serum protein electrophoresis showing a monoclonal spike in the gamma region.

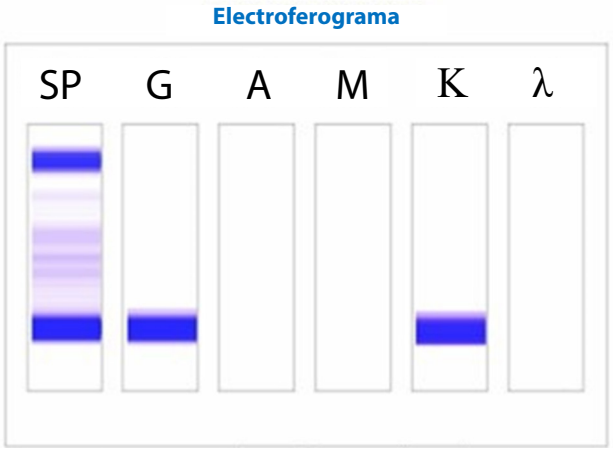

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Figure 3. Serum immunofixation electrophoresis, showing an IgG kappa monoclonal band.

Following the diagnosis, urgent treatment was initiated with daratumumab 16 mg/kg administered intravenously once weekly, bortezomib 0.7 mg/m^2 subcutaneously (dose-adjusted for hyperbilirubinemia) administered twice weekly, lenalidomide 25 mg orally once daily on days 1-21, and dexamethasone 40 mg once weekly. After the first treatment cycle, the patient's acute liver failure resolved, with normalization of bilirubin levels, and she achieved a partial hematologic response (50% reduction in the monoclonal component). After completion of the first cycle, treatment was continued on an outpatient basis; she is currently receiving the third cycle and remains in partial response.

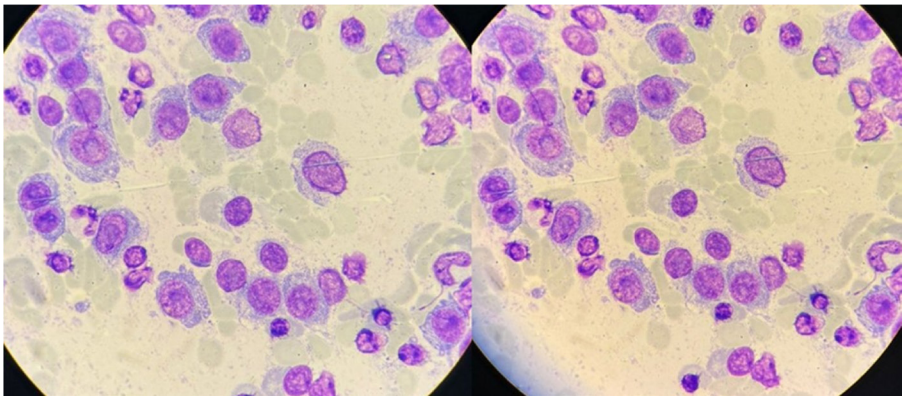

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Figure 4. Giemsa-stained bone marrow smear: evidence of infiltration by cells with round or oval, eccentric nuclei, suggestive of plasma cell dyscrasia.

