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Cytological diagnosis of typical carcinoid on bronchoscopic brush smears in an HIV-positive patient

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ABSTRACT

We report a case of typical carcinoid of the lung in a 60-year-old human immunodeficiency virus (HIV)-positive man diagnosed on brush cytology smears. Bronchial carcinoids are rare tumors, accounting for 1% to 2% of all lung tumors. Although the exact incidence in HIV-infected individuals is not known, the paucity of their documentation in the literature indicates that they may be equally rare. Cytological diagnosis on brush smears is rarely documented as the tumor is covered with mucosa and cellular yield is often not good. In this case, bronchial brushings showed distinctive cytological features of typical carcinoid. The awareness of its characteristic cytological features and differential diagnosis is required for an accurate diagnosis. Clinical awareness that non–acquired immunodeficiency syndrome (AIDS)-defining cancers can also occur in HIV-infected individuals in the context of the prolonged survival in the antiretroviral era is equally important. This case emphasizes the clinical importance of a broad differential diagnosis for lung lesions in HIV-positive patients.

Key words: Bronchial; brush cytology; carcinoid tumor; human immunodeficiency virus; lung; neuroendocrine.

Introduction

Bronchial carcinoids are rare, low-grade malignant tumors that account for 1% to 2% of all lung tumors.[1] Our literature search elicited only one published case report in an human immunodeficiency virus (HIV)-infected individual.[2] We present a case of bronchial carcinoid diagnosed on brush smears in an HIV-positive man. The characteristic cytological features on brush smears, differential diagnosis and causes of diagnostic pitfalls are highlighted. The diagnosis of this tumor has been well documented on fine-needle aspiration (FNA);[3] however, brush cytology is considered of limited or no value for its diagnosis.[4,5]

Case Report

This 60-year-old HIV-positive man was admitted with generalized joint pains and fever of three days’ duration. He had been on antiretroviral therapy for the past seven years. The patient had history of shortness of breath and palpitations, weight loss and chronic cough for more than two years. He often had chest pain that was localized to the retrosternal area and lower chest bilaterally. He was given empirical treatment for tuberculosis at another health facility.

On physical examination, the patient was found to be wasted. The predominant signs were elicited in the respiratory system with diminished resonance in the basal regions bilaterally; increased tactile fremitus and crepitations in the basal region of the right lung; and diminished breath sounds in the basal region of the left lung.

His latest viral load was 57 copies/µL, and CD4 count was 400/µL. Sputum was negative for acid-fast bacilli. Chest radiograph showed opacification of the left lung base. Computerized tomography scan showed a left lower lobe mass with surrounding consolidation and abscess formation. The mass measured $6.28 \times 8.1 \times 7.67$ cm.

Bronchoscopy revealed a large polypoid endobronchial mass in the left lower lobe bronchus with a smooth glistening
surface [Figure 1]. Bronchial brushings, washings and biopsy were performed.

Papanicolaou-stained smears of the bronchial brush were highly cellular, composed of a monomorphic tumor cell population. The cells were arranged in small and large nests, branching trabeculae and anastomosing cords. A large population of cells was dispersed singly [Figure 2a]. There were numerous capillaries, and tumor cells were clinging to them [Figure 2b]. Some tumor cells were arranged in rosettes or acini, resembling an adenocarcinoma [Figure 2c]. Individual tumor cells were polygonal to round in shape with moderate amounts of pale cytoplasm and central or eccentric regular nuclei. Nuclei showed salt-and-pepper chromatin and inconspicuous nucleoli with smooth nuclear membranes. There was no nuclear molding, or pleomorphism but an occasional mitosis was seen. The background was generally clean and necrosis was absent. Few naked nuclei were seen; however, there was no nuclear streaking. A cytological diagnosis of typical carcinoid was rendered. The bronchial wash specimen showed, mainly, blood; and a few singly dispersed tumor cells similar to those seen in the brush smears.

Hematoxylin and eosin section from the bronchoscopic biopsy showed solid nests and trabeculae of medium-size polygonal cells with round uniform nuclei and pale cytoplasm [Figure 3a]. There was no nuclear molding. Chromatin was finely stippled. The tumor cells were monomorphic. Mitotic activity was absent and there was no necrosis. The cytoplasmic positivity with synaptophysin in the tumor cells confirmed the cytological diagnosis [Figure 3b].

