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內文：

Introduction

Lymphoepithelioma-like carcinoma of the skin (LELCS) is a rare tumor of unknown etiology, low malignant potential, and microscopic resemblance to undifferentiated nasopharyngeal carcinoma. Clinically, it presents as a flesh-colored firm nodule or plaque on the face, scalp, or shoulder of middle-aged to elderly individuals. Histologically, LELCS is composed of islands of enlarged epithelial cells with large vesicular nuclei surrounded and permeated by a dense lymphoplasmacytic infiltrate. LELCS exhibits immunoreactivity with high-molecular-weight cytokeratins and epithelial membrane antigen, indicating the epithelial origin. The differential diagnosis includes basal cell carcinoma, squamous cell carcinoma, lymphoma, pseudolymphoma, and Merkel cell carcinoma. We report 11 cases of LELCS of the head and neck region with discussion of the clinical, histopathologic, immunohistochemical, and therapeutic aspects of this rare cutaneous neoplasm.

Lymphoepithelioma-like carcinoma of the skin (LELCS) was first described by Swanson et al. in 1988 as a distinctive primary malignant neoplasm with remarkable microscopic similarity to undifferentiated carcinoma of the nasopharynx. There have been only 54 reported cases of primary LELCS of the head and neck in the English-language literature. Clinically, LELCS has a predilection for sun-exposed skin of the head and neck in elderly individuals. There is a tendency toward local recurrence and very limited metastatic potential. The clinical appearance of LELCS is varied and ranges from a solitary flesh colored nodule or plaque. Histologically, LELCS is composed of a neoplastic epithelial component associated with a reactive lymphoid infiltrate. The epithelial component of the tumor is represented by atypical polygonal cells with vesicular nuclei and prominent nucleoli. The histologic diagnosis of LELCS may be complicated by the variable architectural of the epithelial cells and the dense lymphoplasmacytic infiltrate. Immunohistochemical evaluation may serve to exclude other histologically similar lesions. Owing to the close histologic similarity to nasopharyngeal lymphoepithelioma, patients with suspected LELCS should have a thorough examination, including indirect laryngoscopy to rule out a metastatic nasopharyngeal lymphoepithelioma. Although the skin metastasis of nasopharyngeal lymphoepithelioma is extremely rare, they are associated with a worse prognosis. Eleven new LELCS cases are reviewed along with previously reported cases.

MATERIALS AND METHODS

Eleven cases of LELCS of head and neck were identified in the Armed Forces Institute of Pathology(AFIP) files.The clinical findings, including presentation, patient age, gender, location, and clinical differential diagnosis, were reviewed. When necessary, the contributors were contacted for additional material and follow-up information. Additionally, a review of the available English-language literature was

performed.