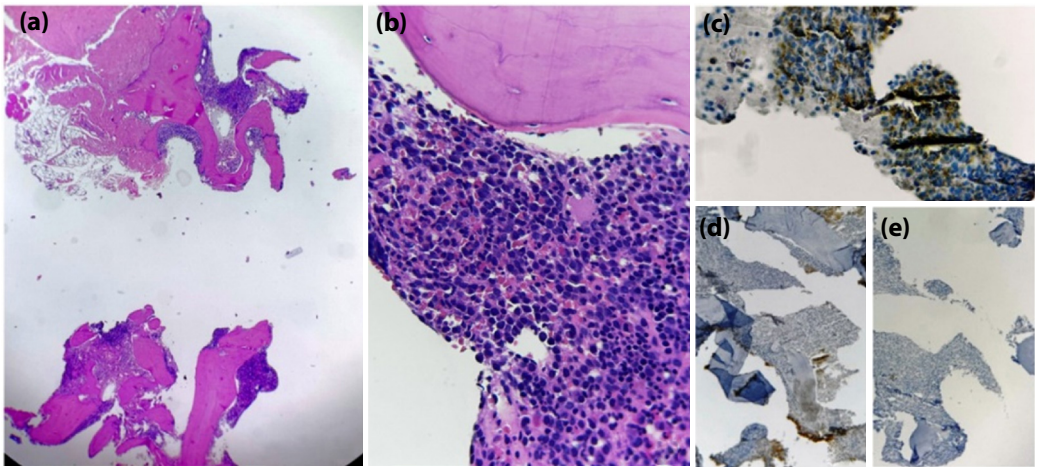

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Figure 5. a and b) Bone core biopsy with some identifiable cells (H&E 4× and 40×, respectively). Immunohistochemistry technique: c) Plasma cells positive for CD138. d and e) Predominance of kappa light chains. Negative Congo red stain.

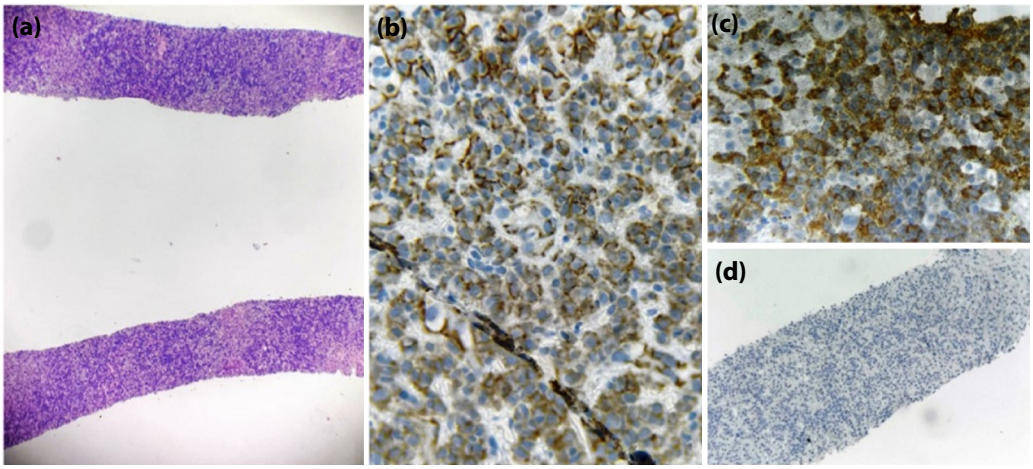

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Figure 6. a) Liver parenchyma biopsy showing involvement by plasma cells interspersed with occasional residual hepatocytes (H&E 4×). b) Immunohistochemistry with plasma cells positive for CD138; c) Kappa light chain restriction and negative lambda light chains; d) Negative Congo red stain.

DISCUSSION

This case describes a woman who presented to the emergency department with anemia and acute liver failure and was ultimately diagnosed with MM with diffuse hepatic infiltration.

Although MM is typically confined to the bone marrow niche, a subset of cases exhibits extramedullary spread, reflecting an aggressive biological phenotype in which a clone or subclone becomes less dependent on the marrow microenvironment and is often enriched for high-risk genetic features.[8] At the time of initial diagnosis, extramedullary involvement is reported in approximately 5% of patients and increases to around 30% at relapse.[2-4]

The most frequently involved sites include skin and muscle, pleura, lymph nodes, liver, and the central nervous system.[9-11]

Hepatic abnormalities in patients with MM have a broad differential diagnosis. In addition to common non-myeloma-related etiologies (e.g., viral hepatitis, autoimmune liver disease, ischemic injury, or drug-induced liver injury), myeloma-associated mechanisms include AL amyloidosis, light-chain deposition disease, focal hepatic plasmacytomas, and – more rarely – diffuse sinusoidal or parenchymal infiltration by plasma cells.[9,10] While autopsy studies suggest that plasma cell infiltration of the liver is not uncommon, clinically significant hepatic dysfunction directly attributable to infiltration remains rare, with most reports limited to isolated cases.[12] The clinical spectrum ranges from incidental or mild biochemical abnormalities to fulminant liver failure. Acute liver failure has been reported in a small proportion of patients with MM (approximately 0.4%), most often in the relapsed setting; presentation at initial diagnosis, as in our patient, is distinctly uncommon.[3,13]

