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Short communications

Skin eruptions following treatment with Iodine-131 for hyperthyroidism. A rare and un-reported early/intermediate side effect

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Abstract

BACKGROUND: Iodine-131 (^{131}I) is a well-established method for the treatment of hyperthyroidism. Following such therapy, patients may experience symptoms relating to early or delayed side effects that can be prevented or minimized if necessary measures are taken. We have noticed an unusual side effect of ^{131}I therapy in the form of a skin eruption (iododerma) and aimed at assessing the frequency and severity of this side effect.
MATERIAL AND METHODS: Retrospective review of 141 patients treated with ^{131}I between January 1994 to December 2000 (86 F, 55 M; mean age 41.35 ± 11.02 years) was performed. The dose of ^{131}I ranged from 250–500 MBq. Post therapy clinical and biochemical evaluation of thyroid function was done at 6 weeks, 3, 6, and 9 months then annually.
RESULTS: Of the 141 treated patients, 3 patients (2.1%) presented with iododerma 4–6 weeks after ^{131}I therapy administration. Lesions were observed at both ankles & lower legs in all 3 cases. All lesions disappeared within 6 months with no residual effect. No other skin lesions were seen thereafter during the follow-up period.
CONCLUSION: Iododerma is a rare complication of ^{131}I therapy that has not been reported before. It appears within 4–6 weeks after therapy and is a self-limiting condition.
Key words: hyperthyroidism, ^{131}I therapy, complications, iododerma

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Introduction

Hyperthyroidism is a common endocrine disorder caused by a multitude of conditions, the most common of which are Graves' disease, toxic multinodular goitre and autonomously functioning thyroid nodule(s). The classic methods of treatment of hyperthyroidism i.e. antithyroid drugs, ^{131}I and surgery, are effective but have their individual advantages and disadvantages. The most significant of the latter is the development of hypothyroidism, which can take place after any of the above treatment modality with variable duration, frequency and severity.

Treatment with ^{131}I was introduced in 1942 [1] and was reserved for patients over the age of 40 years or those unfit for surgery or suffer of side effects of antithyroid medications, due to fear of radiation-induced carcinogenesis or teratogenesis. Since then various studies have shown that its use is not associated with increased risk of carcinogenesis or teratogenesis [2, 3] and confirmed its efficacy and safety compared to antithyroid medications and surgery [4]. The ease of administration and low cost of ^{131}I combine to make it an attractive method of treatment for the majority of hyperthyroid patients worldwide. It is however not free from side effects that are relatively less severe than other treatment modalities and include hypothyroidism and rarely radiation

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thyroiditis, gastritis and sialadenitis. The development of exacerbation of hyperthyroidism and hypersensitivity to iodine are considered extremely rare.

We have noticed the development of a bilateral skin eruption in the ankles and feet of one of our patients following therapy with ^{131}I. There was no history of a previous dermatological disorders nor a clinical or laboratory test to confirm other aetiology. The purpose of this study was to review the case notes of all patients treated with ^{131}I between 1994 and 2000 to assess the frequency and severity of this complication.

Material and methods

We studied the case notes of 141 patients with hyperthyroidism who received ^{131}I therapy and maintained regular follow-up in the Center for Nuclear Medicine & Ultrasound, Khulna, Bangladesh between January 1994 to December 2000. The mean age of the patients was 41.35 $\pm$ 11.02 years (range 21–67 years) and the female/male ratio was 1.56:1. Of these, 120 (85.1%) patients had diffuse toxic goitre (Graves' disease), 14 (9.9%) had toxic multinodular goitre and 7 (5%) had autonomously functioning thyroid nodules (toxic adenoma).

Diagnosis was done based on clinical manifestations and biochemical criteria including elevated triiodthyronine (T_3), thyroxine (T_4) and suppressed thyroid stimulating hormone (TSH). Thyroid scintigraphy with ^{99m}Tc- pertechnetate was done in all patients to assess the size and nodularity of the gland.

