Aluminum Welding Fume-Induced Pneumoconiosis

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Chronic exposure to high concentrations of fumes during aluminum arc welding causes a severe pneumoconiosis characterized by diffuse pulmonary accumulation of aluminum metal and a corresponding reduction in lung function. Aluminum fume-induced pneumoconiosis is a rarely reported entity, of which the true incidence is unknown. We report the clinical, radiographic, microscopic, and microanalytic results of 2 coworkers, employed by the same aluminum shipbuilding facility, who died of complications from this disease. Scanning electron microscopy and energy dispersive x-ray analysis of the exogenous particle content in the lung tissue of these cases revealed the highest concentrations of aluminum particles (average of 9.26 billion aluminum particles per cm^3 of lung tissue) among the 812 similar analyses in our pneumoconiosis database. One patient had an original clinical diagnosis of sarcoidosis but no evidence of granulomatous inflammation. HUM PATHOL 33:819-825. Copyright 2002, Elsevier Science (USA). All rights reserved.

Key words: aluminum welding, pneumoconiosis, sarcoidosis, misdiagnosis, pathology, scanning electron microscopy.

Abbreviations: FEV$_1$, timed forced expiratory volume; FVC, forced vital capacity; LM, light miscroscopy; SEM/EDXA, scanning electron microscopy and energy dispersive x-ray analysis; TEM, transmission electron microscopy.

A wide range of pulmonary pathology is attributed to aluminum dust exposure, including interstitial fibrosis, granulomatous disease, desquamative interstitial pneumonia, and pulmonary alveolar proteinosis.[1-5] Clusters of interstitial pulmonary fibrosis in aluminum powder and potroom workers have been documented in Europe, New Zealand, Canada, and the United States.[6-9] Reports of disease as a result of exclusive exposure to vaporized aluminum and alumina—as found commonly in aluminum arc welding—are very rare, however.[2,10,11]

BACKGROUND

Shaver and Riddell[12] first described lung disease in conjunction with aluminum fume exposure in 1947. The discovery of "peculiar lung shadowing" and spontaneous pneumothorax in several employees of different corundum (an aluminum oxide) abrasive manufacturers launched an industry-wide study. More than 300 furnace operators at 4 different companies who were heavily exposed to alumina and silica fumes were identified as being at risk. Of these, 23 laborers had "well-established" and 12 had "early" radiologic evidence of pulmonary disease. The clinical presentation included cough, white frothy sputum, dyspnea, "tightness in chest," and constitutional symptoms. Autopsies of 7 employees who died during the study revealed patchy pleural thickening, emphysematous blebs and pneumothorax, and considerable nonnodular fibrous replacement of lung tissue. In 1989 Kilburn[11] and coworkers correlated aluminum fume exposure with the development of constitutional symptoms in a cohort of non-smoking, mostly aluminum welders in a shipyard. They found that the incidence of "metal fume fever"—a syndrome comprising fatigue, headache, muscle aches, metallic taste, hoarseness, and sore throat—was much higher in aluminum welders than in stainless steel or mild steel welders. Welders also reported an increased incidence of pulmonary and cardiac symptoms when compared to case-controlled hospital maintenance workers.

Although notable, these studies failed to clarify a direct causal relationship between aluminum welding exposure and lung disease. Byproducts of welding such as oxidant gases, including ozone and nitrogen oxides, are also known to cause irritation, chest pain, shortness of breath,[13] and fibrosis.[14] Others have studied aluminum exposures. Nielson et al[15] measured the exposure of 25 aluminum welders who experienced more respiratory symptoms than a control group of warehouse workers, including nonspecific bronchial hyperreactivity, nasal congestion, pharyngitis, nasal secretions, chronic bronchitis, asthma, and dry cough. The median total dust in the welding areas was 2.8 mg/m^3. Aluminum (median, 1.4 mg/m^3) and water-soluble chromium (median, 8 mg/m^3) levels were increased. Ozone and nitrogen oxides had respective medians of <0.01 and <0.1 parts per million. All of these concentrations were below regulatory limits. Even so, by the end of the work week, the welders had elevated urinary levels of aluminum, consistent with retention and solubility of aluminum with continuing exposure. The lungs have been proposed as the organ responsible for long-term storage of inhaled aluminum fumes.[16]

