A Rare Case of IgM Multiple Myeloma with a Skull Neoplasm

Elena Chertok Shacham MD[1,2], Shay Brikman MD[1,4], Dafna Chap Marshak MD[3], Veronika Denisov MD[1] and Guy Dori MD PhD[1,4]

Departments of [1]Internal Medicine E and [3]Hematology and [2]Endocrinology and Diabetes Unit, Emek Medical Center, Afula, Israel
[4]Rappaport Faculty of Medicine, Technion–Israel Institute of Technology, Haifa, Israel

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Immunoglobulins M (IgM) multiple myeloma (MM) is a hematologic disease characterized by elevated IgM protein levels. MM is a rare disorder found in about 0.5% of myeloma cases. The symptoms of MM include renal failure, hypercalcemia, painful lytic bone lesions, and the presence of less than 10% monoclonal plasma cells in the bone marrow. Solitary plasmacytomas are malignant tumors of neoplastic plasma cells. They are classified into two types according to the growth pattern: intraosseous (skeletal) or extra skeletal. Up to 60% of solitary plasmacytomas progress to multiple myeloma.

We present a case of a patient with MM and a rapidly growing skull neoplasm with a myeloma diagnosis concomitant with a diagnosis of a bone plasmacytoma.

PATIENT DESCRIPTION

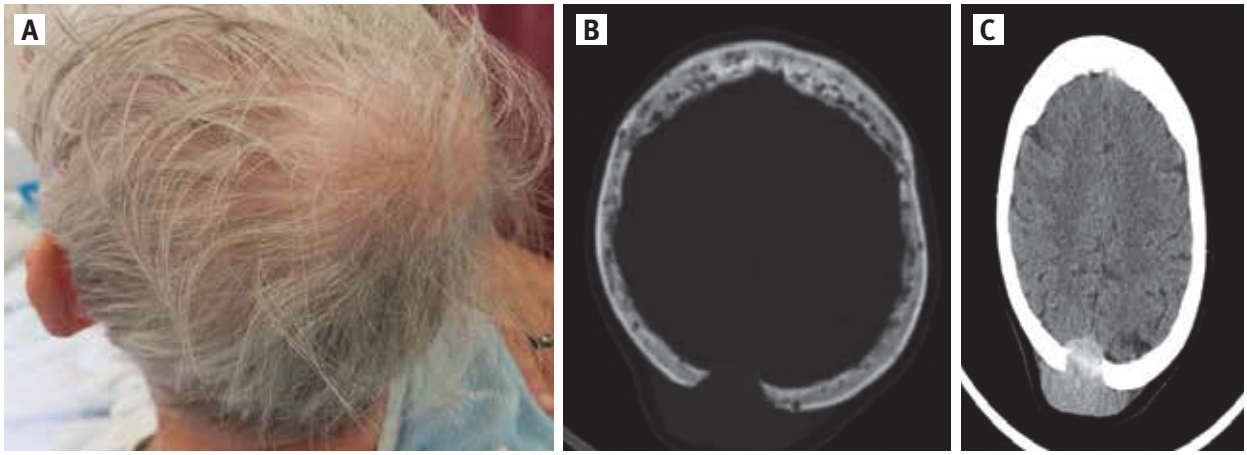
A 73-year-old woman was referred to the emergency department following 2 days of weakness, bone pain, and confusion. Her past history included unprovoked deep vein thrombosis and pulmonary embolism in 2012, which was treated with anticoagulation therapy, hypothyroidism, and essential tremor. The use of new medications was ruled out as a cause of the confusion.

On admission to our medical center, vital signs were normal without fever. Physical examination revealed a deteriorated mental status, no focal neurologic deficits, and pain on palpation of the left scapula and left ribs. In addition, we noted a firm, large, not tender, mobile, tissue mass palpated at the parieto-occipital area of her head [Figure 1A].

Laboratory tests demonstrated significant hypercalcemia (13.5 mg/dl), acute kidney injury with a creatinine level of 1.8 mg/dl (baseline creatinine level 1.1 mg/dl), urea 57 mg/dl, estimated glomerular filtration rate (eGFR) 27 ml/min, hemoglobin 11 mg/dl, and C-reactive protein 0.6 mg/dl. The severe hypercalcemia was treated immediately with an intravenous saline infusion and subcutaneous calcitonin, followed by intravenous bisphosphonates.

During the patient's hospitalization, additional laboratory tests revealed an elevated level of total protein 10 g/dl and 24 hour urine protein excretion of 5.7 gram. An elevated level of IgM 6705 mg/dl (normal range 40–230 mg/dl) was determined using immunoglobulin quantitation analysis. Serum protein electrophoresis revealed elevated g-globulin 4.3 g/dl with monoclonal IgM lambda levels of 3.8 g/dl. Elevated levels of serum free light lambda chains 3510 mg/dl (normal range 5.7–26 mg/dl) with a

Figure 1. The parieto-occipital mass demonstrating erosion of skull bone and invasion into skull vault and multiple lytic bone lesions on computed tomography scans **[A]** Parieto-occipital mass, **[B]** Multiple bone lesions, **[C]** Skull vault invasion



kappa/lambda ratio of 0.0039 (normal range 0.26–1.65). Free lambda light chain excretion was found in urine electrophoresis and immunofixation. Bone marrow aspiration demonstrated over 90% plasma cell infiltrations and flow cytometry of bone marrow aspirate revealed that 32% plasma cells were CD138+, CD38+, Lambda +, CD20dim, CD19-, and CD56-. Polymerase chain reaction (PCR) of bone marrow aspirate for MYD88 (L265P) was negative, supporting the differential diagnosis of MM in contrast to Waldenström macroglobulinemia (WM). A bone marrow biopsy was not conducted due to the patient's deteriorating condition.