Elderly patients and all those with cardiac disease and severe hyperthyroidism were pretreated with a short course of antithyroid drugs in full dosages until they were clinically and biochemically euthyroid. Medications were stopped 3 days before ^{131}I treatment, restarted 3 days later, and continued for 1 to 2 months depending on the patient's symptoms.

^{131}I was not administered to female patients who were pregnant or wishing to become so very soon after therapy. The likely consequences of the treatment were fully explained to the patients and/or relatives and partners. Full consent was obtained and precautions aiming at radiation protection of the public were discussed.

The dose of ^{131}I given to the patients was empirical with single dose ranged from 250-500 MBq. Follow-up was done at 6 weeks, 3 months, 6 months, 9 months and then annually. Clinical and biochemical evaluation of thyroid function was done in follow-up visit. If the first dose was found to be ineffective in controlling disease activity, then a second dose was considered after proper clinical and biochemical evaluation. The amount of ^{131}I given in the second dose was either the same or 50% more than the first dose. During follow-up, patients were classified as cured if the functional status was either euthyroid or hypothyroid within 1 year without further treatment of hyperthyroidism by drugs or ^{131}I.

Results

A single dose of ^{131}I was given to 119 (84.4%) patients, and a second dose was required in 22 (15.6%) patients. Of the 141 patients treated, 11 had severe hyperthyroidism and/or cardiac disease necessitating treatment with antithyroid medications for more than four weeks before treatment. These medications were stopped 3 days before, restarted 3 days after ^{131}I treatment, and continued for 1 to 2 months. None of those patients developed any skin manifestation relating to the use of antithyroid medication.

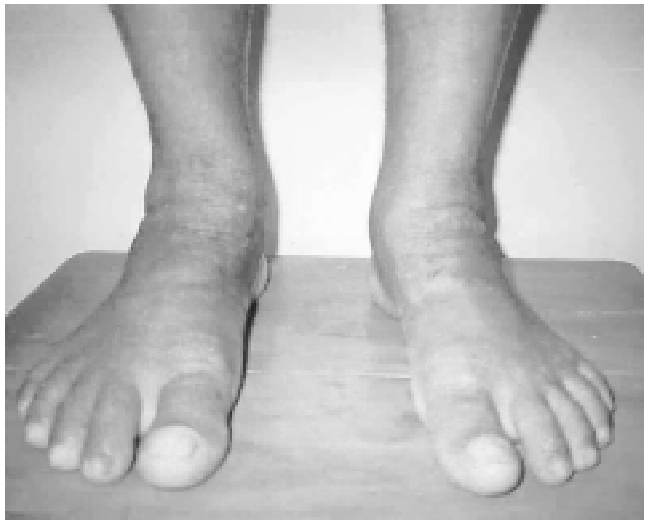

Figure 1. Photograph of lower limbs of patient number 1 showing iododerma involving both ankles and hind feet.

In our study, all patients were followed–up for at least one year following ^{131}I treatment. One hundred and twenty five patients (88.7%) were diagnosed as cured within one year. Hypothyroidism at one year after ^{131}I therapy was observed in 12 (8.5%) patients.

Three patients (2 males and 1 female), comprising 2.1% of all treated cases, presented with skin lesions at 4–6 weeks after ^{131}I administration. The lesions were diagnosed as iododerma and were observed on ankles and lower legs bilaterally in all cases, with multiple inflamed follicular pustules and bullous formations that become ulcerated and crusted (Figure 1).

No such lesions were seen in any other patient who received ^{131}I therapy from the same source. The amount of sodium iodide component of the dose was less than 4.2 μg in all patients. All three patients had Graves' disease. The female patient was pretreated with antithyroid medication for 2 weeks prior to ^{131}I treatment due to severe hyperthyroidism, while the two male patients did not receive any antithyroid medication. The biochemical status of the thyroid and the administered dose of I-131 of these three patients are shown in Table 1. All skin lesions disappeared within 6 months with no residual effect (Figure 2).