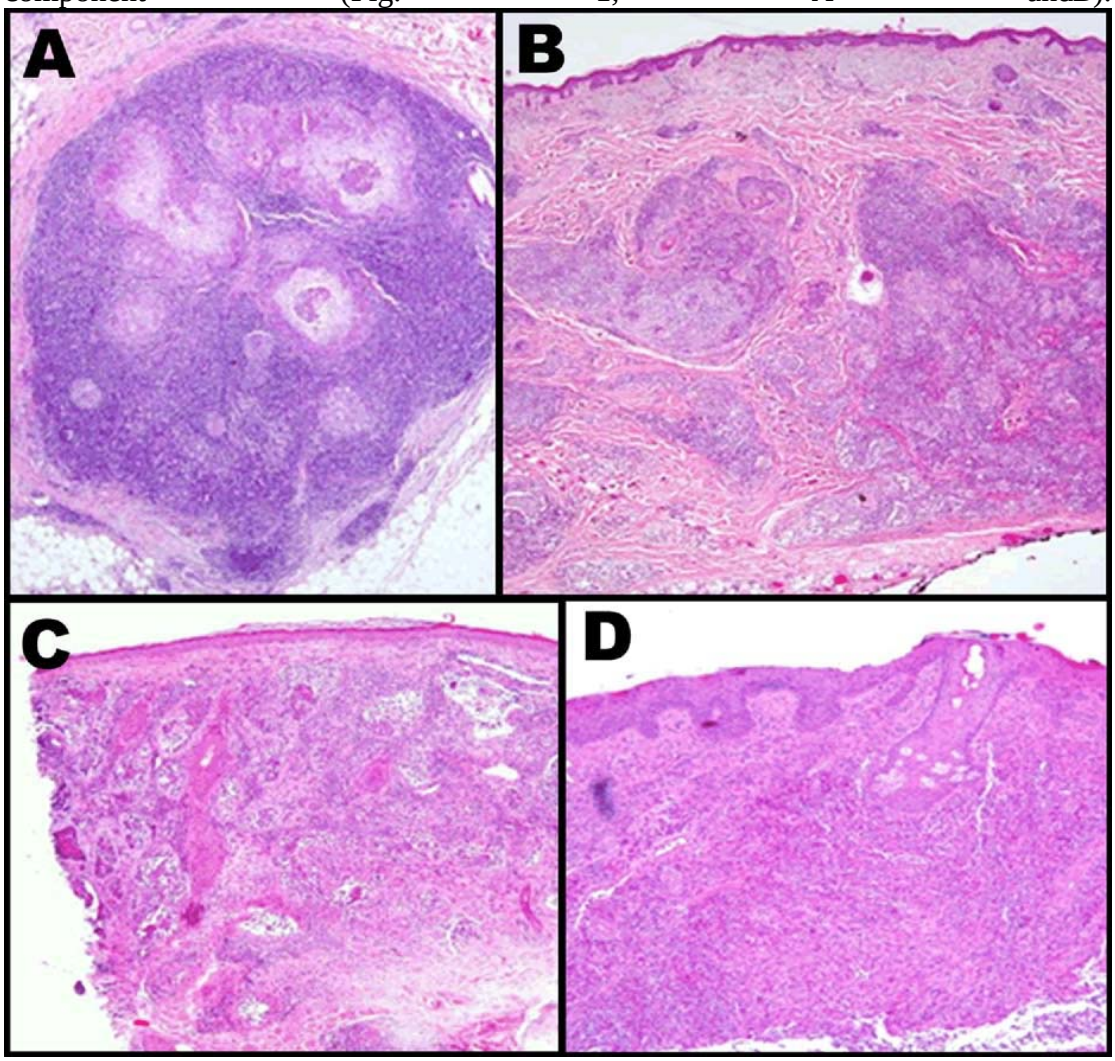
RESULTS

Clinical findings

Eight patients (72%) were male and 3 (28%) female. Patients ranged in age from 47 to 84 years, which is similar to the previously reported cases. As in the previously reported cases, all lesions were located on sun-exposed areas of head and neck, involving forehead (2), cheek (2), ear (2), zygoma (1), scalp (1), temple (1), eyebrow (1), and upper lip (1). Most cases presented as a solitary flesh-colored pearlescent or erythematous firm nodule or plaque, often roughened. The most commonly offered clinical differential diagnosis was basal cell carcinoma. The treatment modalities for the cases included local surgical excision, reexcision of residual tumor after incomplete removal. The clinical follow-up was available for 8 patients: 5 patients were alive without evidence of recurrent disease, and 3 died of unrelated causes with no evidence of disease.

