

CLINICAL STUDY

Thyroid examination in highly radiation-exposed workers after the Chernobyl accident

Bernhard O Boehm^{1,*}, Marianna Steinert^{2,*}, Johannes W Dietrich¹, Ralf U Peter³, David Belyi⁴, Gerald Wagemaker⁵, Silke Rosinger¹, Theodor M Fliedner² and Melanie Weiss²

¹Division of Endocrinology, Department of Internal Medicine and ²Radiation Medicine Research Group and WHO-Collaborating Centre for Radiation Accident Management, University of Ulm, D-89081 Ulm, Germany, ³Department of Dermatology, Federal Armed Forces Hospital, D-89081 Ulm, Germany, ⁴Scientific Centre of Radiation Medicine, UKA-252050 Kiev, Ukraine and ⁵Institute of Hematology, Erasmus University of Rotterdam, NL-3015 Rotterdam, The Netherlands

(Correspondence should be addressed to B O Boehm who is now at Division of Endocrinology and Diabetes, Albert-Einstein-Allee 23, University Medical Centre Ulm, D-89081 Ulm, Germany; Email: bernhard.boehm@uniklinik-ulm.de)

*(B O Boehm and M Steinert contributed equally to this work)

Abstract

Context: Radioactive contamination from the Chernobyl nuclear accident that happened on the morning of 26th April 1986 had a major impact on thyroid health in the Belarus region.

Objective: Observational study of a cohort of 99 adults, most strongly exposed to ionizing radioactivity.

Design, setting and patients: Observational study performed between 1998 and 2000. The cohort comprised 99 workers (92 male) of the Chernobyl nuclear power plant. Examination including physical examination, ultrasonography of the thyroid gland and measurement of serum free thyroxin (fT₄), free triiodothyronine (fT₃) and TSH. Anti-thyroperoxidase (anti-TPO), antithyroglobulin (anti-Tg) antibodies and thyroid stimulating immunoglobulin were also determined.

Main outcome measures: The impact of exposure to high-dose radiation, including radioactive iodine, on the thyroid gland was examined.

Results: Levels of fT₄ in all probands were within the normal World Health Organization-defined range. Elevated levels of fT₃ were found in two workers (2%), high titres of anti-TPO and anti-Tg antibodies were present in four subjects (4%). Mild hypothyroidism was present in one patient. Enlargement of the thyroid gland was observed in 17 workers (17%). There was no evidence of clinically overt thyroid cancer.

Conclusions: The Chernobyl accident showed surprisingly little impact on the thyroid in a cohort of workers strongly exposed to radiation. Our data suggest an age-dependent heterogeneity in response to the short-lived radioiodine isotopes and favours long-term follow-up analysis.

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Introduction

On the 26th of April 1986, reactor 4 at the Chernobyl nuclear power plant severely malfunctioned. The Chernobyl accident is the worst disaster in the history of nuclear power generation. According to recent data, the air at Chernobyl had been contaminated with about 5300 PBq radionuclide activity, including 1760 PBq (131)I and 85 PBq (137)Cs. The highest radiation was received by the liquidators (0.8–1.6 Gy), lower doses were received by the population that was evacuated or inhabited the contaminated areas (1–3). The released radioactivity caused a major increase in thyroid cancer in children, and led overall to an almost 100-fold increase in thyroid cancer incidence in the Belarus region (4). These thyroid cancers demonstrated an aggressive phenotype with a high prevalence of lung metastasis (5).

To evaluate the impact of the Chernobyl accident on thyroid health in a unique cohort of power-plant workers and so-called liquidators, a follow-up study (1998–2000) was conducted. These adults were most strongly exposed to the ionizing radioactivity. In this report, we describe results from a cross-sectional evaluation of 99 probands who were among the most severely irradiated employees of the Chernobyl power plant and who were originally suspected to have had acute radiation sickness (ARS).