Discussion

^{131}I therapy for hyperthyroidism has been well established for more than 60 years. In contrast to surgery and antithyroid drugs, ^{131}I is a simple, inexpensive and effective mode of therapy. It is however not free from side effects that are well documented and can be prevented or minimized if appropriate measures are taken. Hypersensitivity to iodine is extremely uncommon in association with ^{131}I therapy since the quantity of sodium iodide is infinitely small, usually in the order of few micrograms. It is therefore a common practice to prescribe ^{131}I therapy to patients known to be hypersensitive to iodine.

Hypersensitivity to iodine is an idiosyncratic reaction that is not dose-dependent [5, 6] and may cause a wide variety of skin

Table 1. Thyroid hormone levels & administered dose of I-131 in-patient with iododerma

No.	Sex	Age	Dose [MBq]	T_3 [nmol/L]	T_4 [nmol/L]	TSH [mIU/L]
1	M	47	296	4.56	284.05	0.24
2	M	42	370	4.78	293.06	0.12
3	F	40	296	7.71	> 300	Undetectable

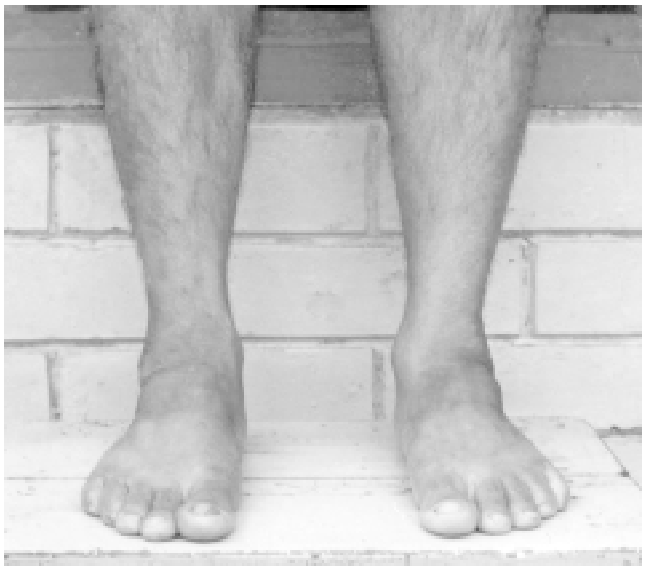

Figure 2. Photograph of same patient as in figure 1 showing disappearance of lesions within 6 months. The difference in skin colour of forefeet and hind feet is due to wearing a sandal.

eruptions referred to as iododerma. The most common type is an acneiform eruption with inflammatory follicular pustules. In mild cases pruritis and urticaria may be manifested but vegetative or fungating lesions may also occur [7]. Bullous lesions are also common with ulceration and crustation. Iododerma may occur in the face, neck, extremities and trunk.

In our study, iododerma of the ankles & lower legs occurred in three (2.1%) patients within 4–6 weeks of treatment despite the fact that they received less than 4.2 μg sodium iodide from ^{131}I therapy. The lesions were self-limiting and disappeared within 6 months with no residual effect.

Other possible causes of the rash have been excluded, as the patients had no previous history of a dermatological or autoimmune disorders. It could not have been caused by idiosyncrasy to carbimazole in our female patient due to the difference in type of eruption and time of onset. The rash that is associated with carbimazole appears within 3–6 weeks of starting therapy [8], and is commonly maculo-papular in type, accompanied by systemic signs such as fever [9]. This is in contradiction to our case in which the rash appeared 8 weeks after starting carbimazole therapy in the form of multiple inflamed follicular pustules and bullous formations followed by ulcerated and crustation.

Conclusion

This is the first report of three cases of iododerma of the ankles and feet developing within 4–6 weeks following ^{131}I therapy for hyperthyroidism. This early/intermediate side effect was seen in around 2% of our treated patients. It is a self-limiting condition that disappears completely within 6 months without any specific treatment. Patient may need to be notified about the possibilities of developing this skin lesion along with other early side effect before administering ^{131}I therapy.

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