Malaysian J. Path., 1: 55–57, 1978

BRONCHIOLO–ALVEOLAR CARCINOMA–UNUSUAL PRESENTATION IN FIVE WOMEN. A BRIEF CYTOPATHOLOGICAL AND CLINICAL APPRAISAL

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Summary

Five women with clinical modes of presentation not suggestive of an underlying malignant disease, were investigated cytologically in the course of routine examinations. The incidental discovery of characteristic malignant cells in the various types of material submitted for study, led to further diagnostic procedures including several more cytological evaluations. The final report of bronchiolo-alveolar carcinoma was confirmed histologically. The value of cytological methods in identifying this tumour and its diverse clinico – pathological manifestations are emphasised.

Bronchiolo-alveolar carcinoma is reported to form 2–5% of bronchogenic carcinomas[1] and is described as a tumour of middle and later life with a peak occurrence in the sixth decade. Though there is a general impression that it is peculiar to women, larger series have shown no significant sex predilictions.[2] In a review of 18 cases diagnosed cytologically between 1976 and 1977, five with unusual clinical pictures were encountered and these are reported here.

CLINICAL DATA

Case 1

A 37 year old Malay female was investigated for cough, chest pain, haemoptysis and low-grade fever of two months duration. Chest X-Rays showed widespread small soft shadows in both lung fields, interpretted as extensive tuberculous pneumonitis. In addition to other procedures to rule out a tuberculous etiology, cytological examination of sputum was carried out. All three specimens of sputum were reported positive. The patient was subsequently bronchoscoped and the bronchial washings were also positive for malignancy.

Cases 2 & 3

Two Chinese females aged 29 and 31 presented at different clinics with massive pleural effusion on the right side of less than a week's duration. There were no preceding symptoms of ill-health. In both cases the clinical diagnosis was tuberculous pleuritis with effusion. Aspirated fluid yielded malignant cells and post aspiration chest films showed sub-pleural parenchymal scarring of the right upper lobes. The second patient, while in the ward and following pleural drainage, developed a productive cough. Sputum examination revealed tumours cells similar to those from the pleural fluid.

Case 4

In the course of a routine medical examination before going abroad, chest X-Rays in a 27 year old Chinese female revealed a solitary peripherally situated mass in the right upper lobe of the lung. On further questioning she admitted to having occasional cough with mucoid sputum which she attributed to smoking. She had been smoking about 20 cigarettes a day for over 5 years. Bronchial washings obtained at a later date were positive for malignant cells.

Case 5

A 27 year old Chinese female presented as an acute medical emergency with cardiac tamponade and pericardial effusion. The fluid drained contained malignant cells while radiographic investigations of the chest revealed multiple confluent densities occupying both lobes of the left lung. Sputum cytology was positive on three consecutive occassions.

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MATERIALS & METHODS

The specimens consisted of sputa, bronchial washings and serous fluids. They were received in a fairly fresh unfixed state. Two smears were made from each specimen and stained by Papanicolaou's technique. Millipore filters were employed for bronchial washings and serous fluids. Criteria described by Roger et al[3] were used to type the tumours cytologically. Histological confirmation was obtained from bronchial biopsies, thoracotomy specimen and pleural biopsies.

RESULTS

The most significant finding was the abundance of characteristic malignant cells in every type of specimen submitted for cytological examination, namely, sputa, bronchial washings, pleural fluids and pericardial fluid. Neoplastic cells were largely arranged in tight papillary clusters with many cell groups showing significant depth of focus. Uniformity of cells with rather characteristic folded nuclei, scarcity and in some cases absence of prominent nucleoli were the diagnostic features of this tumour. Occurrence of single cells was uncommon. The presence of fair numbers of transition forms between perfectly benign respiratory epithelial cells and frankly malignant cells in specimens of sputum and bronchial washing was a point in favour of a primary lung cancer.

DISCUSSION

Though the first specimens from each case were sent for cytologic examination as a routine investigative procedure, a positive result was unexpected. The age of the patients, 27–37 years, which is at least two decades younger that the reported susceptible age, was possibly a misleading factor. Cahan[4] discussing the critical age for primary lung cancer versus a metastastic or benign process, comments that below 35 years, primary tumours are rare and improbable while above this age, it can and does occur with increasing probability. The short history of illness and the mode of presentation were also probably responsible for leading the clinical diagnosis astray. It is a well-documented character of the tumour, that the patients are asymptomatic for a considerable period of time. Delarue et al[5] appraising bronchiolo-alveolar carcinoma, describe it as a tumour most capable of mimicry, producing a fascinating array of radiological appearances which include coin lesions, cavitatary lesions, pneumonic lesions, scar lesions or diffuse multinodular lesions. Because of its diverse radiopathologic manifestations, pulmonary secondaries, pneumoconiosis, miliary tuberculosis and other granulomatous diseases have to be considered in the differential diagnoses. A unusual case which was X-Ray negative but which on exploratory thoractomy had a small primary lesion and a non-resectable metastatic mediastinal mass is described by Watson and Farpour.[6]

