Malignant histiocytosis (or histiocytic sarcoma) is a rare disease characterized by a malignant proliferation of cells resembling mature tissue histiocytes. Median age at diagnosis is 63 years; the prognosis is usually poor, with a median overall survival of 6 months, because no standard treatment has yet been established and responses to conventional chemotherapy at advanced stages are generally poor. Mutations affecting the RAS-MAPK signaling pathway are detected in most cases, and the off-label use of targeted therapies has been reported to yield clinical responses in several cases. It has been suggested that PD-L1 expression is detectable in most cases, but the utility of PD-L1/PD-1 blockade in histiocytic neoplasms remains unclear. We report here the first case of a response to nivolumab in an adult with malignant histiocytosis. Next-generation sequencing appears to be essential for the diagnosis of this rare histiocytic condition, given the therapeutic options available. However, immune checkpoint inhibition may also be a valuable therapeutic option for patients with malignant histiocytosis expressing PD-L1.

Primary Sarcoidosis of the Adipose Tissue: A New Variant of Sarcoidosis

To the Editor: Although sarcoidosis predominantly targets the lungs, almost every organ can be affected. This occasionally renders the diagnosis a difficult task. We describe a patient with isolated adipose tissue sarcoid granulomas, constituting the first ever report on this unique manifestation.

A woman in her mid-50s presented to the emergency department complaining of fatigue. The patient had been in her usual state of health until 3 months before this admission, when she first noticed a feeling of asthenia that gradually deteriorated. Her past medical history was unremarkable, and the physical examination disclosed no abnormalities. Laboratory tests revealed severe hypercalcemia (13.8 mg/dL; to convert to mmol/L, multiply by 0.25) and acute kidney injury (serum creatinine concentration, 1.7 mg/dL; to convert to μmol/L, multiply by 88.4). Additional laboratory test results included excessive urine calcium excretion, low serum parathormone (PTH) level, low serum 25-hydroxyvitamin D level (12.3 ng/mL; to convert to nmol/L, multiply by 2.496), increased activity of serum angiotensin-converting enzyme (211 U/L; to convert to nkat/L, multiply by 2.4), interferon-γ release assay and a tuberculin test response were negative.

The diagnostic process was focused on the dangerously high serum calcium concentration. Suppressed PTH levels narrowed the differential diagnosis to malignant disease–related hypercalcemia and ectopic calcitriol production. Thoracic computed tomography (CT) showed no signs of mediastinal or hilar lymphadenopathy, bone scintigraphy excluded osteolytic metastases, and normal PTH-related protein levels (<1 pmol/L) ruled out PTH-related protein–secreting malignant neoplasm. Serum and urine protein electrophoresis and immunofixation excluded classic secretory multiple myeloma; nonsecretory multiple myeloma was ruled out by a bone marrow biopsy.

The more likely conditions having been eliminated, the probability of a granulomatous disease refocused the diagnostic work-up. Low 25-hydroxyvitamin D levels coupled with inappropriate normal levels of 1,25-dihydroxyvitamin D3.
D could suggest a PTH-independent extrarenal 1,25-dihydroxyvitamin D (calcitriol) production by resident granuloma macrophages. Bronchoscopy with bronchoalveolar lavage was not indicative of an underlying disease, leading us to a diagnostic dead end. This prompted a positron emission tomography/CT (PET/CT) scan that showed diffuse uptake of $^{18}$F-fluorodeoxyglucose exclusively throughout the adipose tissue (Figure). A fine-needle biopsy showed multiple noncaseating epithelioid granulomas, multinucleated giant cells (Langhans cells), and histiocytes, establishing the diagnosis (Figure). Higher resolution images revealed the presence of asteroid formations within the giant cells. The absence of cutaneous or subdermal nodules made the diagnosis of cutaneous...
sarcoidosis/panniculitis unlikely. Systemic corticosteroid treatment led promptly to normalization of both calcium and serum creatinine concentrations. Corticosteroids were tapered in a stepwise fashion for a 12-month period until their withdrawal. An uneventful disease course unfolded during a 2-year follow-up.

Because of the phenotype heterogeneity of sarcoidosis, some cases challenge our diagnostic acuity. Erythema nodosum is among the most common manifestations of sarcoidosis, whereas sole subcutaneous lesions are rarely observed. In the absence of cutaneous nodules and the lack of systemic symptoms, however, both diagnoses were excluded in our patient. Establishing the diagnosis required the detection of granulomas because extensive infiltration of the adipose tissue could be visualized only by PET/CT. The sole, diffuse adipose tissue involvement observed in this patient adds to the rich clinical spectrum of sarcoidosis, being a novel but maybe not the last variant of this unique nosologic entity.

**POTENTIAL COMPETING INTERESTS**

The authors report no competing interests.