Histologic Review of Sarcoidosis in a Neck Lymph Node

Shannon M. Welter¹ · Javier DeLuca-Johnson¹ · Keith Thompson¹

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Abstract Sarcoidosis is a multisystem granulomatous disease of unknown etiology. It may occur at any age, but is most commonly seen in young to middle age adults. Sarcoidosis remains more common in women regardless of geographic or racial boundaries. Although the etiology remains unclear, the most common explanation is that sarcoidosis is a disease of immunologic dysregulation triggered by an as yet unidentified environmental or microbial antigen in genetically susceptible persons. We review a case of sarcoidosis with was initially diagnosed in a neck lymph node that was removed for evaluation of metastatic squamous cell carcinoma with a discussion on the clinical and histologic characteristic of the disease.

Keywords Sarcoidosis · Lymph node · Granuloma · Schaumann bodies · Hamazaki-Wesenbergbodies · Noncaseating · Epithelioid macrophages · Multinucleated giant cells

History

A 75-year-old woman presented with a left parotid mass. Two years prior, she had squamous cell carcinoma of her

left auricle, which was excised and subsequently treated with radiation therapy. Of note, at that time, she was noted to have hilar lymphadenopathy (Fig. 1).

Radiographic Features

A contrast enhanced CT scan showed a 2.7 cm cystic rim enhancing mass in the left retrostyloid parotid space compatible with necrotic parotid lymph node, with extension to the base of the styloid mastoid foramen. A PET scan demonstrated increased FDG activity of this same region, as well as increased FDG activity of an 8 mm left level 1B lymph node. The subsequent MRI showed abnormal enhancing tissue along similar anatomic boundaries consistent with the PET scan as well as new findings of perineural spread along styloid mastoid foramen and inferior mastoid segment of facial nerve (Figs. 2, 3).

Diagnosis

A parotidectomy and neck dissection was performed and in addition to expected findings of metastatic squamous cell carcinoma, a subset of the cervical lymph nodes contained numerous well circumscribed non-caseating granulomas. These granulomas were composed of epithelioid histiocytes and multinucleated giant cells (Fig. 4) which contained asteroid bodies (Fig. 5), Schaumann bodies (Fig. 6), and Hamazaki-Wesenberg bodies. Special stains for fungal and acid fast bacilli were negative. In the clinical setting, these findings were consistent with sarcoidosis.

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✉ Shannon M. Welter
shannon.m.welter.mil@mail.mil

¹ Department of Anatomic Pathology, Naval Medical Center San Diego, 34800 Bob Wilson Drive, San Diego, CA 92134-5000, USA

Fig. 1 CT scan with hilar lymphadenopathy

Fig. 2 CT scan axial view with cystic mass in the left retrostyloid parotid space

Fig. 3 CT Scan sagittal view

Discussion

Sarcoidosis is a multisystem granulomatous disease of unknown etiology. It may occur at any age, but is most commonly seen in young to middle age adults. Incidence varies widely by geography, with the highest rates observed in the Northern European countries (5–40 cases per 100,000). In the United States, incidence among African Americans is three times as high as compared to Caucasians (35.5 cases per 100,000 in African Americans vs. 10.9 cases per 100,000 in Caucasians). Sarcoidosis remains more common in women regardless of geographic or racial boundaries [1]. Although the etiology remains unclear, the most common explanation is that sarcoidosis

is a disease of immunologic dysregulation triggered by an as yet unidentified environmental or microbial antigen in genetically susceptible persons [2].

Sarcoidosis may affect any organ. Bilateral hilar lymphadenopathy is the hallmark finding, and is often accompanied by peripheral lymph node involvement. Besides lymphadenopathy, respiratory, ophthalmologic and dermatologic involvement is common. Other less common sites of involvement include the heart, liver, kidney, central nervous system, bone and salivary glands [1]. Typical laboratory findings include elevated ESR, ACE, reversed

Fig. 4 Multiple granulomas

Fig. 5 Granuloma with asteroid body

albumin-globulin ratio, hypergammaglobulinemia, hypercalcemia, and abnormal LFTs [3].

The overall rate of spontaneous remission is high, with about half of cases remitting within 12–36 months, and the majority within 5 years. In addition, acute presentations, which often encompass Lofgren's syndrome (erythema nodosum, bilateral hilar adenopathy, arthritis) are associated with good prognosis. However, there are several important prognostic factors which are associated with longer and more severe disease course, including race, age of onset greater than 40, and CNS or cardiac involvement [4]. Due to the overall high spontaneous remission rates, the decision to begin treatment is individualized and tailored to degree of patient symptomatology. Steroids are first-line treatment. In persistent disease or in patients

unable to tolerate steroids, non-steroid immunomodulators may also be used [5].

Histologically, sarcoidosis is characterized by the presence of noncaseating granulomas. Within involved lymph nodes, the usual architecture is effaced by multiple well-defined, “tight”, and discrete granulomas which in some instances may coalesce [6]. The granulomas consist of epithelioid macrophages and multinucleated giant cells, and typically display a concentric rim of predominantly CD4+ lymphocytes. CD8+ lymphocytes, plasma cells, B lymphocytes and fibroblasts may also be observed in the concentric rim to lesser extent. The increased CD4+/CD8+ lymphocyte ratio surrounding the granulomas is not reflected in the peripheral blood. In newly formed granulomas, the concentric rim is often entirely absent [3]. In later stages, fibroblasts and collagen with associated sclerosis gradually replace the lymphocyte predominant rim [6].

The epithelioid macrophages are large, polygonal and distributed in concentric rows within the granuloma. These cells lose their phagocytic potential but gain significant secretory functions. Notable enzymes secreted by these epithelioid macrophages include ACE, lysozyme, glucuronidase, collagenase, and calcitriol. Giant cells are formed by the fusion of epithelioid macrophages and have similar morphologic features. In early granulomas giant cells usually demonstrate random distribution of nuclei (foreign body type giant cell), but in later stages granuloma nuclei are distributed to the periphery in a Langerhans-type giant cell pattern [3].

Central immunoglobulin deposits and inclusion bodies are common, nonspecific findings within granulomas, the most important of which include asteroid bodies, Schaumann bodies, and Hamazaki-Wesenberg bodies. Asteroid bodies are 10–25 micron lipoproteins that appear as pink,

Fig. 6 Granuloma with Schaumann body

stellate inclusions (Fig. 5). They are present in 2–9% of cases. Schaumann bodies are found in 48–88% of cases. They are concentric, laminated, strongly basophilic inclusions consisting of complex matrix proteins and calcium phosphate. Hamazaki-Wesenberg bodies are giant lysosomes found in 11–68% of cases. In contrast to asteroid and Schaumann bodies, Hamazaki-Wesenberg bodies are most often extracellular and appear outside of the granuloma. They stain with Gomori Silver stain and are identified as clusters of small rice-like bodies with occasional budding which may be mistaken for a fungal organism [3].

Necrosis is uncommon in sarcoid granulomas, however small central foci of fibrinoid necrosis may occasionally be seen, and so the presence of necrosis in itself does not exclude sarcoidosis. Special stains for acid-fast bacilli (Ziehl-Neelsen) and fungi (Gomori methenamine silver) should be performed in these cases to exclude infectious etiologies [7].

Compliance with Ethical Standards

Conflict of interest All three authors declare that he/she has no conflict of interest.

Ethical Approval This article does not contain any studies with human participants or animals performed by any of the authors.

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