Patients and methods

Subjects

Ninety-nine patients exposed to ionizing radiation from the Chernobyl accident and available for

follow-up at clinical centres in Kiev, Moscow and Ulm were examined between 1998 and 2000. The cohort comprised 92 male and 7 female patients with a mean age at the time of exposure of 33 years (range 21–60 years) and a mean age at follow-up examination (1998–2000) of 47 years (range 35–74 years).

Twenty-four of 99 (24%) reported regular oral iodine administration, with a maximal dose of 200 µg/day before and after the accident. Blocking of radioiodine uptake by thyroid using potassium iodide (KI) according to International Atomic Energy Agency recommendations (KI prophylaxis) had not been used in this cohort.

These patients were among the most severely exposed to high local doses of β-particle and γ radiation, either as working personnel within the reactor immediately after the accident or as members of the immediate clean-up forces (so-called liquidators) in the days following the accident. Table 3 gives histories of patients with an impairment of the thyroid gland during or immediately after the accident.

The whole-body exposure radiation dose was reported as 0.3–8.7 Gy (2). All patients were classified into four groups based on the severity of ARS in the acute phase after the accident, as previously described (6). Patient characteristics with respect to ARS severity are presented in Table 1. Twenty-two patients in the study cohort suffered from first-degree ARS, 24 from second-degree ARS, 10 from third-degree ARS, and one from fourth-degree ARS. The study cohort also included 42, so-called non-confirmed patients, who were exposed to radiation doses that were not sufficient to induce ARS. The ARS radiation doses received were, however, high enough to cause mild clinical signs and symptoms, including changes in peripheral blood counts. In 1989, a re-evaluation of the so-called non-confirmed showed that these patients did not in fact have ARS.

Physical examination

Detailed case histories were obtained and physical examinations were performed in all patients. Thyroid enlargement was determined using inspection and palpation in accordance with the WHO definition of 4 degrees: 0a, no goitre; 0b, palpable but not visible goitre; I, palpable and visible goitre at reclined head position; II, visible goitre.

Ultrasonography

The thyroid gland was examined using a high-resolution linear ultrasonographic 7.5-MHz transducer (Aloka 630, Japan). The volume of the thyroid gland was determined as reported by Brunn and coworkers (7). Subsequently, thyroid gland enlargement, i.e. goitre, was diagnosed when the thyroid gland volume exceeded 25 ml in male or 20 ml in female patients respectively. If present, nodules were classified according to the following features: no/diffuse microcalcifications, regular/irregular margins, regular/irregular sonolucent halo and no/regional lymphadenopathy. No fine-needle biopsies have been performed and no thyroid surgery was performed after the accident.

Lab analysis

Serum concentrations of fT₄, fT₃ and TSH were measured using highly sensitive immunometric technology (Ortho-Clinical Diagnostics GmbH, Neckargmünd, Germany). Serum levels of anti-thyroperoxidase (anti-TPO) and antithyroglobulin (anti-Tg) antibodies were determined using a commercially available variable ELISA (Vita Diagnostica GmbH, Freiburg, Germany). The ELISA test was considered, according to the criteria of the European Thyroid Association, as detecting anti-TPO in preparations of thyroid microsomes (8). Thyroid stimulating immunoglobulin (TSI) titres were measured using a commercially available

Table 1 Patient characteristics according to acute radiation sickness (ARS) severity.

ARS severity	Primary diagnosis 1986	ARS re-evaluation ^a 1989	Deaths in the acute period ^b	Survivors of the acute phase	Deaths 1986–2000 ^c	Survivors at the end of 2000	Number of examined patients 1998–2000 ^d	Patients with thyroid impairment 1998–2000
Non-confirmed	0	103	0	103	6	97	42	5
I mild	131	41	0	41	4	37	22	5
II moderate	59	50	1	49	6	43	24	6
III severe	26	22	7	15	3	12	10	0
IV very severe	21	21	20	1	0	1	1	1
Total	237	237	28	209	19	190	99	17

^aARS was confirmed in 134 cases in 1989 re-evaluations on the basis of clinical symptoms, dynamics of neutrophils, lymphocytes, and thrombocytes in peripheral blood, and chromosomal aberrations of peripheral lymphocytes.