In 1982, Vallyathan et al[10] reported a case of a 35-year-old exclusively aluminum welder with a 60-pack-year smoking history. After finding "ill-defined, nodular, infiltrative lesions in the lung" on x-ray and evidence of restrictive and obstructive disease on pulmonary function tests, it was decided that a left upper lobectomy was justified to rule out malignancy. Both the outer and cut surfaces of the lobe displayed "a metallic sheen resembling tarnished aluminum." Histologic assessment revealed fibrosis, collagenous nodular

FIGURE 1. Case 1: Chest x-ray showing right pneumothorax and fibrotic changes on presentation in 1991.

welder for 8 years. Both jobs were performed concurrently within the confined compartments of aluminum ship bodies with minimal ventilation. A handkerchief tied around his face provided the only dust and fume protection. He smoked 4 cigarettes per day for 5 years. He presented in 1991 with acute onset of pleuritic chest pain and fever. Chest x-ray revealed a 10% left pneumothorax. Diffuse bilateral infiltrates and numerous left-sided emphysematous blebs were also noted. At this time, severe fibrotic lung disease was noted; however, no indication of hilar adenopathy was seen. A chest tube provided relief. His pulmonary function tests, after resolution of the pneumothorax, demonstrated a forced vital capacity (FVC) of 46% predicted and a ratio of timed forced expiratory volume to FVC (FEV_1/FVC) of 80%. He was diagnosed clinically with stage III sardoidosis and received treatment with high-dose corticosteroids and methotrexate. A few months later, he again presented with chest pain. Chest x-ray revealed a large tension pneumothorax with near-total collapse of the right lung with a right-to-left mediastinal shift (Fig 1). Chest x-ray still showed chronic diffuse infiltrates, and the entire process was attributed to sarcoidosis flare-ups. After a remission, he presented again in 1993 with acute onset of right-sided pleuritic chest pain accompanied by fever and chills. Chest x-ray ("consistent with, but not diagnostic of, sarcoidosis") showed, in addition to previous changes, dense parenchymal scarring involving the upper 2/3 of each lung. Bilateral bulla and bleb formation persisted. Follow-up x-rays in 1994 and 1995 (Fig 2) showed progressive disease, and the lungs were noted to have "compensatory emphysema in the lower lung zones, probably compensating for contraction of the upper two-thirds." By 1995, he was increasingly short of breath and cachetic, and had scattered wheezes and rhonchi over all lung fields. In 1996, he presented the final time for a lung transplant evaluation, for which he was found ineligible.

lesions, and areas of coagulative necrosis. Macrophage aggregates, found in the interstitium, nodules, and air spaces, contained a "granular, gray-brown, metallic material." Scanning electron microscopy and energy dispersion x-ray analysis (SEM/EDXA) showed that the pigmented material found in the macrophages was aluminum; however, there was no quantification of lung particulate burden. The patient had a pneumonectomy several years later, and by late 2001 was totally disabled.

Here we report the clinical history, radiographic, gross, histopathologic, and microanalytic findings (including quantification of lung burden) in 2 welders with intense chronic aluminum exposure. Employed by the same Louisiana shipbuilding company, these men were coworkers of Vallyathan's patient. One had an initial clinical misdiagnosis of sarcoidosis. This study is the first to quantify lung burden in pulmonary disease related to intense exposure to aerosolized aluminum produced during aluminum arc welding and grinding in areas of minimal ventilation.

SUBJECTS AND METHODS

Subjects

Case 1

This 43-year-old African-American man worked for a Louisiana shipbuilding factory as an aluminum weld-grinder for 16 years, grinding down the welding irregularities on seams of aluminum plating, structural aluminum fittings, and aluminum piping. He then worked as an aluminum arc

FIGURE 2. Case 1: Chest x-ray taken in 1995, 4 months before death, showing severe fibrosis. Hilar adenopathy was never mentioned in radiologic reports.

