A case of thymoma was diagnosed by fine-needle aspiration cytology based on an intimate admixture of a biphasic cell population consisting of epithelial cells and lymphocytes from an intrathoracic mass. The diagnosis was later confirmed by light and electron microscopic examination of the tissue. 

**Key Words:** Fine-needle aspiration cytology; Thymoma

Percutaneous fine-needle aspiration cytology (FNAC), under the guidance of television fluoroscopy and an image intensifier, is a minimally invasive, low-risk, and valuable diagnostic procedure in establishing the diagnosis of a variety of intrathoracic tumors. In recent years, the increasing use of this method has resulted in providing a quick, simple, and reliable preoperative cytologic diagnosis. This is of great benefit to the patient, since it facilitates timely decisions regarding management.

Thymoma commonly occurs in the mediastinum, and the intimate relationship of the pulmonary hilar structures and thymus in this region can pose serious problems in differential diagnosis among thymomas, bronchogenic carcinomas, metastatic tumors, and lymphomas on the basis of clinical and radiologic findings alone. In our institution, we have recently diagnosed one case of thymoma by FNAC; we herein report our findings.

**Case Report**

A 44-yr-old male was admitted with shortness of breath, orthopnea, weight loss, and marked lethargy. He denied any history of hemoptysis, chest pain, edema, or night sweats. The family and social histories were unremarkable. Physical examination was unremarkable except for a mild bilateral piosis, weakness of shoulder abduction, and extension and abduction of fingers. These findings were not accentuated by exercise. A chest x-ray revealed a large lobulated mass in the anterior mediastinum (Fig. 1). A clinical impression of lymphoma or carcinoma was suggested. Computed tomography (CT) revealed the wide extent of the tumor (Fig. 2). Laboratory work-up showed hemoglobin (Hb) to be 11.5 g/100 ml, with a normal platelet count, normal total and differential WBC counts, an erythrocyte sedimentation rate (ESR) of 36 mm/hr, and a mild normochromic anemia. Other hematological and biochemical investigations, including protein electrophoresis, were normal. A Tensilon test and electromyogram (EMG) were normal.

Bronchoscopy was negative. An FNAC of the tumor mass was performed, using a size 22 needle under guidance of fluoroscopy and an image intensifier, and a diagnosis of thymoma was made. At operation, the tumor was found to be nonresectable with extension to surrounding structures. A biopsy of the tumor was obtained for histological and EM study. In view of widespread mediastinal and hilar involvement, the size of the tumor, and, consequently, the size of the lung fields that would be exposed to radiation, a decision for radiotherapy was deferred, and chemotherapy was given on a regimen of six thrice-weekly courses of cyclophosphamide, vincristine, prednisone, and epirubicin (COPE). During the first pulse, the patient developed an episode of profound muscle weakness and respiratory distress. This was well controlled with Tensilon. To date, the patient has undergone a full course of chemotherapy with a considerable reduction in the size of the mass and improvement in his general condition.
Diagnosis of thymoma by FNAC

Cytopathic Findings

Four aspiration smears were wet-fixed in 95% alcohol and stained by the Papanicolaou method while two smears were air-dried and stained by May-Grünwald Giemsa (MGG) stains. The MGG-stained smears showed a biphasic population of cells composed of loose to moderately cohesive clusters of benign-appearing epithelial cell groups of intermediate to large size with minimal pleomorphism, moderate to abundant cytoplasm, and distinct cell borders. The nuclei were regular and round to ovoid with a rare spindly appearance with a slight variation in size, finely granular chromatin, regular delicate nuclear membrane, and small uniform discernible nucleoli. No Hassall's corpuscles were seen. The epithelial cell groups were admixed with varying proportions of lymphocytes (Fig. 3). The majority of the lymphocytes appeared to be of mature type with only a rare activated type. On the basis of the biphasic population of cells, the diagnosis of lymphoepithelial thymoma was suggested.

Histologic Findings

The biopsy from the mediastinal mass on gross examination measured 2.5 x 2 x 1.5 cm and was firm to rubbery in consistency, resembling lymphoid tissue. Multiple sections were studied. These showed a fibrous capsule that extended in the tumor in the form of fibrous trabeculae. The tumor showed a predominant population of epithelial cells with an intimate intermingling of mature lymphocytes (Fig. 4). The epithelial cells were mainly large to intermediate size with ovoid or round nuclei with a well-defined nuclear membrane, fine chromatin, and uniform nucleoli. Only a few nuclei showed an indented nuclear membrane and stippled chromatin. The cytoplasm was pale to eosinophilic. No abnormal mitoses were seen, and other differentiating cells of squamous, spindly, or glandular type were found to be absent.

Electron Microscopic Findings

Electron microscopic (EM) examination of tumor tissue showed two types of cells. The lymphocytes appeared mainly as the resting type, with smooth surface and a rare transformed type with prominent nucleolus. The intervening epithelial cells showed the presence of numerous desmosomes and prominent broad intracytoplasmic tonofilaments. The findings were interpreted as lymphoepithelial thymoma (Fig. 5).
Discussion

Our findings on FNAC were similar to the few recent studies that have described the features of thymomas. Also, in other clinical and morphologic studies, it has been emphasized that the diagnosis of thymomas is not difficult, especially if a biphasic population of cells of lymphocytes and of thymic epithelial cells is found in the specimen from an intrathoracic mass. However, a differential diagnosis from other tumors—for example, malignant lymphomas, seminomas, bronchogenic carcinomas (presenting as a perihilar mediastinal mass), nonneoplastic cysts, and teratomas—needs to be excluded. The absence of cytologically malignant cells of various types seen in bronchogenic carcinomas should exclude these without much difficulty. Malignant lymphomas and seminomas may rarely present a difficulty in differential diagnosis in some cases, especially when the epithelial nature of thymoma is not obvious; an EM study may be necessary for their exclusion. Nonneoplastic cysts and teratomas may sometimes have a few fragments of benign epithelium; although these may cause an initial difficulty of interpretation by FNAC, a lack of intimate admixture of lymphocytes and thymic epithelial cells in these is an important criterion with which to differentiate them from a thymoma.

In studying an anterior mediastinal mass by FNAC, the clinical setting of a patient is important for the diagnosis of thymoma. This setting, for example, can include some cases in whom symptoms of myasthenia gravis, anemia with red cell aplasia, and hypogammaglobulinemia may be present at the time of presentation. In the patient described in this report, initial physical signs did suggest a possible developing myasthenia gravis and a mild anemia along with an anterior mediastinal mass by CT. However, FNAC was most instrumental in the diagnosis of thymoma due to the biphasic population of cells and a subsequent confirmation on histology and EM study of tissue from the tumor.

References


Fig. 4. The tumor shows intimate intermingling of epithelial cells and mature-appearing lymphocytes (hematoxylin-eosin, x 400).

Fig. 5. EM findings of epithelial cells with desmosomes (D) and tonofilaments (T) shown by arrows (uranylacetate and lead citrate, x 9,000).