Interstitial Pneumonia Developed in a Worker Dealing with Particles Containing Indium-tin Oxide

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The use of indium compounds in the electronics and semiconductor industry has risen sharply from the 1990s, and indium demand increased to a record 335 tons in 2000 in Japan, which was about 5 times that in 1990¹. Indium-tin oxide (ITO) is a sintered alloy containing a large portion of indium oxide and a small portion of tin oxide, and is used in the making of thin-film transistor liquid crystal displays (LCDs) for television screens, portable computer screens, cell phone displays and video monitors. Japan was the world’s largest consumer of indium, with three-fourths of it going for ITO coatings in 2000. More than one-half of the world’s indium consumption is for ITO coatings². Due to the increasingly frequent industrial use of ITO, the potential occupational exposure to this material has attracted much attention.

Although there are no available data about the potential of ITO to induce lung damage in humans, pulmonary and testicular toxicity was reported recently when ITO was given to hamsters in intermittent intratracheal instillations², ³. This is the first case history to our knowledge describing a man with interstitial pneumonia consistent with the inhalation of ITO particles.

Case History

A 27-yr-old man was referred from his general practitioner in January 1998. He had smoked 10 cigarettes per day for ten years, sometimes drank alcohol, had no other medical history and was on no medication. He complained of 10 months of increasing dry cough, night sweats, increasing breathlessness, and anorexia with about a 10 kg weight loss over 10 months. On examination, he was 174.0 cm tall and weighed 48.8 kg. His temperature was 37.2°C, and he had clubbed fingernails. Fine crackles and high pitched squeaks were present on auscultation. Arterial blood gases showed a pO₂ of 6.1 kPa and a pCO₂ of 6.0 kPa. A leukocyte count of 13,000/µl, CRP 1.95 mg/dl (normal range 0–0.2 mg/dl) and liver damage was recognized with AST 108 IU/l, ALT 45 IU/l. Chest radiography showed ground glass opacities in all lung fields (Fig.1). Chest CT scan showed subpleural honeycomb, ground-glass opacities, minor pneumothorax and subcutaneous emphysema (Fig.2). Further questioning revealed that he had been...
engaged in the metal processing industry as an operator of a wet surface grinder for 3 yr, from 1994 to 1997, where ITO sputtering targets are produced for transparent conductive films used in flat panel displays such as liquid crystal displays. Video-assisted thoracoscopic lung biopsy was performed. On histopathological examination, the alveolar spaces were seen to be filled with red blood cells, fibrin, cholesterol clefts and alveolar macrophages, but few neutrophils. In the interstitial spaces, perivascular lymphocyte and plasma cell infiltration was seen. Numerous fine particles were observed within the alveolar macrophages and the alveolar spaces. Lymphocytes and plasma cells had infiltrated the interstitial spaces, and there were lymph follicles everywhere. Numerous fine particles, most of which were less than 1.0 µm in diameter, were observed within the alveolar spaces, alveolar septum and bronchiolar lumens. The presence of indium and tin was demonstrated by X-ray energy spectrometry (EMAX Energy, Horiba Ltd., Kyoto) of these fine particles with a scanning electron microscope (S-3000N, Horiba Ltd., Kyoto) (Fig.4). From these results, he was diagnosed with interstitial pneumonia consistent with the inhalation of ITO particles. He was started on a treatment with
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predonisolone, but he became worse, and bilateral pneumothorax occurred. He died in April 2001 of bilateral pneumothorax. The serum collected one year prior to his death was analyzed for indium and tin by inductively coupled plasma mass spectrometry (ICP-MS (ELAN 5000, Perkin Elmer Japan)) after acid digestion. The serum concentration of indium was 290 µg/l, but that of tin was not quantified because of contamination through acid digestion in the draft.

Discussion

Recent studies have revealed the pulmonary toxicity of indium compounds by using laboratory animals2–6). Tracheal instillations of indium phosphate (InP) or indium arsenide (InAs), which are semiconductor materials, in hamsters showed severe lung-toxic effects and very slow elimination of indium, at 60 wk half-time6). On the other hand, indium distribution after intratracheal instillation of InP in rats showed relatively even distribution among the major organs such as the liver, kidneys, lungs, spleen, and testes5, 6). From the pathological findings in this case, interstitial pneumonia was defined and numerous fine particles were scattered throughout the lungs. Furthermore, an extremely high indium level (290 µg/l) was found in the patient’s serum, compared with a mean indium value of 0.1 µg/l obtained from healthy male serum (n=377)7). Although we have no information on indium or tin concentrations in the working environment, it seemed that this patient who was engaged in wet surface grinding of ITO target was exposed to ITO particles over 3 yr, and inhaled ITO particles may have caused interstitial pneumonia. The adverse effects of indium compounds such as ITO, InAs and InP, have not been paid much attention so far. Since the occupational exposure limit of indium has not been established in Japan, there was no measurement of the indium or tin concentration in the working environment. Although the solubility of ITO particles both in vitro and in vivo has not been reported, this high concentration of indium in serum showed indium dissolution from ITO particles. Indium in the blood seems to be distributed to the organs and may cause chronic adverse health effects, as demonstrated by our patient’s severe emaciation, liver damage and splenomegaly. Although we have no evidence, we speculate that the cause of his liver damage is drug-induced, is auto-immune, indium induced or due to an unknown virus.

To date, we have found no data showing that indium is a respiratory, gastrointestinal, or nervous system health hazard for workers at electronics or semiconductor factories. This is the first report of possible adverse health effects of indium in humans consistent with exposure to ITO particles containing a high percentage of indium. Further study is required to clarify the toxic effects of indium, because the demand for electronics or semiconductor materials is expected to increase.

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References