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Rheumatoid Pneumoconiosis: A Comparative Study of Autopsy Cases between Japan and North America

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In order to elucidate the prevalence of rheumatoid pneumoconiosis (RP), an extensive review was conducted of pathological specimens from a large series of autopsy cases both in Japan and the USA (National institute for Occupational Safety and Health). Twenty-two cases were pathologically identified as having RP among 2450 autopsied coal workers with pneumoconiosis in the USA (0.89%) and its prevalence was comparable with that of Japanese RP cases (n = 9) among 1217 pneumoconiotics (0.74%). RP consisted of two subtypes, Caplan type and silicotic type. All Japanese cases were of the silicotic type (0.82%). In the USA 14 were of Caplan type (0.37%) and 8 silicotic (1.5%). Although RP is an uncommon disease, silicotics are relatively more prone to develop RP compared with other types of pneumoconiotics. The incidence of tuberculosis was significantly higher (9.1%) among RP cases than the non-rheumatoid population (1.5%) only in the US cases ($P < 0.01$).

Keywords: pneumoconiosis; rheumatoid arthritis; rheumatoid nodule; silicosis

INTRODUCTION

Rheumatoid pneumoconiosis (RP) is an uncommon lung disorder described originally by Caplan (1953) in coal miners having rheumatoid arthritis. The reported incidence of RP varies greatly among different areas of the world and very few cases of RP have been reported from North America (Benedek, 1973; Jones Williams, 1991; Parkes, 1994). To investigate the difference in the prevalence of RP and re-evaluate the cases, an extensive comparative study has been conducted since 2000 between Japan and the USA.

MATERIALS AND METHODS

A total of 1217 Japanese cases with a pathological diagnosis of pneumoconiosis were used in the present study. They represented unselected consecutive autopsies conducted in four institutions for 33 yr, from 1966 to 1999, and having detailed documentation on occupational history, chest X-rays and clinical findings. An average of 12 tissue blocks (3–20) taken from both lungs and stained with hematoxylin–eosin and Elastica-Goldner stains were available for histopathological examination.

An ongoing extensive review of autopsy cases registered with the National Institute for Occupational Safety and Health (NIOSH) has advanced so far as to be able to analyze 4601 coal workers registered over 15 yr from 1971 to 1985. The available material per case included a detailed occupational history and 3–10 tissue blocks obtained from both lungs and processed for histopathological examination. The relevant clinical information, including the status of rheumatoid factors as well as radiological findings, was not available in NIOSH cases.

Pathological diagnosis was made based on the predominant type of pneumoconiosis-specific lesions present in the lungs (Honma *et al.*, 1997). They include dust macules (Green and Vallyathan, 1998), nodules (silicotic nodules and mixed dust fibrosis), massive fibrosis (confluent fibrotic masses measuring >2.0 cm) and diffuse interstitial fibrosis coupled with the deposition of asbestos bodies in the lung. According to these criteria for diagnosis, the disease was categorized into the following four entities: macular pneumoconiosis (MP) which presents only with macules (Honma *et al.*, 1997), silicosis, mixed dust pneumoconiosis (MDP) (Honma *et al.*, 2000) and asbestosis. To avoid possible confusion in the analysis, the authors did not use coal

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workers' pneumoconiosis (CWP), based on the recognition that CWP *per se* comprises pathologically heterogeneous diseases (Green and Vallyathan, 1998). As a result, CWP may fall into MDP, MP or silicosis in this study. A high profusion of macules may give rise directly to massive fibrosis in a minority of cases with coal pneumoconiosis (Parkes, 1994). These cases were classified arbitrarily as MDP in this study.

To make a diagnosis of RP it is necessary for the lungs to bear rheumatoid nodules (Gardner, 1992) in the parenchyma. Pathological characteristics of these rheumatoid nodules include extensive central necrosis and a peripheral rim of fibro-inflammatory tissue composed of palisaded fibrohistiocytic cells, occasional multinucleated giant cells, varying amounts of dust, lymphoplasmacytic infiltrate and bundles of collagen. Particularly important as a hallmark of active rheumatoid inflammation is infiltration of the peripheral areas of the nodule by polymorphonuclear leukocytes, both viable and degenerate. To rule out tuberculosis, the elastic fiber stain was particularly useful (Honma *et al.*, 1998), as was the Ziehl-Neelsen stain for acid-fast bacilli. Lungs with only non-specific or burned-out fibronecrotic nodules were not regarded as having RP.

Two subtypes of RP were distinguished (Honma and Taguchi, 1999): (i) classic (Caplan) type, characterized by larger nodules with uniform necrosis and associated with MP, which is often very mild, or almost no pneumoconiosis; (ii) silicotic type, characterized by smaller nodules in which the necrotic area retains some characteristics of a silicotic nodule. The background disease of silicotic-type RP was silicosis or MDP of considerable profusion with or without massive fibrosis. A mixed form of RP between (i) and (ii) may be present.

