Eur Respir J.
1991, 4, 1296–1298

CASE REPORT

Metastatic prostatic adenocarcinoma - diagnosed by bronchoalveolar lavage and tumour marker determination

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Metastatic prostatic adenocarcinoma - diagnosed by bronchoalveolar lavage and tumour marker determination. A. Verstraeten, M.-C. Sault, B. Wallaert, P. Lemonnier, B. Gosselin, A.B. Tonnel.

ABSTRACT: We report a patient who presented with a diffuse interstitial lung disease in whom clinical and radiologic investigation led to the suspicion of lymphangitis carcinomatosa. Bronchoalveolar lavage (BAL) was performed and revealed the presence of prostatic specific antigen (PSA) positive cells. A prostatic needle aspiration confirmed the diagnosis of adenocarcinoma. This case demonstrates the value of tumour marker determination in BAL.

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Keywords: Bronchoalveolar lavage; prostatic specific antigen.

Received: May 1990; accepted after revision November 20, 1990.

Supported by INSERM (CJF 90-06) and by Université de Lille II.

Bronchoalveolar lavage (BAL) is used by many in the clinical investigation of diffuse interstitial lung diseases. Most attention has been paid to the cellular components which allow a differential diagnosis in accordance with the predominant cell type [1]. However, in some cases a definite diagnosis can be made by demonstration of a specific feature, such as lipoproteinaceous material in alveolar proteinosis, OKT6+ cells in histocytosis X, malignant cells or microorganisms [1]. We advocate the value of tumour marker determination in BAL.

We present the case of a patient where the diagnosis of metastatic prostatic adenocarcinoma was made by the demonstration of prostatic specific antigen (PSA) positive cells in BAL.

Case report

A patient, 57 yrs old, was admitted complaining of weight-loss and dyspnoea. He had been treated for pulmonary tuberculosis 15 yrs previously and had a longstanding smoking history. Clinical examination revealed some inspiratory crackles in the lower lobes. Lung function showed a predominantly restrictive defect forced expiratory volume in one second (FEV_1) 1455 ml (50% of predicted), vital capacity (VC) 2400 ml (57% of predicted), residual volume (RV) 2350 ml (92% of predicted), total lung capacity (TLC) 4750 ml (70% of predicted) with a lowered diffusing capacity for carbon monoxide (D_{LCO}) of 16.5 $ml \cdot min^{-1} \cdot mmHg^{-1}$ (68% of predicted) and a Po_2 at rest of 51 mmHg breathing air. The chest radiograph showed the sequelae of tuberculosis and a diffuse interstitial infiltrate (fig. 1). A CT scan confirmed the interstitial involvement as well as bronchial wall thickening (fig. 2).

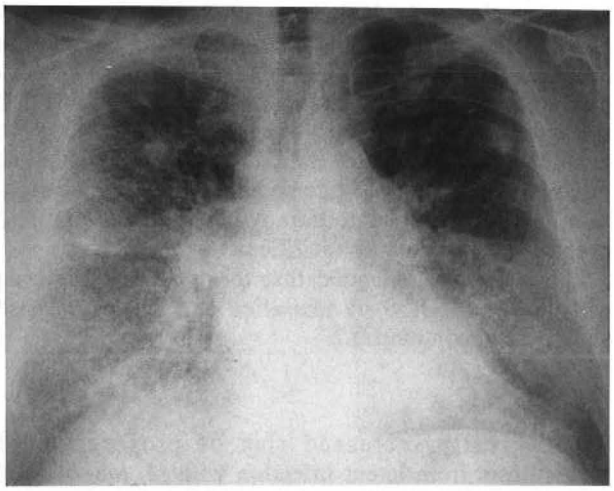

Fig. 1. – Chest radiograph: diffuse interstitial infiltration of lungs predominantly in lower parts in association with nodular lesions.