While in the hospital he developed aspergillus pneumonia and hemoptysis due to diffuse hemorrhage from all airways. Chest x-ray again demonstrated large coalescing emphysematous blebs, diffuse bilateral infiltrates, and, for the first time, cardiomegaly. His respiratory function deteriorated rapidly, and he died. The cause of death was deemed progressive respiratory failure due to pulmonary sarcoidosis. His body was exhumed for autopsy 11 months after death. The examiner confirmed cardiomegaly (embalmed heart weight, 550 g) with right-sided hypertrophy further characterized by dilation of both chambers and pulmonary artery. The coronary vessels were all <10% occluded. Severe pulmonary edema, congestion (embalmed lung weight, 2050 g), and visceroparietal pleural adhesions were also noted. The well-preserved lungs were then sent for further study.

Case 2

This 45-year-old, white, hypertensive man with a 13-to-40 pack-year smoking history presented in May 1991 with progressive dyspnea, severe hypoxia, hypersomnolence, and narcolepsy. A coworker of case 1, he had welded aluminum inside boats and tanks at the same Louisiana shipbuilding company for 22 years. Case 2 also worked in small compartments without wearing a protective mask and without access to a ventilation hood. His wife confirmed heavy snoring and nightly instances of sleep apnea. He also would fall asleep suddenly and inappropriately, such as during a conversation and when driving. The patient, 5'6" and 190 lb, reported a gradual weight gain over several years. Dyspnea restricted him from walking comfortably beyond 200 feet, causing a noticeable decline in activity. Occasionally he would have morning mucus production. He was negative for any other illnesses, known allergies, hemoptysis, and medication use. His father had died of lung cancer, but 3 siblings and his mother were living and in good health. Heart catheterization and chest x-ray in 1985 after an incident of "substernal burning" had revealed no coronary disease or other abnormalities. He denied any other known occupational exposures.

Physical examination revealed a slightly dusky and plethoric man with rare, intermittent crackles heard over both lung bases, "very early clubbing" of the fingers, and an excess of pharyngeal tissue contributing to a narrow oropharynx. His chest x-rays were abnormal with "bilateral diffuse small densities in both upper lung fields." Pleural thickening on the lateral chest walls, a 2-cm nodular density on the left superior hilum, and mildly increased heart size were also noted. Pulmonary studies showed "moderate air flow obstruction with mild reduction in vital capacity" with a FVC of 77% predicted and FEV_1/FVC of 57% predicted. On admission he was hypoxemic at room air oxygen levels (pH, 7.42; partial pressure of carbon dixide, 43; partial pressure of oxygen, 53) and had a pulse oximetry reading of 87%. Laboratory studies confirmed erythrocytosis (hemoglobin, 19.3; hematocrit, 58) that was treated with phlebotomy. He underwent a sleep study and was subsequently diagnosed with "sleep apneic disorder." His "chronic obstructive lung disease" and "probable pulmonary siderosis from arc welding" were treated with theophylline and albuterol, and he was placed on oxygen therapy. A sample from a lung biopsy performed in 1991 was sent for evaluation. He developed lung cancer, which proved inoperable due to pneumoconiosis, and expired in 1999. No autopsy was performed.

FIGURE 3. Case 1: Sagittal section of the left lung showing dense bands of scar tissue and consolidation.

Methods

Gross

Whole lung autopsy specimens were available for examination in case 1 only.

Histopathology

Paraffin sections of surgical and autopsy lung tissue were stained with hematoxylin and eosin and examined with brightfield, darkfield, and polarized light microscopy (LM). Iron-stained sections were examined for asbestos bodies.

Lung-Retained Particulate Microanalysis

Lung parenchyma from each case was available for analysis of nonfibrous inorganic particulate burden, using methods described previously.[17] Briefly, the lung concentration of nonfibrous inorganic particulates was measured using morphometric in situ analysis of tissue sections. This involves placing a paraffin section of lung tissue on a carbon disk, removing the paraffin, and quantifying and

FIGURE 4. Case 1: Closer inspection of Figure 3 reveals the unusual slate-gray metallic appearance of the scarred areas and also of peribronchial lymph nodes.

characterizing the lung burden of inorganic particulates using SEM/EDXA. Transmission electron microscopy (TEM) provided further morphologic data on the particulate matter.