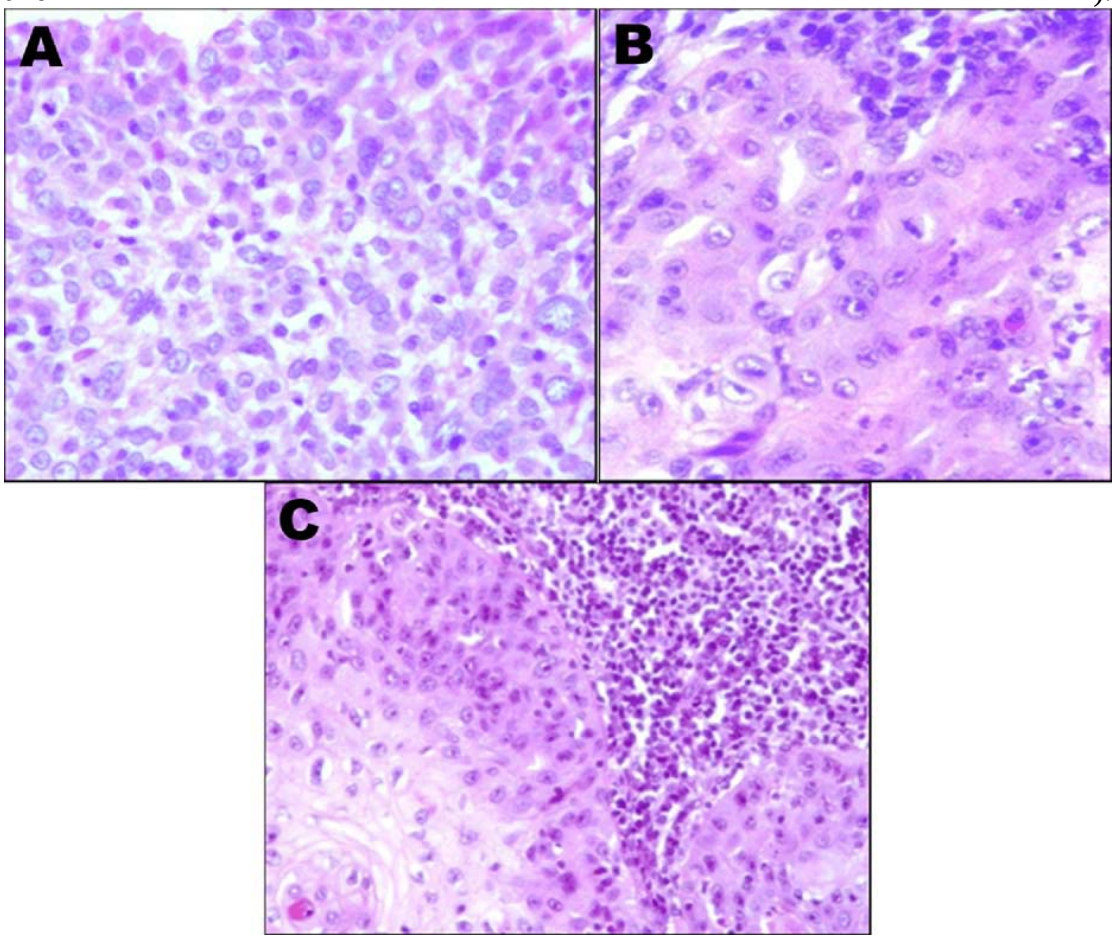
Histologic findings

The 11 cases revealed 2 distinct histologic growth patterns. Seven cases were characterized by nodular growth of atypical epithelioid cells in the middle and deep dermis associated with a dense lymphoid infiltrate with a variable plasma cell component (Fig. 1, *A* and*B*).