RESULTS

A total of nine cases with RP were found in 1217 Japanese autopsy cases with pneumoconiosis (0.74%). Clinical rheumatoid arthritis (RA) was seen in 15 cases (1.2%), with eight cases with silicosis and seven with MDP. All RP cases had RA (9/15, 60%) and were of silicotic type, associated with silicosis (n = 607) in six cases and MDP (n = 493) in three. Thus, the prevalence of RP (silicotic type) in nodular pneumoconiosis (n = 1100) was 0.82%. No RP case was seen associated with MP (n = 96) or asbestosis (n = 21).

A total of 22 RP cases were found among 2450 NIOSH cases with pneumoconiosis (0.89%), with 14 Caplan type and eight silicotic type (seven with silicosis and one with MDP), respectively. There were 288 cases with silicosis, 238 cases with MDP, 1924 with MP and 1865 cases with evidence of dust exposure but no pneumoconiosis. As a result, the Caplan type accounted for 0.37% (14/1924 + 1865) and silicotic type for 1.5% (8/288 + 238).

Massive fibrosis was seen in four cases with RP in Japan (4/9, 44.4%) and in three cases in the NIOSH data (3/22, 13.6%). Tuberculosis was seen in four cases with RP in Japan (4/9, 44.4%) and in two cases in the NIOSH data (2/22, 9.1%). The prevalences of massive fibrosis were 61.5% (748/1217) and <9.8% (229/2338) in the Japanese and NIOSH cases with pneumoconiosis, respectively. Similarly, the prevalences of tuberculosis were 25.4% (309/1217) and 1.5% (35/2338). Statistical analysis (normal distribution test) revealed a significantly higher incidence of tuberculosis among cases with RP (2/22) than without (33/2316) in the NIOSH cases ($P < 0.01$).

DISCUSSION

An extensive review of autopsy cases with pneumoconiosis registered with NIOSH disclosed a typical pathology of RP in 22 of 2450 cases (0.89%). Although there is almost no clinical data available to support the pathological diagnosis, it is very likely that, contrary to previous thinking (Benedek, 1973; Parkes, 1994), RP does exist in North America. The actual prevalence may be a little higher than that estimated here, because only nodules with active rheumatoid inflammation were considered to be diagnostic of RP in this study.

It was found in Japanese cases that the majority of pneumoconiotics with clinical RA developed RP (60%). All cases were of silicotic type. According to the original report of Caplan (1953), concerning about 14000 coal workers, the incidence of RP (classic type) was much lower (25.5%). In South Africa only one case of active RP (0.17%) out of 11 cases with RA (9.1%) was found among 576 autopsied silicotics (Chatgidakis and Theron, 1961). Our study suggests that lungs with silicosis or MDP develop RP more frequently than do MP or non-pneumoconiotic lungs with 'minimal change'. It appears that the collagen fibers constituting pneumoconiotic nodules (silicotic nodule mixed dust fibrosis) may induce rheumatoid inflammation (Caplan, 1953; Jones Williams, 1991; Gardner, 1992). Our data indicate that silicotics develop RP more often (1.0% in Japan and 2.4% in the NIOSH data) than MDP (0.61% in Japan and 0.42% in the NIOSH data). The high incidence of RP in lungs with nodular pneumoconiosis presents a striking contrast to the extremely rare occurrence of intrapulmonary rheumatoid nodules in the general population with RA (Katzenstein, 1997). A question remains as to the pathogenesis of Caplan-type rheumatoid nodules which develop in the lungs with only mild or almost absent pneumoconiosis (Jones Williams, 1991).

There is a tendency for RP to develop in lungs with tuberculosis, suggesting that an etiological relation-

ship may exist between the two conditions. In the NIOSH cases the prevalence of tuberculosis presented a 6-fold increase in lungs with RP ($P < 0.01$). Although in typical examples tuberculosis and RP represent quite different processes, there are certainly difficult cases to distinguish from each other, since bacteriological studies are of no help with formalin-fixed tissue. One of the authors (K.H.) has seen a case with RP in which collagen fibers constituting the fibrous capsule of a tuberculous caseation necrosis were secondarily involved in active rheumatoid inflammation. Older rheumatoid nodules which are composed of non-specific fibronecrotic tissue are virtually impossible to distinguish from other similar conditions, including tuberculosis (Gibbs and Wagner, 1998). Therefore, we excluded cases suspected of showing RP but with only old inactive nodules. Gough *et al.* (1955), in their original pathological description of RP, found three cases with positive bacteriology out of 11 pathologically proven RP cases and postulated that RP represents a modified form of infective pneumoconiosis. In the German literature RP has drawn little attention (Petry, 1954) and tends to have been regarded as an unusual phenotype of tuberculosis (Könn *et al.*, 1983), except for an early report (Niedobitek, 1969).

CONCLUSIONS

RP does exist in North America with a prevalence comparable with that in Japan. Silicotics develop RP more frequently than any other type of pneumoconiosis. The association of tuberculosis with RP is much higher than with non-rheumatoid pneumoconiosis.

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