Available online at www.sciencedirect.com
ScienceDirect
Leukemia Research 32 (2008) 523–525
Leukemia Research
www.elsevier.com/locate/leukres

Editorial

Have we been wrong about ionizing radiation and chronic lymphocytic leukemia?

Abstract

It is almost axiomatic that chronic lymphocytic leukemia (CLL) is not caused by ionizing radiation. This assumption has been challenged recently by a critical re-appraisal of existing data. A recent paper implicated radon exposure in Czech uranium miners as a possible cause of CLL and in this issue of *Leukemia Research* the first paper examining the incidence of CLL among those exposed to radiation from the accident at the nuclear power plant in Chernobyl is published. It suggests that CLL occurring among the clean-up workers was of a more aggressive form than is normally seen in the community.

Keywords: CLL; Ionizing radiation

Although ionizing radiation is a well-known cause of leukemia, most papers alluding to the topic exclude chronic lymphocytic leukemia (CLL) from consideration since it is believed to be well established that CLL is not caused by radiation [1]. Just how secure is this assumption?

The primary data come first from studies of atom bomb survivors at Hiroshima and Nagasaki [2–4]. Only 10 cases of CLL were identified in survivors between 1945 and 1980, and of those 10, 7 turned out to be acute T-cell leukemia/lymphoma (ATLL) when examined more closely. ATLL is endemic in the area around Nagasaki being associated with infection with the human T-cell lymphotropic virus type I (HTLV-1). These findings point out two of the hazards in interpreting the epidemiological data: CLL is an extremely rare diagnosis among those who were bombed (and indeed among the Japanese in general), and the definition of CLL has changed down the years. Many who would have been diagnosed as CLL in the past are now recognized as having different sorts of lymphoid malignancies, and since, even as recently as 1975, the diagnosis of CLL required a lymphocyte count of over $15 \times 10^9\,L^{-1}$ [5], many low count cases would have gone unrecognized.

The second primary sources of data come from studies of patients treated with ionizing radiation for benign conditions. The initial study [6] of 14,000 British patients with ankylosing spondylitis treated with radiotherapy between 1935 and 1954 with an average bone marrow dose of 4400 mSv showed an excess of acute leukemia and chronic myeloid leukemia in the first 5 years post-irradiation, but no excess of CLL. It is believed that CLL have a very long latent period, making a follow-up of less than two decades unacceptable, but later reports of this study in 1994 and 1995 [7,8] found only seven deaths attributable to CLL, and while this was greater than expected, it was not significantly so. Similarly, a study of 12,955 women irradiated for benign gynecological disorders found no significant excess of CLL-related deaths [9].

These studies illustrate other difficulties in the epidemiological data. CLL is seldom recorded as a cause of death in patients who have been diagnosed with it. For many patients, especially those with mutated IgVH genes, it is a very trivial condition that seldom causes ill health. The traditional methods by which epidemiologists acquire cases – from death certificates and hospital admissions – are ineffective in CLL; many patients never require hospital admission and they die from causes unrelated to their CLL. In one series 75% of cases were diagnosed because they had a blood test for a different condition [10]; presumably there are undiagnosed cases in the community who have not had blood tests.

A recent analysis of the Surveillance Epidemiology and End Results (SEER) database puts the annual incidence in the USA at 3.5 per 100,000 (males 5.0: females 2.5) [11]. However, the Leukaemia Research Fund Data Collection Study which gathered data from individual hematologists responsible for laboratories covering about one third of the population

0145-2126/$ – see front matter © 2007 Elsevier Ltd. All rights reserved.
doi:10.1016/j.leukres.2007.08.015