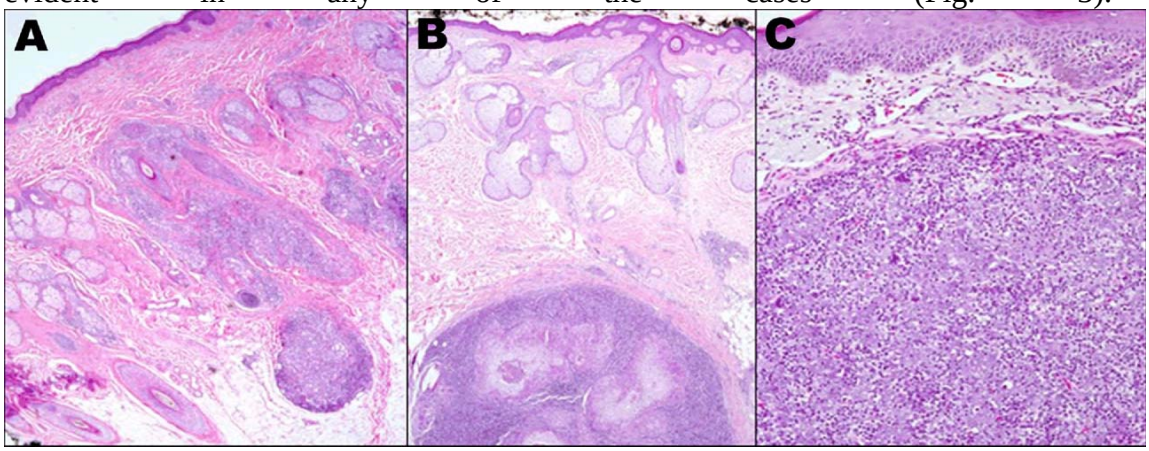


Four cases exhibited diffuse growth of a cohesive more sheet-like atypical epithelioid cells with scant lymphoid component approximating surface epidermis (Fig. 1, *C* and *D*). The tumor cells appeared to be of moderate size with vesicular, monotonous, and

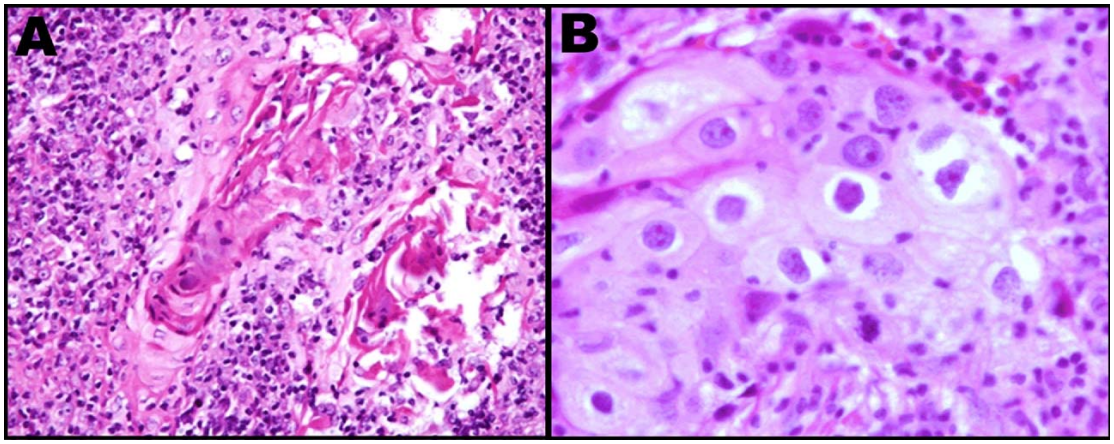
polymorphic nuclei. Mitotic figures ranged from 1 to 8 per high-power field (Fig. 2, *A* and *B*).



