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Can environmental factors contribute in triggering vitiligo and associated autoimmune thyroid diseases? Possible connection to the Chernobyl nuclear accident

After the Chernobyl nuclear accident an increased incidence of some autoimmune disorders has been reported in people exposed to the radioactive fallout.[1] Herein we report three cases of non-segmental vitiligo patients referring to our department in which the disease occurred with concomitant autoimmune thyroid disorders (ATD), in close timely correlation with the abovementioned accident. Such women lived near to Chernobyl, at the moment of the nuclear accident, during their childhood or adolescence, and moved to Italy several years later.

A 46-year-old Belarusian woman referred to our Dermatology Department with a history of stable non-segmental vitiligo localized on the upper and lower limbs. The disease appeared 7 months after the nuclear accident. Blood tests at the moment of our observation showed high levels of circulating antithyroglobulin (TgAb) and antithyroperoxidase autoantibodies (TPOAb), while thyroid ultrasonography was suggestive of a chronic thyroiditis. Such laboratory findings were in accordance with the diagnosis of Hashimoto's thyroiditis which was made 2 years after the radioactive fallout. Anti-parietal cell autoantibodies were negative.

Family history was positive for autoimmune disorders, since a daughter was affected by Hashimoto's thyroiditis and a brother suffered from type-1 diabetes mellitus.

A 40-year-old Ukrainian woman reported a history of Hashimoto's thyroiditis, which firstly occurred about 6 months after the Chernobyl accident. Three months after she also developed several vitiligo patches, which firstly appeared on the hands. Four years later, she developed an autoimmune atrophic gastritis. We observed multiple achromic patches localized on the eyelids, the corners of the mouth, nipple, surrounding areola, and on the perianal region. Hair leucotrichia was also detected. Her family history was negative for autoimmune disease.

A 43-year-old Belarusian woman reported a personal history of Hashimoto's thyroiditis, which was discovered 9 months after the nuclear accident. One year later she developed achromic macules on the hands and lower limbs, which were still detectable at the moment of our observation. Clinical examination under both natural light and Wood's lamp was suggestive of non-segmental vitiligo. Anti-parietal cell autoantibodies were negative. Family history revealed a positive family history of Hashimoto's thyroiditis.

The Chernobyl nuclear accident, which occurred on April 26th, 1986, induced a widespread radioactive release of radioiodines and cesium into the environment. Such radioactive cloud was also carried by wind predominantly in westward direction. Hence, a few days later it reached Western Europe, where rainfall gave rise to significant levels of radioactivity at ground level. Consequently, a large population both in Ukraine, Belarus, Russia and in Western Europe had been potentially exposed to ionizing radiation, mostly from ingestion of radioiodine-contaminated food, inhalation of radioactive isotopes dispersed in the environment or skin contamination. Epidemiological studies report an increased long-term risks of thyroid cancer and non-malignant diseases, such as ATD, in individual living in the neighboring areas and exposed as children and adolescents.[1]

Herein we report three cases of patients previously living in neighboring areas where the nuclear accident occurred and there-

TABLE I.—*Summary of clinical series.*

	Case 1	Case 2	Case 3
Age (years)	46	40	43
Vitiligo: months after radioactive fallout	7	6	21
Autoimmune thyroid disorders: months after radioactive fallout	24	9	9
Anti-thyroglobulin (TgAb)	Yes	Yes	Yes
Anti-thyroperoxidase autoantibodies (TPOAb)	Yes	Yes	Yes
Anti-parietal cell autoantibodies	No	Yes	No
Other associated autoimmune diseases	No	Autoimmune atrophic gastritis	No
Family history of vitiligo	No	No	No
Family history of autoimmune thyroid disorders	Yes	No	Yes
Sites of vitiligo macules	Upper and lower limbs	Eyelids, corners of the mouth, nipple and surrounding areola, perianal region	Hands, lower limbs

fore possibly exposed to ionizing radiation through inhalation or skin contamination (Table I). All our patients developed autoimmune disorders such as vitiligo and Hashimoto's thyroiditis shortly after the Chernobyl radioactive fallout, to which were exposed during childhood or adolescence.

Vitiligo and ATD can be associated, as reported by a recent systematic review.[2] The chronic inflammatory milieu of vitiligo, sustained by a continuous immune system activation and a consequent release of pro-inflammatory cytokines, can lead to local and systemic reactive oxygen species (ROS) accumulation.[3] It is conceivable that increased ROS levels might be toxic for thyroid, as previously reported.[4] Namely, an oxidative stress might lead to the release of large amounts of thyroglobulin proteins that could be more accessible to immune system attack. At the same time, increased ROS levels have been demonstrated in patients with thyroid autoimmunity, possibly able to modify tyrosinase or other melanogenic proteins into neo-antigens, leading to the appearance of vitiligo. Thus, melanocytic and thyroid system might interact, creating a vicious cycle in which thyroid autoimmune processes give rise to vitiligo lesions, and in turn vitiligo sustains the formation of thyroid autoimmunity.[3] In case of the Chernobyl nuclear plant, we hypothesize that environmental exposure to endocrine disruptors, able to impair thyroid function through a wide range of molecular toxic mechanisms, including increased ROS levels, might have a causal role for autoimmunity. In different regions of Belarus an increased exposure to nitrates in drinking water due to usage of fertilizers has been reported after the Chernobyl accident.[5] Such an exposure seems to be responsible, together with ^{131}I exposure, of the increased incidence of childhood thyroid cancer in Belarus after the Chernobyl accident, since ingested nitrate is considered as a thyroid disruptor.[5] Therefore, an increased ROS accumulation due to an environmental exposure could induce changes of both melanocytic structures and thyroid proteins, leading to the frequently reported association of vitiligo and thyroid diseases. In addition, it is conceivable that the psychological stress following the nuclear accident might have triggered vitiligo and associated ATD, since both of them recognize stress as a triggering or worsening pathogenic factor.

Thus, the synergic action of low doses of radiations, endocrine disruptor exposure and psychological stress in a genetically predisposed individual might have induced an immune system activation and ROS production, thus leading to vitiligo development. In turn, the inflammatory and oxidative milieu due to vitiligo might have unmasked or modified some thyroid structures, thus leading to the development of thyroid neo-antigens, specific antibody formation and thus an overt ATD.

In the light of our cases, we hypothesize that an exposure to environmental factors connected with Chernobyl accident might have triggered vitiligo and ATD. Nevertheless, since the causal role of ^{131}I exposure in eliciting thyroid autoimmunity and benign thyroid diseases is still controversial, we cannot provide a certain evidence for a synergistic causative role provoked by radioactivity and endocrine disruptors exposure from the accident. Further epidemiological studies on vitiligo patients exposed to Chernobyl radioactive fallout might be useful to support our hypothesis.

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Conflicts of interest.—The authors certify that there is no conflict of interest with any financial organization regarding the material discussed in the manuscript.

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Leukemia cutis in a Ph+ ALL patient treated with ponatinib

Leukemia cutis (LC) is a dissemination of leukemic cells within the skin. Clinical presentation consists of isolated or disseminated, erythematous to purplish-like papules, plaques or nodules, which usually involve the lower extremities.[1] In ten to 15% of cases, LC is akin to acute myeloid leukaemia,[1-3] while the incidence in acute lymphoid leukemia (ALL) is rare, ranging from 0.5% to 3%.[2] B-cell lineage ALL LC cases occurring in the non-pediatric population