^bTwenty-eight patients died within a few weeks of the accident, mainly due to local injuries rather than bone marrow failure.

^cIn the period between the end of 1986 and 2000, 19 patients died from bone marrow failure ($N=12$); accidents and/or suicide ($N=7$).

^dNinety-nine of the original 237 patients were re-examined between 1998 and 2000.

luminescence receptor assay (BRAHMS Diagnostica GmbH, Henningsdorf, Germany). Autoantibody titres are presented in units of IU/ml (anti-TPO, anti-Tg) or IU/l (TSI) according to a World Health Organization reference. The normal ranges for these thyroid hormones and thyroid antibodies are: fT_4 , 10–23 nmol/l; fT_3 , 1.4–2.8 nmol/l; TSH, 0.2–4.2 mIU/l; anti-Tg and anti-TPO, 0–100 IU/ml; TSI, <9 IU/l. Hypothyroidism was defined as fT_4 < 10 nmol/l and TSH \geq 3.5 mIU/l. Positive thyroid autoantibodies were defined as anti-TPO and anti-TG concentrations > 100 IU/ml and TSI concentrations > 9 IU/l.

Study probands provided written informed consent for the follow-up study.

Results

Physical examination

No clinically apparent signs of thyroid dysfunction were present in the cohort. Various degrees of thyroid gland enlargement were present in 17 of 99 patients. Nine patients had 0b-degree goitre, seven patients had degree-I goitre, and one patient had degree-II goitre (Table 2). No evidence of pressure to adjacent structures, infiltration, lymph-node enlargement or regional or distant metastasis was found on physical examination.

Ultrasonography

Using ultrasonography, a nodular goitre was diagnosed in 10 and a diffuse goitre in seven of the above-mentioned patients respectively (Tables 2 and 3).

All nodules determined were lacking microcalcifications, irregular margins, irregular sonolucent halo and regional lymphadenopathy. Four probands revealed a solitary thyroid nodule, and six probands showed multinodularity. All nodules appeared with a regular margin and/or a well-defined sonolucent halo. No fine-needle biopsies have been performed.

Laboratory examination

Thyroid hormones could be determined in 74 out of 99 patients. Serum fT_4 levels were within the normal range in all cases (mean + s.d. 18 nmol/l + 2.46, range 12.4–23.3 nmol/l). In one patient, the serum TSH level was slightly above the normal range (4.49 mIU/l), and fT_4 was close to the reference minimum (11 nmol/l). This male patient had suffered from fourth-degree ARS. In 1986, he was 25 years old; at the time of examination, he was 39 years old. Two patients had elevated serum fT_3 levels (2.98 and 4.15 nmol/l). There were, however, no abnormalities in fT_4 , basal TSH, or thyroid antibodies. Both patients were reported as having suffered second-degree ARS; their age at exposure was 25 years, and their age at examination was 40 years.

Autoantibodies

In four cases (three males, one female), anti-TPO antibodies were present at a markedly high concentration (mean + s.d. 1104 IU/ml + 1275, range 234–3000 IU/ml). Three out of these four patients also had increased anti-TG antibody titres (mean + s.d. 1119 IU/ml + 1629, range 202–3000 IU/ml). In three of these patients, serum fT_3 , fT_4 and TSH concentrations

Table 2 Laboratory findings.

Patient number	ARS severity	Age at examination (years)	Goitre	Thyroid hormones			Thyroid antibodies		
				TSH (mIU/l)	fT_4 (nmol/l)	fT_3 (nmol/l)	Anti-Tg (IU/ml)	Anti-TPO (IU/ml)	TSI (IU/l)
1	n.c. ^a	63	0b	1.47	17.6	2.05	69	234	<1
2	n.c.	45	0b	3.1	20.4	2.65	13	15	<1
3	n.c.	48	I	1.12	14.4	2.09	22	<10	<1
4	n.c.	61	I	3.71	22.6	2.27	<10	<10	<1
5	n.c.	73	0b	2.63	15.7	2.14	33	<10	<1
6 ^b	I	58	0b	2	23	2.07	202	580	<1
7	I	45	I	2.32	17	1.91	45	<10	<1
8	I	55	0b	2.12	16	1.84	<10	<10	<1
9	I	56	I	1.35	13.3	1.8	<10	<10	<1
10	I	70	0b	2.35	21.4	2.03	<10	<10	<1
11	II	61	I	3.56	19.2	2.04	154	>3000	<1
12	II	64	I	9.4	18.9	2.19	>3000	600	1.4
13	II	37	0b	0.6	17.6	4.15	41	<10	<1
14	II	38	0b	3.33	23.3	2.98	12	<10	<1
15	II	68	I	2.95	17.7	1.94	25	<10	<1
16	II	52	II	2.18	20.2	2.18	17	<10	<1
17	IV	40	0b	4.49	11	1.36	13	11	<1