Though there is some debate in the literature on the need for or the validity of cyto-histologic typing of bronchiolo-alveolar carcinoma as a separate entity[7], the weight of microscopic evidence supports this categorization. The International Histological classification of the World Health Organization[8] describes it as a very well differentiated tumour orginating in the peripheral part of a lung beyond a recognizable bronchus with a tendency to grow upon pre-existing alveoli and forming papillary clusters in large numbers. Cytologic diagnostic accuracy improves with the number and quality of specimens examined. Mears, Kirklin and Woolner[9] report 63.7% accuracy with cytologic material while Roger et al[3] identified 90% of bronchiolo-alveolar carcinoma purely from cytological material. When this tumour exfoliates cells, it does so profusely, a feature not noticable with epidermoid or anaplastic carcinomas. Apart from the distinctive appearances discernible under the light microscope, there are electron microscopic data supporting the concept that bronchiolo-alveolar carcinoma is a histologic entity.[10,11]

The role of known carcinogens in the evolution of this tumour is uncertain. Though not as decisively etiologic as in epidermoid and anaplastic carcinoma, cigarette smoking appears to play some role. 91% of males and 65% of females were smokers in a report of 256 cases of terminal bronchiolar cancer by Watson and Farpour.[6] There is some thought of a viral etiology based on the similarity of the tumour histologically to a disease of S. African sheep called "jagziekte' and the occurrence of the tumour in two persons exposed to the diseased sheep.[12] Reporting this tumour in male identical twins, Joishy *et al*[13] advance a view that genes not only determine the susceptibility to

malignant change of pulmonary cells but also the character of the resultant tumour.

The importance of identifying this tumour is not merely of academic interest but is also of great value in determining management and prognosis since the cure rate of localised or single nodule is extremely good.[1,4] Delarue *et al*[5] document a 58% resective cure rate in their series. There appears to be a period of restricted growth before the tumour spreads by air spaces and lymphatic channels to produce metastases. Approximately 50% of tumours do not metastasise beyond the thoracic cavity even if they are widespread in the lungs.[8] Diffuse disease invariably has a dismal outlook.

CONCLUSION

Bronchiolo-alveolar carcinoma is an interesting pulmonary tumour that lends itself readily to cytological identification by virtue of its abundantly exfoliating nature and by the distinctive morphological characteristics of its component cells. Its occurrence in an unsuspected age group and particularly the benign modes of presentation are highlighted in this paper with brief comments on its clinicopathological features as observed in the literature.

REFERENCES

1 Yesner R, Gerstl B and Auerbach O: Application of the World Health Organization classification of lung carcinoma to biopsy material. Ann Thorac Surg, 1: 33–49, 1965.

2 Heitzman ER: Bronchiolar Carcinoma of the lung *In* The Lung – Radiologic – pathologic correlations. The C.V. Mosby Company, St. Louis, 1973, p. 300–313.

3 Roger V, *et al:* Cytologic differential diagnosis f bronchiolo – alveolar carcinoma and bronchogenic adenocarcinoma, Acta Cytol, 20: 303–307, 1976.

4 Cahan W G: Multiple primary cancers of the lung, oesophagus and other sites. Cancer, 40(4Suppl): 1954–1960, 1977.

5 Delarue NC, *et al* Bronchiolo-alveolar carcinoma. A reappraisal after 24 years. Cancer, 29: 90–97, 1972.

6 Watson WL and Farpour A: Terminal bronchiolar or "alveolar all" cancer of the lung. Cancer, 19: 776–780, 1966.

7 Bennett D E and Sasser W F: Bronchiolar carcinoma: A valid clinicopathologic entity? A study of 30 cases. Cancer, 24: 876–887, 1969.

8 Kreyberg L: Histological classification of lung tumours. International Histological Classification of Tumours, No. 1, World Health Organization, Geneva, 1967, p. 22.

9 Mears TW, Kirklin JW and Woolner LB: The fate of patients with alveolar – cell tumour of the lungs. J Thorac Cardiovasc Surg, 27: 420–424, 1954.

10 Kuhn C: Fine structure of bronchiolo – alveolar cell carcinoma. Cancer, 30: 1107–118, 972.

11 Jacques J and Currie W: Bronchiolo – alveolar carcinoma: A Clara cell tumour? Cancer, 40: 2171–2180, 1977.

12 Stephens HB and Shipman SJ: Pulmonary alveolar adenomatosis, cancerous pulmonary adenomatosis, alveolar cell carcinoma of the lung, Jagziekte? J Thorac Surg, 19: 589–603, 1950.

13 Joishy SK, Cooper RA and Rowley PT: Alveolar cell carcinoma in identical twins – similarity in time of onset, histochemistry of site of metastasis. Ann Intern Med, 87: 447–450, 1977.

14 Jackman RJ, Good CA, Clagett OT, et al: Survival rates in peripheral bronchogenic carcinomas up to four centimeters in diameter presenting as solitary pulmonary nodules. J Thorac Cardiovasc Surg, 57: 1–8, 1969.