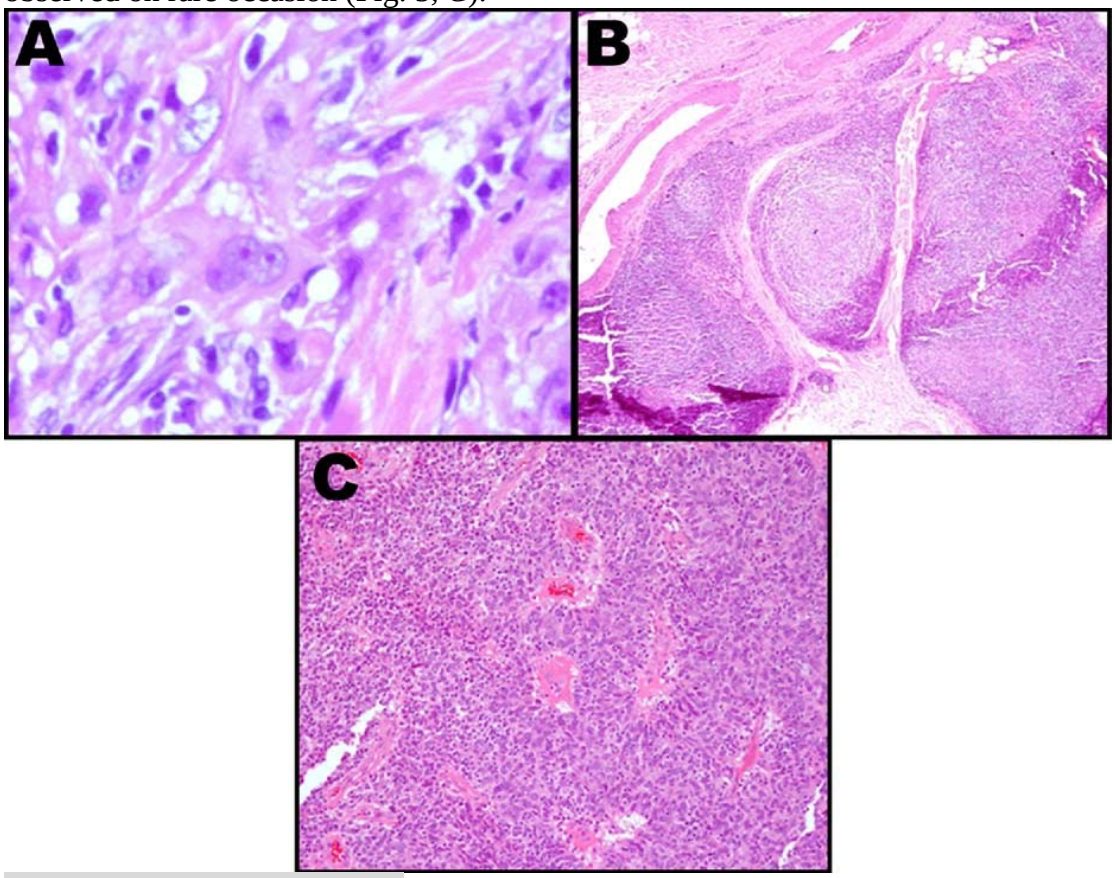
The borders of the atypical epithelioid component were often indistinct, blending with the lymphoid stroma (Fig. 2, *C*). No connection to the overlying epidermis was evident in any of the cases (Fig. 3).



Two of the present cases displayed evidence of squamous differentiation (Fig. 4, *A*), and a sebaceous differentiation was independently observed in another (Fig. 4, *B*).

