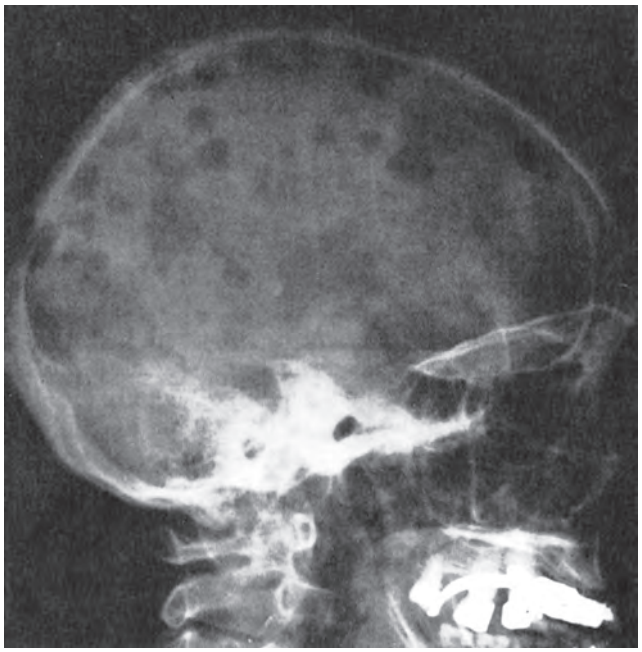

Figure 13-16 Multiple myeloma of the skull (radiograph, lateral view). The sharply punched-out bone lesions are most obvious in the calvarium.

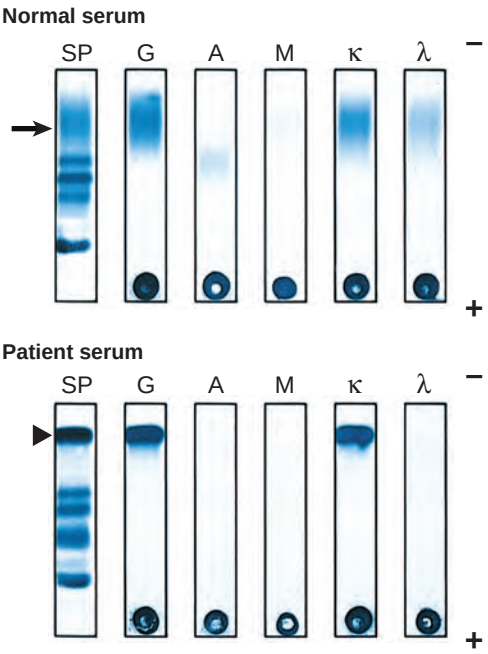

Figure 13-18 M protein detection in multiple myeloma. Serum protein electrophoresis (SP) is used to screen for a monoclonal immunoglobulin (M protein). Polyclonal IgG in normal serum (*arrow*) appears as a broad band; in contrast, serum from a patient with multiple myeloma contains a single sharp protein band (*arrowhead*) in this region of the electropherogram. The suspected monoclonal Ig is confirmed and characterized by immunofixation. In this procedure, proteins separated by electrophoresis within a gel are reacted with specific antisera. After extensive washing, proteins that are cross-linked by antisera are retained and detected with a protein stain. Note the sharp band in the patient serum is cross-linked by antisera specific for IgG heavy chain (G) and kappa light chain (κ), indicating the presence of an IgGκ M protein. Levels of polyclonal IgG, IgA (A), and lambda light chain (λ) are also decreased in the patient serum relative to normal, a finding typical of multiple myeloma. (Courtesy Dr. David Sacks, Department of Pathology, Brigham and Women's Hospital, Boston, Mass.)

tissues, particularly the bones; (2) the production of excessive Igs, which often have abnormal physicochemical properties; and (3) the suppression of normal humoral immunity.

Bone resorption often leads to *pathologic fractures* and *chronic pain*. The attendant *hypercalcemia* can give rise to neurologic manifestations, such as confusion, weakness, lethargy, constipation, and polyuria, and contributes to renal dysfunction. Decreased production of normal Igs sets the stage for *recurrent bacterial infections*. Cellular immunity is relatively unaffected. Of great significance is *renal insufficiency,* which trails only infections as a cause of death. The pathogenesis of renal failure (Chapter 20), which occurs in up to 50% of patients, is multifactorial. However, the single most important factor seems to be *Bence-Jones proteinuria*, as the excreted light chains are toxic to renal tubular epithelial cells. Certain light chains (particularly those of the λ6 and λ3 families) are prone to cause *amyloidosis* of the AL type (Chapter 6), which can exacerbate renal dysfunction and deposit in other tissues as well.

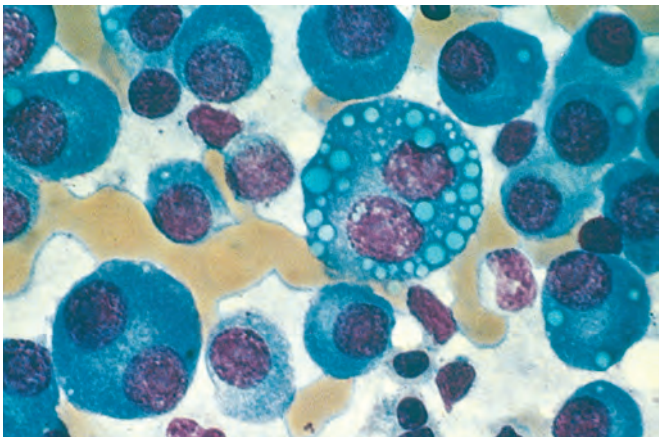

Figure 13-17 Multiple myeloma (bone marrow aspirate). Normal marrow cells are largely replaced by plasma cells, including forms with multiple nuclei, prominent nucleoli, and cytoplasmic droplets containing Ig.

In 99% of patients, laboratory analyses reveal increased levels of Igs in the blood and/or light chains (Bence-Jones proteins) in the urine. The monoclonal Igs are usually first detected as abnormal protein "spikes" in serum or urine electrophoresis and then further characterized by immunofixation (Fig. 13-18). Most myelomas are associated with more than 3 gm/dL of serum Ig and/or more than 6 mg/dL of urine Bence-Jones protein. The most common monoclonal Ig ("M protein") is IgG (approximately 55% of patients), followed by IgA (approximately 25% of cases). Myelomas expressing IgM, IgD, or IgE occur but are rare. Excessive production and aggregation of M proteins, usually of the IgA and or IgG_3 subtype, leads to symptoms related to hyperviscosity (described under lymphoplasmacytic lymphoma) in about 7% of patients. Both free light chains and a serum M protein are observed together in 60% to 70% of patients. However, in about 20% of patients only free light chains are present. Around 1% of myelomas are nonsecretory; hence, the absence of detectable M proteins does not completely exclude the diagnosis.

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