Head and neck lesions in a cohort irradiated in childhood for tinea capitis treatment

We read with interest Shifra Shvarts and colleagues' Historical Review on the tinea capitis treatment campaign in 1950s Serbia.[1] Treatment of tinea capitis infection that included radiation was also used in Portugal in the same period, in accordance with the same Kienbock-Adamson technique.[2] We had access to the registries of a cohort treated in the north of Portugal, which included patients' details, treatment dates, tinea diagnoses (type of infection), and doses received (table).

In March, 2006, we started to locate and contact the cohort members; this was a difficult task because 40–50 years have passed since their tinea capitis treatment. Nevertheless we have traced 3548 individuals, to whom we sent information letters with a free-phone contact number. This method allowed us to clinically examine 1287 individuals, all by the same clinician (TG), and report that 292 are dead and 85 are living abroad.

We recommended neck ultrasounds, and 886 (70%) of the participants had the examination. A fine-needle aspiration biopsy was advised in 221 patients who had nodules with suspicious features. Surgery was proposed for 45 people whose biopsy samples showed malignant or follicular lesions. At clinical examination, 18 individuals had been previously diagnosed with thyroid carcinoma, and we diagnosed 15 more. In total, we recorded a 2·6% prevalence of thyroid carcinoma; similar to the 2·1% reported for survivors of the Hiroshima and Nagasaki atomic bombs in a survey study by Misa Imaizumi and colleagues[3] that used a similar protocol (thyroid ultrasonography). If we exclude from our study the previous diagnoses, the prevalence decreases to 1·4%, which is similar to the 0·95% reported by Siegal Sadetzki and co-workers.[4]

Our data seem to agree with the high risk of thyroid tumours reported in Shvarts and colleagues' study.[1] We have observed in our cohort a high prevalence of meningiomas and basal-cell carcinoma (data not shown), not mentioned by Shvarts and colleagues. We have also shown in this cohort that the favus tinea infection gives an eight-times increase in risk of alopecia when compared with trichophytic tinea, even after adjustment for age and irradiation dose.[5]

Our data support and emphasise the arguments presented by Shvarts and colleagues, that physicians should be aware of particular subsets of population that might be at risk of late radiation-associated health effects. These data justify a close follow-up of the irradiated tinea capitis cohorts to identify those head and neck lesions that are undiagnosed.

	Cohort member (n=5358)	Participants (n=1287)
Sex		
Female	2804 (52%)	767 (60%)
Male	2554 (48%)	520 (40%)
Type of infection		
Favus tinea	1164 (22%)	215 (17%)
Microsporic or trycophitic tinea	4191 (78%)	1072 (83%)
Not known	3 (<1%)	0
Age (years) at irradiation		
≤5	1352 (25%)	419 (33%)
>5 and ≤15	3765 (70%)	850 (66%)
>15	185 (4%)	18 (1%)
Not known	56 (1%)	0
Irradiation dose		
325–475 roentgens	5024 (94%)	1206 (94%)
≥630 roentgens	318 (6%)	74 (6%)
Not known	16 (<1%)	7 (<1%)
Thyroid pathology		
Thyroid carcinoma	..	33 (3%)
Follicular adenoma	..	18 (1%)
Thyroid nodules	..	462 (36%)

Data are number (%).

Table: **Registry variables of the tinea capitis irradiated cohort in the 1950–63 study, from the Dispensário de Higiene Social do Porto, and participants of the present study**

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Balkan NDM-1: escape or transplant?

The December, 2010, issue of *The Lancet Infectious Diseases* carried further correspondence related to our article about NDM-1,[1] and reported cases worldwide. Several patients had travelled to the Indian subcontinent—the epicentre of the enzyme's distribution.[1] A minority, however, in Belgium, Denmark, and Germany had no such links, but had been admitted to hospitals in Balkan countries, including Bosnia, Kosovo, Montenegro, and Serbia. A Balkan link was also highlighted by Marc Struelens and colleagues[2] after the reporting of these same cases and two in Slovenia (one with hospital admission in Serbia) to the European Centres for Disease Control. Among 55 patients with bla_{NDM-1} positive bacteria and a travel history, Struelens observed that 31 had visited the Indian subcontinent and five had visited Balkan countries.

Two hypotheses might explain a Balkan association for bla_{NDM-1}. First, the bla_{NDM-1} gene was recruited to plasmids from an external origin, probably an environmental organism without clinical relevance. Such bacteria are the source of many resistance genes now prevalent in Gram-negative opportunists. The escape of bla_{NDM-1} might have occurred independently in the Indian subcontinent and the Balkans, just as bla_{CTX-M} genes, which code for cephalosporin-hydrolysing extended-spectrum β lactamases, have escaped repeatedly from *Kluyvera* spp.[3] Alternatively, the NDM-1 enzyme, which was already circulating in India in 2006[4] (versus the first Balkan-linked case in 2007[5]) could have been imported from the subcontinent to the Balkans. We are struck, in this context, by a report[6] that patients from the Balkans travelled to Pakistan for commercial kidney transplants, many with poor outcomes and frequent infection. At least four of the UK patients with NDM-1-positive bacteria had a history of renal transplant in Pakistan.[1] Medical tourism of this sort could have introduced NDM-1 to the Balkans.

Insufficient data are available to confirm or refute either hypothesis, although an answer might come from comparison of bla_{NDM-1} flanking sequences, or host plasmids, found in patients linked to the Balkan states and India or Pakistan. If these sequences are different, the Balkan cases likely represent a second gene escape; if they are identical, then import to the Balkans is the more probable explanation. But this hypothesis cannot be definitively proven without a clear epidemiological trail.

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