Comparison With Pneumoconiosis Database

We compared data from the 2 cases with our updated pneumoconiosis database of inorganic particulate lung burden[18] comprising 812 analyses (including the cases reported here). We plotted the fraction of total inorganic particle concentration composed of aluminum metal particles against the total inorganic particle concentration for each of these analyses, to compare the aluminum lung burden of these welders with the entire database.

RESULTS

Gross

The primary and most striking finding from case 1 was the dense metallic, slate-gray cut surface of the left upper lobe (Fig 3). The lung parenchyma demonstrated focally dense fibrosis, more severe in the upper lobes, with peripheral honeycombing sparing the lung bases. Mucopurulent material was found in the bronchi. Furthermore, apical bullae, consolidation, and abscesses were noted in the right upper lobe. The hilar
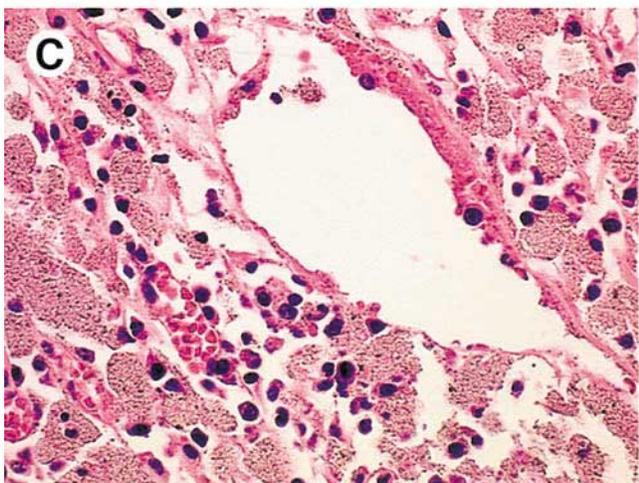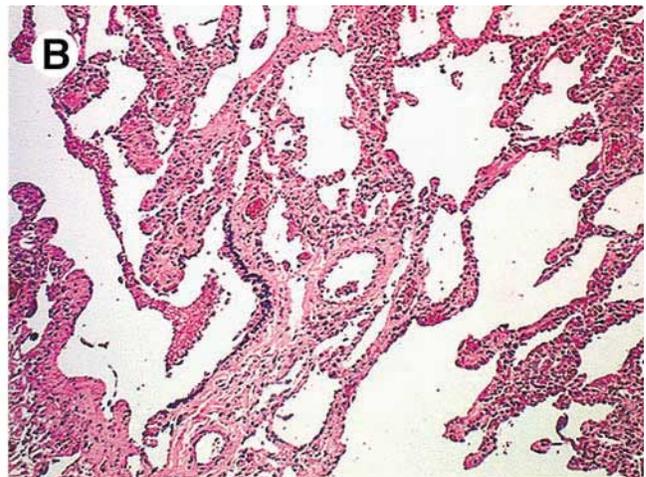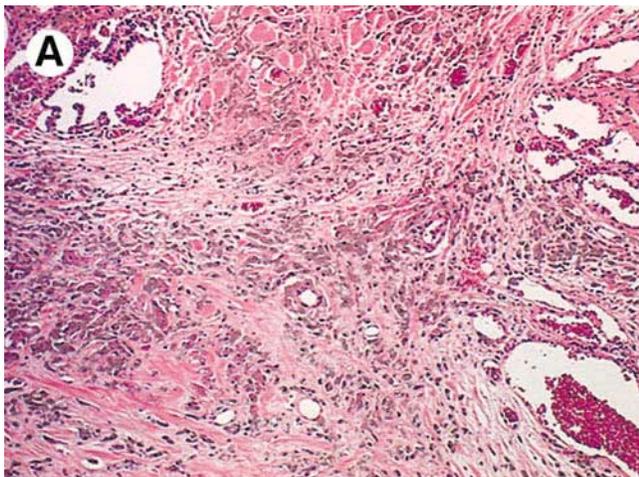
FIGURE 5. Case 1, LM: (A) Dense fibrotic area of the lung with many aluminum-containing macrophages. (Original magnification × 10.) (B) Lung parenchyma showing peribronchiolar and interstitial aluminum-containing macrophages. (Original magnification × 10.). (C) Aluminum-containing macrophages in lymph node. (Original magnification × 180.)
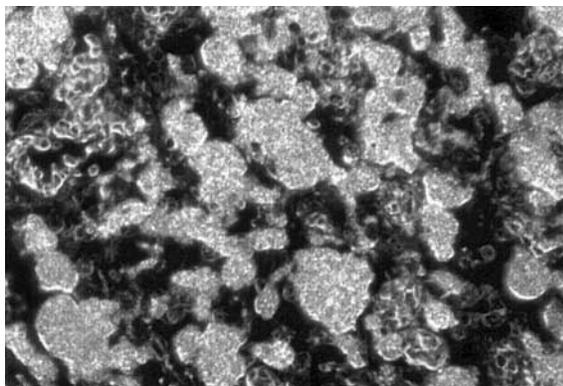
FIGURE 6. Case 1, LM: Bright appearance of aluminum-containing macrophages with darkfield illumination. (Original magnification × 400.)

