Marginal Zone B-Cell Lymphoma of the Parotid Gland Associated with Epithelioid Granulomas
Report of a Case with Fine Needle Aspiration

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BACKGROUND: Although granulomas can occur in association with malignant neoplasms, including some subtypes of lymphoma, they have been described rarely in marginal zone B-cell lymphoma (MZCL). To our knowledge, the cytologic features of this association have not been documented. We present the cytologic findings with fine needle aspiration cytology (FNAC) of an unusual case of MZCL with concomitant granulomas.

CASE: An 82-year-old male presented with a mass in the left parotid gland. The lesion was evaluated by FNAC. The smears showed syncytial aggregates of epithelioid histiocytes intermixed with small and medium-sized lymphoid cells containing round to irregular-shaped nuclei and small nucleoli. Some of these cells had a greater amount of cytoplasm and frequently had a plasmacytoid appearance. The lesion was removed, and histopathologic study showed MZCL associated with extensive nonnecrotizing granulomas.

CONCLUSION: Granulomatous reactions can be seen in rare cases of MZCL. However, the cytologic features of the lymphoid infiltrate can suggest the possibility of MZCL in the clinical setting of FNAC performed from an extranodal location, such as the parotid gland. (Acta Cytol 2004;48:420–424)

Keywords: lymphoma, B-cell; parotid cancer; granuloma; aspiration biopsy; marginal zone B-cell lymphoma.

Epithelioid granulomas are a common finding in disorders with different causes, including sarcoidosis, foreign body reactions and a variety of infectious diseases, such as tuberculosis, toxoplasmosis, histoplasmosis, brucellosis and tularemia.10 Granu-
lomatous reactions have also been reported in solid neoplasms, including carcinomas, Hodgkin’s disease and some types of non-Hodgkin’s lymphomas, among which have been a few cases of marginal zone B-cell lymphoma (MZCL). However, to our knowledge, the cytologic features of this association have not been documented before. We present the cytologic findings of MZCL of the parotid gland associated with a florid granulomatous reaction.

Case Report

An 82-year-old male with a previous history of recurrent enlargement of the left parotid gland for 10 years presented with a firm, painless, enlarged parotid gland. Ultrasound and computed tomography revealed a 7-cm parotid mass. No lymphadenopathy or other abnormalities in the thoracic or abdominal organs were identified. All laboratory analyses were within normal limits, and cultures, including *Mycobacterium tuberculosis*, were negative. Fine needle aspiration cytology (FNAC) of the parotid gland was performed.

Cytologic Findings

The material obtained was air dried and stained by the May-Grünwald-Giemsa method. The smears showed abundant lymphoid cells intermixed with variable number of epithelioid histiocytes with round or elongated, footprint-shaped nuclei arranged as single cells and, more commonly, in syncytial aggregates (Figure 1). Giant multinucleated cells were not observed. The lymphoid popula-

Figure 1 Smear showing 1 syncytial aggregate of epithelioid histiocytes surrounded by lymphoid cells (May-Grünwald-Giemsa stain, ×200).

Figure 2 Small and medium-sized lymphoid cells with round to irregular-shaped nuclei and occasional micronucleoli. Note the presence of some cleaved nuclei (arrow) (May-Grünwald-Giemsa stain, ×400).

tion was composed of small to medium size cells with scant cytoplasm and round or mildly irregular, occasionally cleaved nuclei, frequently with small nucleoli (Figure 2). In addition, other lymphoid cells had a greater amount of cytoplasm, some with eccentric nuclei, showing a plasmacytoid appearance (Figure 3). Isolated ductal cells were present in the smears, although lymphoepithelial clusters were not seen.

Histologic Findings

The normal architecture of the parotid gland was effaced by confluent areas composed of a dense, lymphoid infiltrate. Between the lymphoid cells was a prominent epithelioid histiocytic reaction that ranged from small clusters to florid granulomas, with some giant multinucleated cells of Langhans type. Necrosis or caseation within the granulomatous areas was not observed (Figure 4). The lymphoid population was heterogeneous, composed of small lymphocytes, centrocytelike cells, monocytoid cells and lymphocytes with a plasmacytoid appearance. These cells surrounded and invaded numerous myoepithelial islands (Figure 5). In the immunohistochemical analysis, the neoplastic cells showed immunoreactivity for CD20 and CD79a (Figure 6). Immunostaining for CD3, CD5, CD10, CD23, CD43 and CD30 was negative. The epithelioid histiocytes were stained with CD68.

