OBJECTIVES

We describe a case of war correspondent with lung cancer and unknowns pneumoconiosis. In the literature were noted sporadically cases of lung cancer in war correspondent (e.g Oriana Fallaci). Inhaled microscopic dust particles laden with toxic metals and a toxic stew with the use of impoverished uranium (but also tungsten) during the bombardments can be real etiology. The IARC recently considered thin dust or nanoparticles as a responsible for death for lung cancer. Hard metal nanoparticles generated by high temperature during a bombing can induced a pneumoconiosis. Dust deposits are not readily identified by either routine or polarizing light microscopy. The individual fine metal particles can be observed by analytical electron microscopy. Tungsten particles and cobalt are the suspected causative agent of the disease but may or may not be identified, since its water solubility makes it susceptible to removal from tissue. After Chemotherapy and Radiotherapy some mineral elements and nanoparticles identified in lung tissue can be endogenous and so it is difficult to discriminate an occupational etiology.

MATERIALS and METHODS: CASE REPORT

Male born in 1941, no smoker, lived in Reggio Calabria until 1963, after in Genova until 1970 and then in Torino. He was war correspondent from 1976 until 2004 in Cambogia, Libano, Algeria, Kuwait, Marocco, Chad, Libia, Salvador, Nicaragua, Panama, Colombia, Iraq, Afganistan, Somalia, Congo, Ruanda.

In 2005, in Miami, incidental not small cells tumor was diagnosed. The cancer was inoperable. The patient was processed to Chemotherapy for 3 mounts and Radiotherapy for 45 sessions, with experimental trial, and after apical lobectomy was done. Today is free of the neoplasia.

In the lung near the cancer was present fibrosis and granulomatous reaction, with cholesterol crystals and elastic fibrosis with nodular aspect and with diffuse calcification and aggregate of particles of iron and carbon especially around terminal and respiratory bronchioles. In some areas there was an aspect of desquamative alveolar lesion with type 2 pneumocytes hyperplasia without chronic inflammatory infiltrate.

The patient asked to Nanodiagnostic SRL (di San Vito di Spilamberto - Modena) an investigation on lung lobectomy to evaluate the possible presence of nanoparticles by FEG-ESEM (Field Emission Gun – Environmental Scanning Electron Microscope). He asked to us other investigation to exclude the presence of eventually inhaled fibers (coated and not coated). We used different techniques: optical microscopy with direct and polarized light; Raman spectroscopy, and scanning electron microscopy (SEM) with energy dispersive spectrometry (EDS).
METHODS

The patient gave us 9 white paraffin sections on slights of lung parenchyma. Two of them were used by laboratory of Nanodiagnostic SRL to FEG-ESEM (European Community project QRLT-2002-147 nanopathology). The patient has given to us his consent to use the remaining histological lung sections on the slight for other analysis. We processed one of them with routine coloration (hematoxylin-eosin) and another with a specific coloration for iron (Prussian blue). After chemical digestion of the lung tissue of the third section we investigated the inorganic particles and fibers by SEM-EDS (Belluso et al., 2006). Another section was analyzed by Raman Spectroscopy (micro-Raman) that have some advantages: no sample preparation needed, non-destructive technique, Raman spectra can be collected from a very small volume (< 1µm in diameter) (Rinaudo et al., 2009).

RESULTS

Dusts deposit was identified in the surgical lung routine technique (H-E) in the area of elastotic fibrotic reaction, sclerosis and desquamative alveolites (Fig. 1), in irregular fibrotic lesion like so Mixed-Dust Nodule (Fig. 2) with type 2 pneumocytes hyperplasia without inflammatory infiltrate (Fig. 3) and giant cell reaction (Fig. 4). There wasn't birefringent particles under polarizing light microscopy. There was abundant iron oxide deposits in the Mixed-Dust Nodule (Fig. 5). There were not particles with birefringent effect under polarizing light microscopy.

We concluded that these lesions can be attributed to siderosis with associated antrachosis. The presence of multinucleate giant cells and the hyperplasic alveolar type 2 pneumocytes could suggested an hard metal lung disease. The only morphological aspect doesn't allow to identify the submicroscopic particles. Therefore it is mandatory to do the mineralogical analysis with electron microscopy.

Fig. 1 H-E (20x0,40)  Fig. 2 H-E (60x0,80)  Fig. 3 H-E (20x0,25)  Fig. 4 H-E (40x0,65)  Fig. 5 Iron (60x0,80)
Nanodiagnostic SRL by FEG-ESEM (range from 500x to 60,000x) identified calcified spherules composed by Ca, P, O, Na, C, Mg and aggregate of particles (5 µm in diameter) composed by Al, C, O, Si, Na, Mg. Some particles (0.1-0.8 nanodiameter) are composed by O, Si, C, Na, Cr, Fe, Mg, Al, Ti, Zr, Zn. In other white paraffin sections of the bronchial biopsy were also founded particles (0.2-0.4 µm in diameter) composed by Ti, Fe, P, Zr, Sn. Their conclusions are that these are ceramic dusts, and hard-metals particles. After digestion of the lung tissue we identified, by SEM-EDS (2,000x), only some particles rich of iron oxide (the smaller 2.0 x 0.8 µm and the biggest 6.4 x 2.2 µm) (Fig. 6). Micro-Raman (Fig. 7) showed a fine granular refractive particles with deposit of Ca-P, Fe and more little particles under the resolution powder of Light microscopy (Figg. 8, 9, 10).

Fig. 6 Backscattered electron SEM image of some particles of iron and EDS-SEM spectrum

Fig. 7 Raman Spectroscopy and raman spectrogram

Figg. 8, fine granular refractive particles
The identification of the non neoplastic lesions associated to carcinoma, in this case, is not easy to explain. The morphological lesions must be distinguished from UIP, desquamative interstitial pneumonia (DIP), and hypersensitivity pneumonitis secondary to radio and chemotherapy. The presence of a history of exposure and the presence of alveolar giant cells may be required an analytical electron microscopy investigation to confirm the diagnosis of hard metal lung disease. Optical observation, SEM-EDS (under 20,000x) and Raman investigation are not sufficient to investigate this type of possible pneumoconiosis, in fact they have shown only deposit of particles of iron oxide. Only the FEG-ESEM (like so used to Nanodiagnostic SRL of Modena) can be an appropriate instrument for analyze the nanoparticles present in the lung and in particular exogenous nanoparticles. Probably, in this case, the pneumoconiosis could be caused by air pollution, by the inorganic nanoparticles inhaled during war occupation and can be the cause of the lung cancer. This case report shows also the importance, in the diagnosis of pneumoconiosis, of the use of different techniques and the inevitable interdisciplinary approach. The conclusive anatomo-pathological diagnosis in fact must be done only after a recollection of some information: clinico anamnestical data, mineralogical analyses. It is important in this type of diagnosis to have appropriate biological materials (at least four sections of non neoplastic lung). In this century the diagnosis of pneumoconiosis must be considered the toxicity of nanoparticles in the lung with the use of ancillary Techniques (like so FEG-ESEM: Field Emission Gun - Environmental Scanning Electron Microscope).

References