TABLE 1. Total, Metal, and Aluminum Concentrations in 2 Analyses Each of 2 Cases of Aluminum Fume-Induced Pneumoconiosis

	Case 1		Case 2	
	Concentration*	(%)†	Concentration	(%)
Total (a)§	9.68‖		11.01	
(b)	7.42¶		11.43	
Metal (a)	8.97	(92.6)	10.82	(98.3)
(b)	6.12	(82.4)	11.42	(100)
Al (a)	8.97	(92.6)	10.62	(96.4)
(b)	6.12	(82.4)	11.33	(99.1)

*billions of particles/cm^3 lung tissue
†percent of total lung particulates
§2 analyses (a, b) of each case
‖left upper lobe (case 1 only)
¶left lower lobe (case 1 only)

lymph nodes exhibited a similar metallic, slate-gray sheen (Fig 4).

Histopathology

LM examination of case 1 (Fig 5) confirmed severe dense fibrosis with interspersed macrophages containing nonbirefringent, extremely fine, gray-to-brown refractile particulate matter. Macrophages in less-fibrotic interstitial areas, in some airspaces, and in lymph nodes displayed this same cytoplasmic content, which was best revealed with darkfield illumination (Fig 6). Polarized light revealed focal birefringent dust. A cavitating aspergillus infection was seen in the right lung. Case 2 showed numerous interstitial macular and alveolar aggregates of macrophages with cytoplasm containing abundant granular pigment, as seen in case 1. There was also evidence of emphysema. No asbestos bodies, silicotic nodules, or granulomas were noted in either case.

Lung-Retained Particulate Microanalysis

In case 1, specimens from the left upper lobe and left lower lobe base were analyzed using the in situ technique. The analyses of each demonstrated similar results (Table 1), with the left lower lobe exhibiting a slightly lower particulate concentration. The average total concentration of exogenous inorganic particulates was 8.55×10^9 particles/cm^3 of tissue. Approximately 86% of these were metallic particles, all of which contained aluminum. Aluminum silicates, which were differentiated from aluminum metals, comprised 3.0% of the total exogenous inorganic particles. Silica (0.9%) and gypsum (8.0%) were also detected. The average diameter of the metallic aluminum particles, measured in SEM, was 0.34 μm. However, examination of the tissue at higher magnification using TEM (Fig 7) showed many of the particles to be aggregates of much smaller ultrafine particles than could be resolved at the standard magnification used in SEM. In fact, fumes as small as 10 nm were demonstrated.

