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Review

The association between lung cancer and silicosis: from theory to practice in occupational medicine

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Abstract

Unbound (free) crystalline-silica dust is recognized since 2012 by the International Agency for Research on Cancer as a class I carcinogen. Exposure to this professional hazard was massive at the end of the last century, and it continues to exist today, albeit at lower levels. The number of cases of occupational cancer attributed to this exposure is minimal in Romania due to the absence of adequate post-exposure monitoring and the reporting of cases that encounters multiple obstacles, such as the absence of exposure data or the disappearance of the industrial sites in which the exposure took place. Occupational exposure to free crystalline silica dust can cause silicosis, and the presence of this disease certifies the existence of significant exposure. That is why the declaration of occupational cancer in a patient previously diagnosed with silicosis should be straightforward because the proof of exposure already exists.

This article presents the cancer-silicosis relationship from the perspective of current scientific data and aims to substantiate the decision of the doctors from the public health departments who investigate and declare the reported cases.

Keywords: *unbound (free) crystalline-silica dust, lung cancer, silicosis, occupational disease*

Introduction

The association between cancer and silicosis received different responses after being discussed in the literature for many years. In the '90s, although the genotoxic potential of unbound (free) crystalline silica (FCS) was widely accepted, most publications claimed that more evidence was needed and that the relationship was still controversial [1,2]. Initially, the relationship between FCS and lung cancer and the real carcinogenetic potential of this agent had to be clarified.

In March 2012, the monograph of the International Agency for Research on Cancer (IARC) was published, which reclassified FCS from group IIA, in which it belonged previously, to the group I, respectively in the group of carcinogenic agents for which there is sufficient evidence in both human and experimental studies. The monograph appeared a month after the last edition of the Encyclopaedia of Occupational Health & Safety, which still placed it in the IIA group of possible carcinogens and which, detailing, as will be seen below, sufficiently the carcinogenic action of silica.

Data on the number of occupational cancers induced by exposure to unbound (free) crystalline silica

After its recognition as a carcinogen, the reporting of professional cancers induced by this agent has

increased worldwide. Canada estimates an average of 570 lung cancers annually through exposure to FCS. [5], double compared to the 230 cases in Australia [6]. There are also more detailed statistics, such as the one published in 2018 by a group of researchers from the Republic of Korea, which found 23 lung cancer cases in patients with silicosis and 97 in patients without silicosis in the last ten years [7].

In Europe, the fraction attributable to exposure to FCS in 2020 for lung cancer is 2.35% [8]. Considering the number of 12122 new cases in 2020 [9], the number of occupational lung cancers through exposure to FCS should be 285, while the data centralized by the National Institute of Public Health does not mention any cases reported in 2020 [10].

The reasons for these discrepancies with the reported cases in other countries are manifold. Firstly, the post-exposure surveillance, although legislated, is not implemented. Moreover, none of the public authorities have specific designated competencies in controlling over how the employee surveillance is conducted, in general, and in the post-exposure surveillance, in particular. In theory, the medical record of the worker exposed to silicogenic dust who retires or changes the workplace should be transmitted by the latest treating occupational doctor to the closest occupational medicine clinic to the employee residence. The cccupational medicine clinics should provide the post-exposure surveillance and get paid through one of the means already implemented in European countries: the national oncology programs (i.e., from the public health budget) or the insurance system for occupational diseases and accidents at work.

If these things were to solve the future disease reporting of those currently exposed, they only partially solve the declaration of professional cancers, especially for those with incompletely documented exposure from the past. The latency of occurrence of the tumor can span several decades. As there are no databases that include previous exposure to carcinogens in general, and many enterprises where such exposure existed have ceased their activity, the onsite investigation of the case is frequently impossible. In the case of lung cancer secondary to exposure to FCS, an existing diagnosis of silicosis in that patient is a strong argument for significant exposure. In principle, it should be accepted without the need for new research into the workplace conditions that generated both diseases.

Arguments for recognizing as occupational the lung cancer in patients diagnosed with silicosis

The literature data published in the last decade supports the two diseases' independence through both pathophysiological and epidemiological arguments.

1. Pathophysiological arguments

The mechanism by which the inhalation of respirable particles of CFS contributes to carcinogenesis differs from the pneumoconiogenic mechanism. The pathological process by which the lesions of pneumoconiosis develops may be the substrate of increasing the risk of cancer [4], but the course toward one disease or another is different and independent. For example, although oxygen free radicals (ROS) are involved in both processes, in oncogenesis, ROS alters the structure of DNA, while in silicosis it contributes to the formation of granulomas and fibrotic tissue [11]. In chronic silicosis, CFS is present inside the silicotic node surrounded by collagen and fibroblasts. Besides the CFS trapped inside the silicotic nodules in the patient's lung who still has or has had exposure to silicogenic dust, there are also "free" CFS particles. They come from the inhalation of silicogenic dust. They are more aggressive (in the sense of triggering ROS production) if the exposure is more recent [4]. Given silicosis's histology, it is obvious that it is not the CFS inside the silicotic node but the one outside them that generates ROS that comes into contact with pulmonary alveolar and interstitial cells, the location of the malignant transformation leading to the pulmonary neoplasm. Simple embedding of the CFS particles in epithelial cells and phagocytes can generate ROS[12], this stage being one precursor to the constitution of the malignant lesion. In this regard, IARC experts cite relevant experimental studies in which ROS production and the secondary genotoxic effect occurred in the absence of inflammatory cells [3]. It has also been shown in animal experiments that FCS not only increases ROS levels but directly diminishes the antioxidant capacity in the lung, inhibiting glucose-6-phosphate dehydrogenase with consecutive reduction of intracellular glutathione [13].

2. Epidemiological arguments

Crystallized-free SiO2 is a threshold carcinogen with genotoxic action. There is an exposure threshold

for this carcinogen which, from the European Trade Union Institute's perspective, should be further lowered [14], particularly in light of the results that show an increase in the risk of cancer with the increase in the intensity and duration of exposure [15]. The presence of chronic silicosis generally certifies an average exposure period of 15 -20 years [16] and, from this point of view, is only evidence of sufficient exposure to FCS. In the same trend, epidemiologic data identified a similar risk of lung cancer in people diagnosed with silicosis to those exposed who have not been diagnosed with silicosis [3,15]. Indeed, some epidemiological studies showed that silicosis is associated with a higher incidence of lung cancer, but this incidence is proportional to the intensity and duration of exposure, which is the common risk factor for both conditions [17, 18]. The fact that silicosis is NOT a condition that necessarily precedes lung cancer was clarified earlier in a cohort of 34018 workers exposed to FCS and monitored for 44 years and confirmed by experts from the United Kingdom [19] and the United States of America [20]. Moreover, the International Agency for Research on Cancer defines FCS as a carcinogen, not silicosis [3].

Conclusion

In conclusion, epidemiological and pathophysiological data, as well as the publications from international experts, are convergent in supporting the statement that the lung cancer is NOT a "complication" of pneumoconiosis but an independent condition resulting directly from the action of CFS on lung cells. Therefore, lung cancer in people diagnosed with silicosis is another disease; a new Reporting file 1 (“Fișă de semnalare BP1”) form must be filled out, as the current legislation requires [21].

As it consists of another clinical entity, lung cancer must be declared a new occupational disease of the respective patient with silicosis.

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