Figure 1: Endobronchial growth on bronchoscopy

Figure 2: (a) Bronchial brush smear showing high cellularity composed of monotonous polyhedral cells in nests and scattered singly (Papanicolaou stain, ×200). (b) Tumor cells clinging to capillary (Papanicolaou stain, ×100). (c) Tumor cells forming acini like an adenocarcinoma and scattered singly. Nuclei show salt-and-pepper chromatin (Papanicolaou stain, ×400)
Discussion

Typical carcinoids (TCs) arise from Kulchitsky cells and are classified as neuroendocrine neoplasms of the lung, which also include atypical carcinoid, large-cell neuroendocrine carcinoma and small-cell carcinoma. TC represents the most well-differentiated and least aggressive end of the spectrum with slow growth and infrequent metastasis.[1]

Diagnosing the exact subtype is a challenge to the clinician and the pathologist alike because clinical data is of little help and radiological and bronchoscopic findings are non-specific. Carcinoid syndrome, Cushing syndrome, acromegaly, hyperpigmentation, syndrome of inappropriate excretion of anti-diuretic hormone, and hypoglycemia are rare presentations in bronchial carcinoids as compared to gastrointestinal carcinoids.[1,3,5] Our patient did not have any evidence of a para-neoplastic syndrome. There was no evidence of associated multiple endocrine neoplasia, which is known to occur in about 4% of patients.[1,5]

Approximately 75% of patients present with central tumors, and 52% are symptomatic with cough, hemoptysis, wheeze, recurrent pneumonia or chest pain. The symptoms are related to the presence and degree of endobronchial occlusion and the vascularity of the tumor.[1,5,6]

Tissue sampling is essential for definitive subtyping. Severe hemorrhage can occur after biopsy of a bronchial carcinoid during bronchoscopy. In such a situation, cytologic sampling causing minimal trauma confers an advantage. A variety of cytology specimens can be obtained, such as sputum, bronchial wash, brush and transbronchial FNA. Each specimen has different diagnostic yield, depending upon the location of the tumor, skills of the bronchoscopist and experience of the cytopathologist. Sputum and bronchial wash specimens often fail to yield diagnostic material as the tumor is generally covered with intact bronchial mucosa.[7,8] Transbronchial FNA also has the risk of bleeding similar to that after biopsy.

Bronchial brushing technique has the advantage that the surface of the suspicious lesion is scraped with a brush, thus dislodging the cells from the surface of those lesions that do not exfoliate cells readily. Thus the chances of getting adequate sample with better preserved morphology are high in comparison to the already exfoliated cells sampled in sputum or bronchial wash specimens, as was evident in our case.

The cytological features of TC in brush smears were characteristic in our case and similar to those in FNA.[6,9] TC may be mistaken for a well-differentiated adenocarcinoma due to its polygonal cells with bland cytology often forming acini. Abundant scattered naked nuclei can resemble hyperplastic reserve cells, small-cell carcinoma or non-Hodgkin lymphoma.[7,9] Features that helped to exclude these differential diagnoses in our case included cells with moderate amount of cytoplasm forming loose clusters despite high cellularity and absence of tightly cohesive cells like in a carcinoma; bland monotonous appearance with minimal or no variation in cell size; typical salt-and-pepper chromatin; paucity of naked nuclei; and absence of nuclear streaking and molding. In addition, the tumor cells surrounding, and clinging to, the arborising delicate capillaries was a distinct and noteworthy feature characteristic of carcinoid tumors.[10]

Atypical carcinoid is cytologically similar to the classical type but shows necrosis and mitoses. Tumor cells from small-cell carcinoma show Indian-filing, nuclear molding and rosette arrangement with many naked nuclei and nuclear streaking.[11] The background is often necrotic. The characteristic cytological features of large-cell neuroendocrine carcinoma include large tumor cell size, cohesive cells, fine chromatin, prominent nucleoli, thin nuclear membranes, naked nuclei, nuclear streaking and a necrotic background.[6,9,11] There was no necrosis, and mitotic activity was scant in our case.

The cytological diagnosis of carcinoid lung was challenging in this HIV-infected patient due to its rarity and lack of clinical suspicion. Clinicians and cytopathologists need to be aware that the incidence of non–acquired immunodeficiency syndrome (AIDS)-defining cancers (NADCs) is on the rise in the antiretroviral era. It is also critical to be familiar with the cytological features of TC, its differential diagnoses and potential pitfalls. This is particularly important for those centres where respiratory cytology is performed infrequently. An accurate cytological diagnosis can contribute to appropriate and timely treatment.
The fact that NADCs appear to have an earlier onset and worse prognosis in HIV-infected patients than in the general population has implications for patient care. Surveillance of HIV-infected patients with NADCs is imperative to identify risk factors, risk-reduction strategies, early and accurate diagnosis and optimal treatment.

Conclusion

In conclusion, the case is atypical because it is rare and the diagnosis was clinically unsuspected in light of the HIV status of the patient. A cytological diagnosis has rarely been documented in brush smears. The cytological diagnosis was possible because of the high cellularity of the smears, well-preserved cell morphology and characteristic cytological features in correlation with bronchoscopic findings. This case emphasizes the clinical importance of a broad differential diagnosis for lung lesions in HIV-infected patients.

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