In case 2, in situ analysis of the lung tissue demon-strated an average total exogenous particulate concentration of 1.12×10^{10} particles/cm^3 lung tissue. Approximately 99% of these were metallic. Although iron (4.44×10^8 particles/cm^3 lung tissue) and zinc (1.83×10^9 particles/cm^3 lung tissue) were represented, 98% of the metal particles contained aluminum. Miscellaneous silicates (including aluminum silicates) comprised 0.9% of the total exogenous inorganic particles.
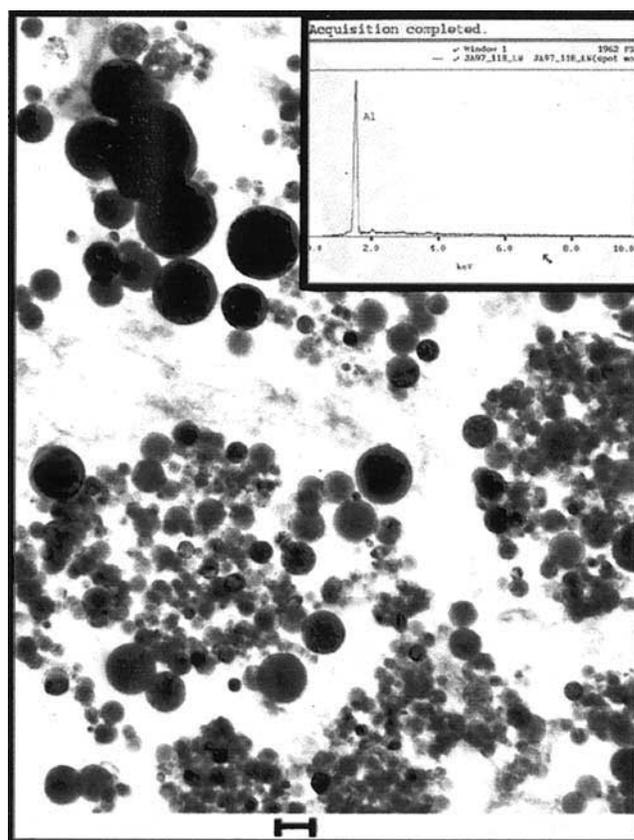
FIGURE 7. Case 1, TEM: Aluminum particles in this section of macrophage. (Black bar, 0.1 μm; original magnification × 112,000.) The inset shows a typical EDX spectrum revealing an aluminum peak.

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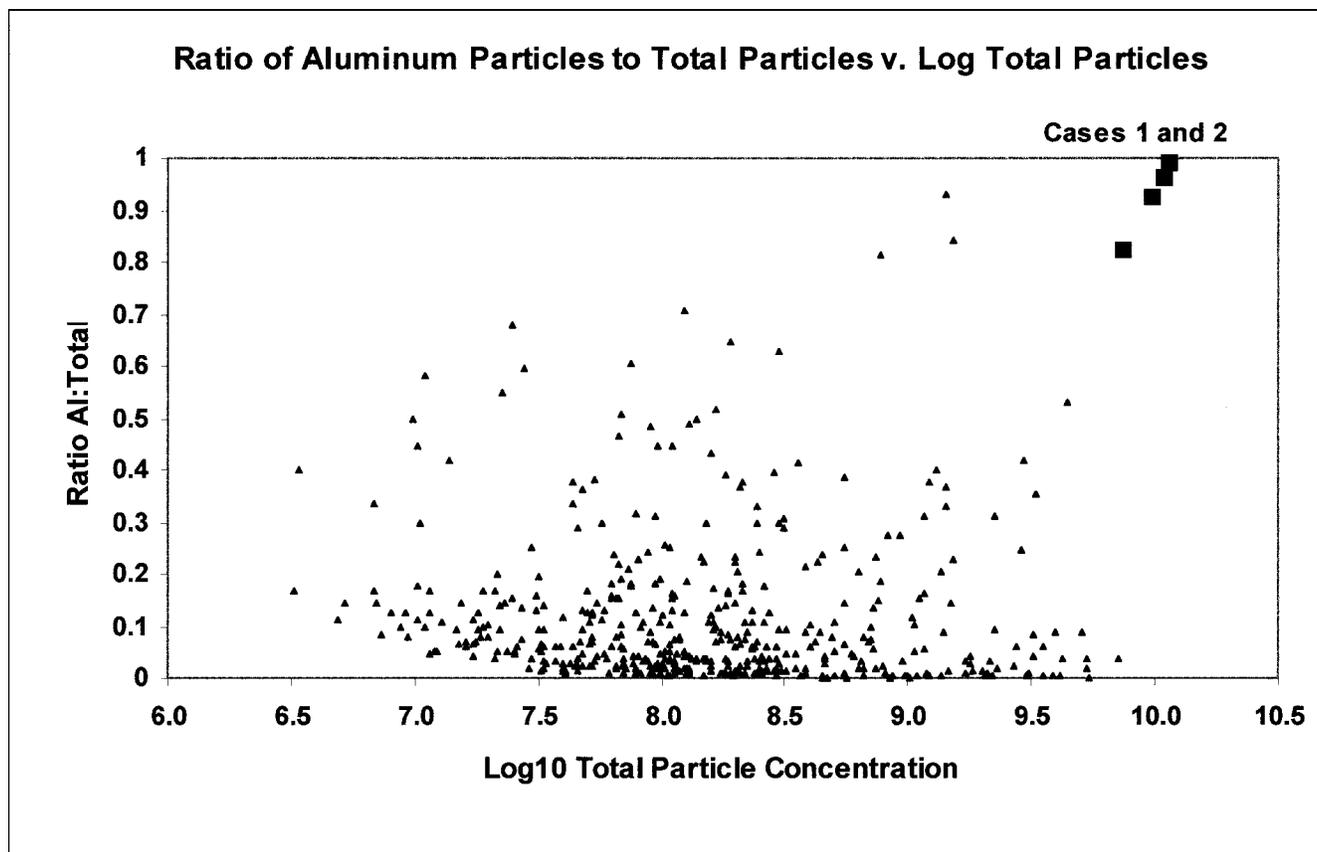
FIGURE 8. Total inorganic particle concentration (log scale) and the fraction of total particle concentration comprising aluminum metal particles in the entire pneumoconiosis database.[18] (Note: Analyses without detectable aluminum are not represented on this graph.) The large square symbols indicate the results for cases 1 and 2.