A head computed tomography (CT) scan demonstrated multiple skull lytic lesions [Figure 1B] and a well-demarcated tissue mass in the occipital region, eroded skull bone [Figure 1C], and penetrated the skull vault. No significant pressure on brain tissue or a brain edema was detected. The mass measured 5.6 × 6.5 × 3.5 cm, which indicated a significant increase in mass compared to a previous CT scan taken 4 months earlier. In addition, an earlier head CT demonstrated that the mass had not penetrated the skull. Invasion and destruction of the skull was noticed during the hospitalization together with the MM diagnosis.

A chest, abdomen, and pelvic CT demonstrated multiple lytic lesions in the skeleton, in particular a fracture of the spinous process of vertebrae T2 and the left 8th rib.

A plastic surgeon was consulted to take a biopsy of the scalp mass; however, the procedure was deferred due to the patient's deteriorating condition. A hematologic consultation recommended initiation of induction therapy for MM; however, the patient and her family preferred palliative care. Morphine was administered for severe bone pain. The patient died 8 days after admission.

COMMENT

Our case study shows a patient with IgM MM and a skull penetrating neoplastic lesion.

Clinical practice guidelines define active multiple myeloma by the presence of clonal bone marrow plasma cells ≥ 10% and any one or more of the following myeloma-defining events: hypercalcemia > 12 mg/dl, renal insufficiency with eGFR < 40 ml/min, anemia < 10 g/dl, osteolytic bone lesions, abnormal serum free light chain ratio ≥ 100 or ≤ 0.01 depending on the chain, or more than one focal lesions larger than 5 mm in magnetic resonance imaging studies [1]. The patient had 32% monoclonal plasma cells on bone marrow aspiration, severe hypercalcemia of 13.5 mg/dl, acute kidney injury (eGFR 27 ml/min), the presence of multiple lytic skull lesions on CT scans, and a free light chain ratio of 0.0039 suggesting a diagnosis of MM.

Monoclonal IgM gammopathy is observed in several hematologic diseases including WM, MM, chronic lymphocytic leukemia, marginal zone lymphoma, and monocloncal gammopathy of uncertain significance [2]. It is important to distinguish between these entities as they differ in clinical course, treatment, and prognosis. Patients with MM are usually classified by immunophenotyping as CD20- CD138+, whereas patients with WM are usually CD20+ CD138- [3]. Our patient was CD 138+ and weakly positive for CD20. The L265P mutation in the MYD88 gene is frequently present in WM, in contrast to MM [3]. In our patient, the gene did not have this mutation, supporting the diagnosis of MM.

Osteolytic calvarial lesions are rare, varying from benign slow growing lesions to highly aggressive, malignant ones. Aggressive malignant lesions are characterized by an erosion of the bone cortex, irregular margins, multiple lesions, and extracranial expansion. Benign lesions usually show frequently sclerotic smooth margins, which expand from within the bone cortex without damaging the inner or external tables of the bone [4]. Metastases and multiple myeloma are the two most common malignant calvarial neoplasms in adults [4]. Multiple lytic skull lesions are found with MM and metastases due to thyroid or lung cancer. Blastic lesions are found with metastases of breast or prostate cancer and these metastases can extend into adjacent soft tissue. The chest, abdomen, and pelvic CT scan showed no evidence of a primary neoplasm that might have metastasized to the skull.

Plasmacytoma is a solid tumor resulting from clonal proliferation of plasma cells. Some plasmacytomas are solitary tumors, and some are related to past or present MM [5]. Solitary plasmacytomas of head and neck are rare. They can have an intraosseous growth pattern or can arise from within soft tissue such as the extramedullary plasmacytoma. Extramedullary plasmacytomas rarely progress to MM in contrast to solitary plasmacytoma of the bone [5].

According to the CT, the patient had a tumor mass in the skull bone without skull invasion just a few months before being diagnosed with MM. Skull invasion and erosion was noticed when MM was diagnosed, supporting the diagnosis of a bone plasmocytoma. Although tissue diagnosis for the patient's calvarial lesion was not pursued due to the patient's rapidly deteriorating condition, it is likely that the calvarial lesion was a plasmacytoma concomitantly emerging with MM. To the best of our knowledge, this is the first report of a plasmacytoma appearing simultaneously with MM.

Correspondence
Dr. E. Chertok Shacham
Endocrinology and Diabetes Unit, Emek Medical Center, Afula 18101, Israel
Fax: (972-4) 814-1506
email: elenachertok12@gmail.com,

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