In MM with diffuse hepatic plasma cell infiltration, one frequently described pattern is marked hyperbilirubinemia (often with a predominantly direct fraction) with relatively preserved or normal ALP, a profile observed in our case.[2,14] This pattern can help distinguish infiltration from hepatic involvement due to AL amyloidosis, which more commonly presents with disproportionate ALP elevation and normal or only mildly elevated bilirubin. Recognizing these patterns may provide an early clue that the liver dysfunction is related to myeloma biology rather than to more prevalent causes of cholestasis or hepatocellular injury.[14,15]

Unlike focal hepatic plasmacytomas, diffuse hepatic infiltration may not produce characteristic or readily identifiable abnormalities on imaging, and ultrasonography or computed tomography may be normal or show nonspecific changes.[5] Consequently, imaging alone is often insufficient to confirm myeloma-related hepatic dysfunction or to exclude mimicking conditions, including primary liver malignancy and metastatic disease. In this context, liver biopsy remains pivotal to establish the diagnosis by demonstrating plasma cell infiltration with light-chain restriction and supportive immunophenotyping (e.g., CD138 positivity).[2,3,6] When coagulopathy is present, as commonly occurs in acute liver failure, the transjugular approach is preferred to mitigate bleeding risk while enabling histologic confirmation.[3,6,15]

In our patient, the initial presentation with jaundice and hemorrhagic diathesis appropriately prompted evaluation for more common causes of acute liver failure, including decompensated chronic liver disease, autoimmune hepatitis, hepatotropic viral infections, and metastatic or infiltrative malignancy. The absence of relevant prior liver disease and negative viral serologies and autoimmune studies necessitated an expanded work-up, ultimately leading to the diagnosis of MM. Following histologic confirmation of hepatic plasma cell infiltration and exclusion of alternative infiltrative processes, MM with hepatic involvement was established as the primary driver of acute liver failure.

Management of MM complicated by acute liver failure is particularly challenging. Hepatic dysfunction limits the use of several antineoplastic agents due to altered metabolism and increased toxicity risk, and it often complicates supportive care because of coagulopathy and infection susceptibility.[16] Nonetheless, when hepatic failure is driven by tumor infiltration, rapid initiation of effective myeloma-directed therapy may

reverse cholestasis and improve hepatic function. In our case, prompt treatment was associated with rapid clinical improvement and reversal of liver failure, emphasizing the importance of early recognition and timely disease-specific intervention.

This case underscores several practical points for clinicians. First, in patients with suspected or confirmed MM who develop otherwise unexplained hyperbilirubinemia, particularly when AST/ALT are near normal and ALP is not markedly elevated, hepatic plasma cell infiltration should be considered, even at initial diagnosis. Second, because imaging may be nondiagnostic, biopsy is often required to establish the mechanism of liver dysfunction and to guide therapy.[3,5,6,15]

Finally, given the rarity of this presentation and the absence of standardized management recommendations, continued reporting of well-characterized cases is essential to refine diagnostic approaches, clarify prognostic factors (including the contribution of high-risk cytogenetics), and inform therapeutic strategies for this aggressive manifestation of extramedullary MM.

CONCLUSION

Despite infrequent hepatic involvement and liver failure due to MM, it should be considered as an etiology, especially when other etiologies are ruled out. Liver biopsy is key to diagnosis, and is necessary for initiating a specific and immediate treatment for the disease because of early recognition, decreasing the mortality for the patients, and improving patient prognosis.

CONFLICTS OF INTEREST

Nothing to declare.

DECLARATION OF USE OF ARTIFICIAL INTELLIGENCE TOOLS

No artificial intelligence was used in the creation of this article.

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DATA AVAILABILITY STATEMENT

All data are presented in the article.

AUTHOR CONTRIBUTIONS

Conceptualization: Olmedo J, Caeiro G. **Investigation:** Danies NO, Milanesio M. **Methodology:** Danies NO. **Formal Analysis:** Sanchez AV. **Data Curation:** Milanesio M. **Project Administration:** Basquiera AL, Caeiro G. **Writing:** Danies NO, Milanesio M. **Supervision:** Basquiera AL. **Final Approval:** Milanesio M.

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Nothing to declare.

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