The metal particles, measured in SEM, ranged in diameter from 0.2 to 1 μm (average, 0.43 μm).

Comparison With the Pneumoconiosis Database

As far as we know, pulmonary aluminum accumulation to the extent measured in these aluminum shipbuilders has not been previously documented. Figure 8 illustrates how the aluminum particle concentrations in these 2 cases stand out at the end of the range observed in the 812 analyses currently in our pneumoconiosis database.[18] Aluminum metal particulates were detected in only 467 (57.5%) of the analyses, with 90% of those containing aluminum having concentrations $<10^8$ aluminum particulates/cm^3 lung tissue.

DISCUSSION AND CONCLUSION

Arc welding uses electrical currents in excess of 200 amperes and a space-filling metal rod to join 2 metal objects together. In the process, some of the liquefied metal is aerosolized. Also, an irregular surface along the seam of fusion is left behind, which must be ground off to produce a smooth finish. In the process of "weld-grinding," metal particulates composed of

fume aggregates are reaerosolized, most likely having an additive effect on respirable material in the workplace when occurring alongside welding. TEM of the lung tissue supports that the aluminum particles are indeed composed of fume aggregates. Therefore, there may have been little difference in occupational exposure for case 1 between his first 16 years as a weld-grinder and his next 8 years as an aluminum welder, particularly given that both welding and grinding of the same materials occurred in the same small enclosed compartments.

Pneumothorax may be a characteristic (though not absolute) finding in aluminum welding fume-induced pneumoconiosis. Several reports document pneumothorax in both aluminum workers and other metal grinders.[12,19,20] The effect of smoking on this disease process is not clear. Our cases demonstrate variable smoking histories (1 and 13 to 40 pack-years, respectively); thus smoking is unlikely to have contributed substantially to the respiratory dysfunction in at least 1 case. The differential diagnosis of noncaseating granulomatous disease, although not demonstrated in these 2 cases, merits brief discussion, because the potential for misdiagnosis increases when typical granulomas are present on biopsy. In 1987, De Vuyst et al[21] reported a 32-year-old chemist, heavily exposed to alu-

minum powder, who developed noncaseating granulomatous lung disease with an initial diagnosis of sarcoidosis on biopsy. The potential to clinically mislabel aluminum (or other) pneumoconioses as sarcoidosis also warrants consideration. Young African-Americans, like case 1, are particularly at risk of such misdiagnosis due to the high reported incidence of sarcoidosis in this ethnic group.[22] Awareness of this rare aluminum welding fume-induced pneumoconiosis, along with a thorough occupational history, should aid its accurate pathologic identification.

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