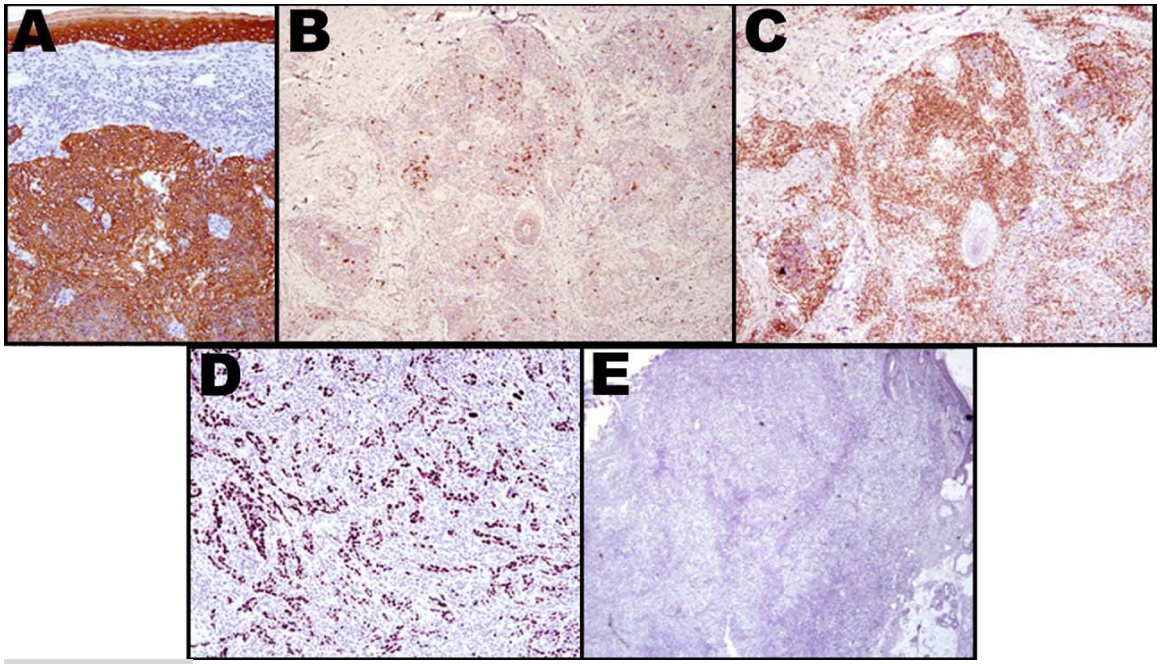


Reed-Sternberg–like cells were noted in 1 case (Fig. 5, *A*). The stromal fibrosis was not uniform, and 1 case demonstrated prominent collagenized fibroblastic stroma dividing the tumor cells into compartments (Fig. 5, *B*). "Pseudorosettes" were observed on rare occasion (Fig. 5, *C*).



Immunohistochemical findings

The neoplastic cells showed strong positive reaction with pancytokeratin (Fig. 6, *A*). The surrounding lymphoid infiltrate exhibited a positive reaction with the T-cell and B-cell markers CD3 and CD20, respectively (CD3 _ CD20; Fig. 6, *B* and *C*). All tumors exhibited strong p63 protein reactivity (Fig. 6, *D*). Stains for Epstein-Barr virus (EBV) latent membrane protein 1 (Fig. 6, *E*) cytokeratin CK- 7, CK-20, neuron-specific enolase, and carcinoembryonic antigen were negative in all of the cases studied (Table III).



DISCUSSION

LELCS is a tumor of low malignant potential that is morphologically similar to undifferentiated nasopharyngeal carcinoma and lymphoepithelioma-like carcinoma occurring in other anatomic sites, such as salivary glands, tonsils, larynx, thyroid, thymus, lungs, stomach, breasts, and uterine cervix. LELCS is usually seen in older individuals and has a male predilection. Our study of 11 cases demonstrated a definite male bias similarly to the data collected from the published literature
(Table II). The most frequent location for LELCS is sun-exposed skin of the head and neck region. Clinically, LELCS appears as an asymptomatic, slowly enlarging, solitary, flesh- or red-colored, firm nodule or plaque. The clinical differential diagnosis of LELCS includes basal cell carcinoma, squamous cell carcinoma, keratoacanthoma, and Merkel cell carcinoma (MCC). Histomorphologically, LELCS is characterized by nests, cords, or sheets of mitotically active polygonal epithelioid cells with hyperchromatic nuclei. The tumor cells display a syncytial or cohesive growth pattern surrounded by variable amounts of a lymphoid stroma composed of small lymphocytes.

The most frequent submitted microscopic differential diagnoses for the present cases were LELCS and atypical lymphoid proliferation.The histologic differential diagnosis of LELCS is wide, including cutaneous lymphadenoma, metastatic nasopharyngeal carcinoma, metastatic lymphoepithelial carcinoma from other organs, follicular dendritic cell tumor, MCC, melanoma, Hodgkin disease, and lymphoma.

The immunohistochemical profile of LELCS aids in differentiating it from other histologic mimics. LELCS expresses high-molecular-weight cytokeratins and epithelial membrane antigen reactivity. The tumor cells are negative for carcinoembryonic antigen, S-100 protein, CK-20, CK-7, and neuron-specific enolase. Surrounding lymphoid cells show reactivity with T-cell and B-cell markers.