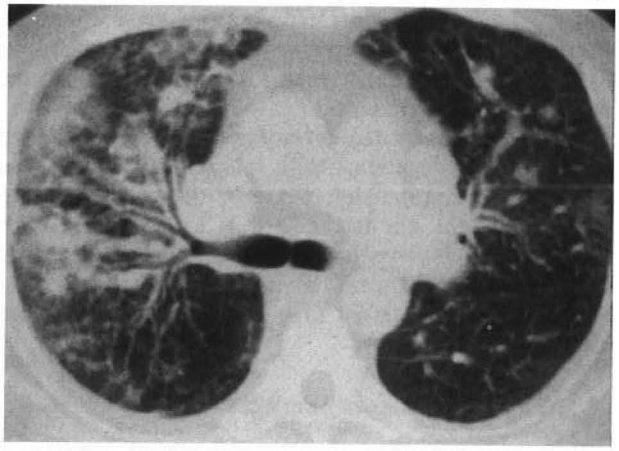

Fig. 2. – CT scan at the level of right upper lobe: interstitial and peribronchial infiltration.

BAL was performed using 5×50 ml saline. The first aliquot was considered as bronchial specimen whereas the next four aliquots were pooled as the alveolar specimen. The alveolar specimen slides were obtained after cytocentrifugation and were stained with Papanicolaou, May-Grunwald-Giemsa and Perls. BAL yielded 190×10^3 cells·mm^3 of which were 70% macrophages, 27% lymphocytes and 3% polymorphonuclear cells. For immunocytochemistry, air dried smears were stored at -20°C. Post fixation with ethanol was performed before immunoperoxydase procedure. Antibody was a polyclonal anti-PSA (dilution at 1/100) (Dakopatt Copenhagen, Denmark). Papanicolaou staining detected four clusters of small round cells, with hypercromatic nuclei, scarce cytoplasm, identified as carcinomatous cells. Immunostaining by anti-PSA antibody was positive on the same cells.

Ultrasonography of the prostate demonstrated a hypoechogenic left lobe; serum PSA was elevated to more than 50 $\mu g \cdot l^{-1}$ (N 0–2.5 $\mu g \cdot l^{-1}$) and prostatic acid phosphatase to 43.2 $U \cdot l^{-1}$ (normal <2.5 $U \cdot l^{-1}$). A needle aspiration biopsy of the prostate confirmed an adenocarcinoma grade 3 + 5, Gleason 2 to 10. There were also diffuse bone metastases on an isotope bone scan.

The patient underwent a surgical resection (pulpectomy) and antiandrogens were started (Nilutamide - Flutamide). Initially, there was a dramatic response to therapy with clinical and functional improvement. Serum PSA dropped to 7 $\mu g \cdot l^{-1}$, with partial radiological improvement. Repeated BAL did not demonstrate any malignant cell. Ten months after diagnosis however the tumour relapsed and chemotherapy and radiotherapy were started.

Discussion

In recent years the search for tumour markers to specify the origin and extension of malignant disease has made a lot of progress. In 1979 WANG *et al.* [3] isolated and purified a glycoprotein specific for prostatic epithelial cells [3]. PSA is confined to the cytoplasm of normal and malignant prostatic acinar and ductal epithelium. Its high specificity and sensitivity for both primary and metastatic prostatic cancers allows the confident identification of the origin of what might otherwise be felt to be a case of adenocarcinoma of unknown origin [4].

Using a sensitive immunoassay, increased levels of circulating PSA have been demonstrated in the serum of patients with prostatic cancer. The level of serum PSA closely correlates with the extent of the disease [4]. While the serum half life is 2.2 days it is useful for assessing the response to therapy and in detecting residual and early recurrence of tumour [5]. Similarly MOROTE *et al.* [6] evaluated PSA in spinal fluid. Whereas PSA is not detectable in normal spinal fluid, it was significantly increased in spinal fluid from patients with prostatic carcinoma and metastases of the skull, vertebral bodies or meningeal membranes.