Discussion

Extranodal MZCL is a distinctive clinicopathologic
entity categorized in the revised European-American classification of lymphoid neoplasm, originally described by Issacson and called “malignant lymphoma of mucosa-associated lymphoid tissue.” Although initially MZCL was recognized in the gastrointestinal tract, it has also been seen in other extranodal locations, such as the lung, liver, kidney, bladder, thymus, thyroid, breast, skin, orbit, conjunctiva, lacrimal gland and salivary glands. Its association with infectious agents, such as *Helicobacter pylori*, and autoimmune disorders, such as Hashimoto’s thyroiditis and Sjögren’s syndrome is well known.

Primary salivary gland lymphoma is an uncommon neoplasm, and MZCL is the most frequent subtype. MZCL commonly occurs in the parotid gland of adult females and usually presents with an episodic or chronic enlargement of the gland.

Although the histologic and immunohistochemical findings of MZCL are well documented, few cytologic descriptions have been published. The smears generally show a background with a heterogeneous, lymphoid population of small to medium-sized cells composed of small lymphocytes; centrocytelike cells with mildly irregular, occasionally cleaved nuclei and small nucleoli; and monocytoid cells with a greater amount of cytoplasm and variable number of plasmacytoid lym-
phocytes with eccentric nuclei. Based on the cytologic findings alone, MZCL can be difficult to distinguish from benign reactive conditions when FNAC is performed on lymph nodes. However, the appropriate clinical setting is important to suspect this entity in the diagnosis. Therefore, when a florid, lymphoid infiltrate with these cytologic features is observed in an extranodal location, such as the parotid gland, the possibility of MZCL should be considered, although ancillary diagnostic techniques, including immunohistochemistry and flow cytometry, can be required to determine the clonality.

Epithelioid granulomas have been observed in a wide variety of disorders with different causes, among which are sarcoidosis, numerous infectious diseases and malignant neoplasms, appearing within the tumor and in lymph nodes involved and uninvolved by the tumor. They have been noted in solid tumors, particularly keratinizing squamous cell carcinoma, as well as lymphoproliferative disorders, especially Hodgkin’s disease. This epithelioid histiocyte response has been reported in 2–7% of cases of other lymphoproliferative malignancies, such as Lennert’s lymphoma, mycosis fungoides, lymphoplasmaicytoid lymphoma, diffuse large B-cell lymphoma, lymphoblastic lymphoma, multiple myeloma, lymphocytic lymphoma, follicular lymphoma and Burkitt’s lymphoma. However, only a few cases of MZCL associated with epithelioid granulomas have been described, occasionally in the clinical setting of systemic sarcoidosis.

To our knowledge, the cytologic findings of MZCL associated with granulomas have not been documented before. In addition to the cytologic characteristics described above, the smears in our case showed some syncytial groups of epithelioid histiocytes arranged within the lymphoid infiltrate. The presence of epithelioid granulomas in the background can obscure the underlying lymphoproliferative disorder, exacerbating the difficulty of diagnosing this type of lymphoma since it can be misinterpreted as a reactive granulomatous process. However, because of the association with tumors, when a granulomatous reaction is recognized on FNAC, a detailed evaluation of the background should be performed to exclude malignant neoplasms, including MZCL.

The cause of granulomatous reactions in tumors is not well known. Several mechanisms have been postulated for their development. It has been suggested that antigens produced by the tumor cells could elicit a hypersensitivity reaction mediated by T-helper cells and thereby stimulate the activation of monocytes to form epithelioid histiocytes. Although a host response to the tumor is probably the basic mechanism, the specific characteristics of the host that permit such a response are unknown.

In conclusion, although the presence of granulomas is rarely observed in MZCL, this lesion should be included in the cytologic differential diagnosis of neoplasms associated with epithelioid histiocytic reactions. A careful examination of the background is very helpful in suggesting this diagnostic possibility in the appropriate clinical setting of FNAC performed on a mass from an extranodal location, such as the parotid gland. However, histopathologic examination and ancillary techniques, such as immunohistochemistry and flow cytometry, are required to confirm the diagnosis.

References