Cutaneous lymphadenoma also exhibits a dense lymphocytic infiltrate similar to that of LELCS which surrounds the neoplastic lobules. But unlike LELCS, the neoplastic cells of cutaneous lymphadenoma are monomorphous, there is no mitotic activity. The most complex differential diagnosis of LELCS is a metastatic nasopharyngeal carcinoma. The histopathologic features of metastatic nasopharyngeal carcinoma are akin to those of LELCS, and the only reliable method to differentiate the two lesions

is by testing for EBV. LELCS stains negative to EBV, in contrast to the EBV-positive staining of nasopharyngeal carcinoma.
Follicular dendritic cell tumor (FDCT) is histologically similar to LELCS. The diagnosis of FDCT is confirmed by immunohistochemical studies. In contrast to LELCS, the tumor cells of FDCT stain negative for cytokeratins. FDCT stains positive for FDC markers, namely Ki-M4, CD21, and CD35.
Metastatic lymphoepithelial carcinoma from other organs and primary LELCS are identical both histogically and immunophenotypically, but are different in their association with EBV. Metastatic LELCS are positive for EBV.
Merkel cell carcinoma is histologically characterized by closely approximated hyperchromatic cells. Unlike LELCS, MCC may demonstrate connection to the surface epithelium. The other important histologic criterion that separates these 2 entities is the absence of lymphocytic infiltrate in MCC.
Microscopically, LELCS may also bear resemblance to Hodgkin lymphoma owing to the presence of occasional binucleated cells resembling Reed-Sternberg cells. Negativity for cytokeratin and positivity for CD30 and CD15 support a diagnosis of Hodgkin lymphoma.
The immunohistochemical profile of melanoma is used to distinguish it from LELCS. The neoplastic cells of melanoma stain positively with S-100 and HMB-45 and negatively with cytokeratins.
Although LELCS represents a distinct pathologic entity, its histogenesis still remains unclear. There have been competing opinions regarding the origin of LELCS among different reviewers.
Adnexal origin is favored by many authors because of its location in the dermis .
All of our cases exhibited strong p63 protein reactivity, supporting the epithelial origin with a putative adnexal histiogenesis.
Some authors favor epidermal origin based on the presence of keratinocytic atypia and epidermal involvement. None of the present 11 cases exhibited these features. Like undifferentiated nasopharyngeal carcinoma, LELCS may be a squamous cell carcinoma variant. In spite of the high-grade histologic features of LELCS, the prognosis is good. There have been reports of recurrences after incomplete excision.
The treatment of choice is complete surgical removal. To prevent local recurrence, some reports also recommend micrographic surgery. It is imperative to properly diagnose and adequately treat this type of malignancy with complete excision of the tumor. Close clinical follow-up of the patient is recommended. Metastasis to lymph nodes and internal organs (liver, lungs, and bone), though exceptionally uncommon (only 5 cases), have been reported. In conclusion, LELCS is an uncommon neoplasm that is rarely suspected at the time of presentation. It displays distinctive histologic features and similarities to nasopharyngeal carcinoma. Awareness can serve to prevent a diagnostic and therapeutic misadventure.

題號	題目
1	下列關於basal cell carcinoma敘述何者錯誤 (A) 85%的case發生於頭頸部的skin (B) 主要造成原因是長期暴露於紫外線 (C) 在美國,佔了skin cancer的50% (D) 可分成pigmented ， sclerosing ， superficial ， nevoid四種類型的basal cell carcinoma
答案(C)	出處：Oral & Maxillofacial Pathology second edition P.373

	“representing 80% of all skin cancers in the United States”
題號	題目
2	下列關於nasopharyngeal carcinoma敘述何者錯誤 (A) First sign of disease主要是enlarged , firm 的cervical lymph node metastatic tumor (B) 主要的治療方式是radiotherapy結合chemotherapy (C) Microscopic examination之下，主要呈現squamous cell carcinoma , differentiated nonkeratinizing carcinoma , indifferentiated nonkeratinizing carcinoma三種型態 (D) 承上選項，在每一個biopsy之中，只會發現其中一種型態的病變
答案(D)	出處：Oral & Maxillofacial Pathology second edition P.372