^aNon-confirmed patient.

^bFemale patient.

Table 3 History of patients with structural or functional thyroid abnormalities.

Patient number	History
1	Worked as watchman on the night of the accident ^a and stayed 150 m from the reactor area for 15 min
2	Worked as a fireman for ~4 h on the night of the accident
3	On the night of the accident worked 1400–1500 m from the explosion area in block IV, stayed there until 0500 h, and during the following hour was located 300–400 m from the explosion area. On April 26 at 0600 h experienced headache and nausea and vomited several times
4	Worked as a watchman and spent 8 h walking ~20–30 m around the reactor on the night of the accident
5	Worked as a member of the liquidator team immediately after the accident
6	Worked on the night of the accident and spent 10 min 50–100 m from the explosion area in block IV. On April 26 at 1600 h, experienced nausea and vomited 10 times. Patient was transferred to Hospital Number 6 in Moscow 1 day after the accident
7	Worked at the reactor for 2.5 h on the night of the accident. Immediately after the accident, the patient took 200 µg potassium iodide and put on a gas mask. On April 26 at 0600 h experienced nausea and vomited 3 times. Patient was transferred to Hospital Number 6 in Moscow 1 day after the accident
8	Employee at the Chernobyl power plant since 1977. Arrived at the power plant on April 26 at 0400 h and stayed until 1400 h. On April 30, experienced nausea and was hospitalized at Kiev Region Hospital
9	Worked as a member of the liquidator team for ~5 h on April 26
10	On April 26 worked for 4 h in block IV, 150 m from the explosion area
11	Arrived at the reactor site ~5 h after the explosion, took 200 µg potassium iodide at the entrance gate, and received a protective mask. Spent ~2 h 30–40 m from the explosion area. At 1230 h experienced nausea and vomited several times. Was transferred to Hospital Number 6 in Moscow 1 day after the accident
12	Arrived at the power plant ~3 h after the explosion and spent 30 min in block IV, 300 m from the explosion area. On April 26 at 1330 h experienced nausea, general fatigue, and headache and vomited more than 10 times
13	On April 26 between 0800 h and 0900 h worked in the power plant 300 m from the reactor. At 1000 h experienced headache and nausea and vomited four times. Was transferred to Hospital Number 6 in Moscow 1 day after the accident
14	Worked as a technician at the reactor on the night of the accident. Arrived on April 26 at 0245 h and spent ~5 h 200–300 m from the explosion area. Wore protective overalls
15	Employee at the Chernobyl power plant since 1976. On the night of the accident was working as a senior engineer in technical supervision. On April 26, arrived at the reactor at 0200 h and stayed for ~15 h. Visited different rooms and points of the reactor. On April 26 at 0300 h experienced nausea. Was transferred to Hospital Number 6 in Moscow 1 day after the accident
16	Employee at the Chernobyl power plant since 1977. On the night of the accident worked as watchman at blocks V and VI. On April 26 at 0500 h arrived at the builder's temporary office, 400 m from block IV. At 0800 h experienced nausea, and at 0900 h vomited six times. Transferred to Hospital Number 6 in Moscow 1 day after the accident
17	On the night of the accident worked in block IV 100 m from the reactor. Became severely contaminated by sitting on contaminated pipes. Changed clothes for the first time 3.5 h after the accident. Transferred to hospital Number 6 in Moscow 1 day after the accident. Received bone marrow transplantation