Intrathoracic manifestations of disseminated prostatic adenocarcinoma can cause lung nodules, mediastinal and hilar lymphadenopathy, lymphangitis carcinomatosa, pleural effusion and corpulmonale due to microscopic tumour emboli [7]. Up to 5–10% of patients initially present with intrathoracic metastases. Since the immunohistochemical marker for prostatic cancer is performed on formalin fixed histological sections or cytological preparations, it seems useful to search for it in areas where metastases may occur. Positive PSA stain has previously been found in pleural effusions [7]. We have demonstrated it here on BAL cytospin preparations in a patient suspected of lymphangitis carcinomatosa. To our knowledge no similar case has been described. A lymphocyte predominant pattern on BAL however has been mentioned in lymphangitic spread of adenocarcinoma to the lung [8]. Moreover GOLDSTEIN *et al.* [9] analysed the value of four tumour markers (carcinoembryonic antigen, calcitonin, creatinine kinase-BB and DNA) measured by radio-immunoassay in BAL and concluded that tumour marker levels in lavage are a useful aid in the diagnosis of malignancy in patients undergoing bronchoscopy.

In accordance to the findings of Goldstein we suggest that determination of tumour markers on BAL cells becomes of increasing interest. Since the primary site leading to lymphangitis carcinomatosa is, in decreasing frequency, stomach, bronchus, breast, pancreas or prostate, organ specific tumour markers may help in establishing both the diagnosis and perhaps the site of the primary tumour.

References

1. Rossi GA. – Bronchoalveolar lavage in the investigation of disorders of the lower respiratory tract. *Eur J Respir Dis*, 1986, 69, 293–315.
2. Desligneres S. – Anatomie pathologique de l'Adenocarcinome de la prostate en 1988. *Ann Pathol*, 1988, 8, 91–105
3. Wang MC, Valenzuela LA, Murphy GP, Chu TM. – Purification of a human prostate specific antigen. *Invest Urol*, 1979, 17, 159–163.
4. Nadji M, Tabei SZ, Castro A, Chu TM, Murphy GP, Wang MC, Morales AR. – Prostatic specific antigen: an immunohistologic marker for prostatic neoplasms. *Cancer*, 1981, 48, 1229–1232.
5. Stamey TA, Yang N, Hay AR, McNeal JE, Freiha FS, Redwine E. – Prostate specific antigen as a serum marker for adenocarcinoma of the prostate. *N Engl J Med*, 1987, 317, 909–916.
6. Morote J, Ruibal A, Boada M. – Behaviour of prostatic specific antigen (PSA) in spinal fluid: its correlation with serum levels. *Int J Biol Markers*, 1986, 1, 109–110.
7. Mestitz H, Pierce RJ, Holmes PW. – Intrathoracic manifestations of disseminated prostatic adenocarcinoma. *Respiratory Medicine*, 1989, 83, 161–166.
8. Fedullo AJ, Ettensohn DB. – Bronchoalveolar lavage

in lymphangitic spread of adenocarcinoma to the lung. *Chest,* 1985, 87, 129–131.
9. Goldstein N, Lippmann ML, Golberg SK, Fein AM, Shapiro B, Leon SA. – Usefulness of tumor markers in serum and bronchoalveolar lavage of patients undergoing fibreoptic bronchoscopy. *Am Rev Respir Dis,* 1985, 132, 60–64.

Metastases d'un adenocarcinome de la prostate diagnostiquées par determination des marqueurs tumoraux dans le lavage bronchoalveolaire.. A. Verstraeten, M.-C. Sault, B. Wallaert, P. Lemonnier, B. Gosselin, A.B. Tonnel.

RÉSUMÉ: Nous présentons le cas d'un patient dyspnéique et hypoxémique hospitalisé pour bilan d'une pneumopathie interstitielle diffuse. Le lavage bronchoalvéolaire révélait des amas de cellules tumorales positives pour l'antigène spécifique de prostate, pathognomoniques du diagnostic de lymphangite carcinomateuse d'origine prostatique. Le diagnostic de carcinome de la prostate fût prouvé ultérieurement par la biopsie prostatique. Cette observation illustre l'intérêt des marqueurs tumoraux spécifiques dans le lavage broncho-alvéolaire.

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