^aChernobyl accident occurred on April 26, 1986 at 1:23 AM (Moscow time).

were within the normal range, whereas in one patient TSH was elevated to 9.4 mIU/l without corresponding changes in fT₃ and fT₄ levels. Thyroid antibodies in the antibody-positive patients were associated with clinically and sonographically observed goitre. In the antibody-positive patients, mean thyroid gland volume was 33 ml (range 28–40 ml) in males and 25 ml in the female patient. At the time of exposure, the mean age for all four patients was 47, and was 62 years at examination. Of these patients, two had suffered from second-degree ARS, one from first-degree ARS and one belonged to the non-confirmed group (Table 2 and 3).

Discussion

Twelve to fourteen years after the Chernobyl accident, we studied a cohort of adults who were exposed to particularly high levels of ionizing radioactivity, including a high dose of radioactive iodine (131-I, 132-I, 133-I and 135-I). This unique cohort comprised 99 long-term survivors from a group of 237 Chernobyl

workers including also liquidators originally diagnosed with ARS. By contrast to what has been reported for children from the Belarus area, the impact of the Chernobyl accident on the thyroid condition in this adult cohort was found to be different. No clinically overt thyroid cancer was found.

It is well known that exposure to ionize radiation is associated with an increase in incidence of thyroid abnormalities and in particular thyroid cancer (9–13). An increase in the incidence of thyroid cancer was observed in survivors of the atomic bomb in Japan (14) and in residents of the Marshall Islands exposed to ionize radiation during the testing of hydrogen bombs (15). Of note is the higher rate of thyroid cancer in females. The cohort addressed in our study mostly comprised men therefore reducing the likelihood of thyroid cancer *per se*.

In Belarus, Russia, and the Ukraine there was a marked increase in the incidence of paediatric thyroid cancer following the Chernobyl accident (16–19). Previous studies demonstrated a higher prevalence of nodular goitre in atomic bomb survivors as compared

with individuals in control groups (20, 21). In our cohort, nodular goitre was present in only 10%. Based on the physical examination and ultrasonography thyroid nodules observed were classified as most likely benign lesions. However, there are no ultrasound characteristics that definitively exclude carcinoma. Since fine-needle biopsies or thyroid surgery had not been performed, we can not rule out the presence of thyroid cancer.

In adults, unlike in children, other radiation-induced pathologies of the thyroid gland such as autoimmune thyroiditis may become more prevalent. In atomic bomb survivors and patients treated with external radiation for non-thyroid diseases, exposure to radiation was associated with increased incidence of thyroid autoimmunity (22–24). In our study, we also found evidence of thyroid autoimmunity. Affected patients reported pain over the thyroid gland, which suggests antibody formation due to acute radiation thyroiditis (25, 26). However, it is important to acknowledge that thyroid autoimmunity has also been described in healthy individuals with no documented exposure to ionizing radiation. In two population-based studies from the United Kingdom (Wickham Study) and Australia (Busselton Health Survey) anti-TPO prevalence rates of 6.8% and 6.6% respectively, were reported (28, 29). In a more recent study using the same antibody detection technology as in this study, 5.1% of Caucasian healthy blood donors were anti-TPO positive (30).

A limitation of the study is that it is an observational study with no control group. In addition, the number of probands is low when compared with standard population-based evaluations. Therefore, only observational data of a very unique group of patients can be presented. Long-term follow-up including fine-needle aspiration of thyroid nodules will be needed to define the cancer risk more accurately. In view of previous observations of thyroid malignancy in radiation-exposed patients, there is still a high probability of subsequent development of thyroid malignancies. Therefore, in accordance with published data, and due to the high susceptibility of the thyroid gland to radiation damage, a detailed long-term follow-up of thyroid function during the next several decades would be of great importance in identifying thyroid malignancies and deviation of its function. Our data, however, do suggest that the pathobiology of the thyroid gland after radiation exposure is different in adults versus children (30, 31).

Declaration of interest

The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of the research reported.

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