

## CASE REPORT

# Successful radioiodine treatment in a 3 year old child with Graves' disease following antithyroid medication induced neutropenia

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A 3 year old child with Graves' disease and mitral valve prolapse became neutropenic on carbimazole therapy. She was switched to propylthiouracil but the neutropenia recurred. She was treated with radioiodine but required two doses of 113 MBq and then 198 MBq five months later before becoming hypothyroid. The mitral valve prolapse resolved when she was euthyroid on thyroxine replacement. Antithyroid drugs, surgery, and radioiodine all have a place in the management of the thyrotoxic child.

There is no ideal treatment for the child with thyrotoxicosis.<sup>1</sup> Medical therapy has potentially serious complications such as neutropenia, and young patients usually relapse when treatment is stopped.<sup>2</sup> Surgical management with partial or total thyroidectomy carries the risks of any major operation, as well as problems such as hypoparathyroidism and potentially disfiguring keloid scar formation. Partial thyroidectomy also carries the risk of recurrence.

Radioiodine therapy is an effective way of treating adults with thyrotoxicosis, but there is a reluctance to use this

therapy in childhood in Europe.<sup>3</sup> This may reflect worries about carcinogenesis and impaired fertility, although there is little objective data to substantiate these concerns.<sup>4,5</sup> Royal College guidelines state that radioiodine can safely be given to patients of all age groups, although the long term data on administration in the young child are limited.<sup>5</sup>

### CASE REPORT

A 3 year old child presented with a four month history of neck swelling, sweating, hyperactivity, heat intolerance, and loose stools. Her height was above the 91st centile and her weight above the 50th centile (midparental target approx. 25th centile). On examination she was thyrotoxic with a goitre and thyroid eye disease (fig 1). The pulse rate was 146/min and blood pressure 126/68 mm Hg. Heart sounds were normal, but there was a grade 3/6 pansystolic murmur that radiated to the axilla. There was a strong family history of autoimmune thyroid disease, although both parents were unaffected.

Investigations confirmed the clinical picture with a suppressed TSH (<0.1 mU/l) and raised thyroid hormone concentrations, with a free thyroxine of 130.2 pmol/l (normal range 11–23 pmol/l) and a free triiodothyronine of 27 pmol/l (normal range 3.5–6.5 pmol/l). An isotope scan (technetium-99m pertechnetate) showed increased uptake of 21% (euthyroid range 0.1–3.4%), in keeping with Graves' disease. Thyroglobulin and microsomal antibodies were raised at 1/1 638 400 and 1/26 214 400 respectively. She was assessed by the paediatric cardiology team who confirmed on examination and by echocardiography that there was a mild degree of prolapse of the anterior mitral valve leaflet with resultant mitral regurgitation of mild to moderate degree (fig 2).



**Figure 1** Patient prior to treatment with radioiodine illustrating mild thyroid eye disease.



**Figure 2** Echocardiogram of patient prior to radioiodine treatment, showing mitral valve prolapse. LV, left ventricle; LA, left atrium; MV, mitral valve; MVP, mitral valve prolapse; AO, aorta.

## MANAGEMENT

The child was commenced on carbimazole in a dose of 5 mg three times daily (0.8 mg/kg/day) and propranolol 4 mg three times daily, but presented with a cough six days later. A full blood count showed a white blood cell count of  $5.7 \times 10^9/l$  and neutrophil count of  $2.0 \times 10^9/l$ , which had fallen to  $0.5 \times 10^9/l$  two days later. Carbimazole was stopped and the neutrophil count increased to  $3.3 \times 10^9/l$  two weeks later. Propylthiouracil 160 mg/day (9 mg/kg/day) was started but she became neutropenic after eight days ( $1.0 \times 10^9/l$ ). There was no evidence of intercurrent illness at that stage.

The family discussed management with the paediatric team, thyroid surgeon, and radiotherapist. There were concerns about the risks of surgery in a thyrotoxic child and the family opted for radioiodine treatment. Radioiodine ( $^{131}I$ ) in a dose of 113 MBq was administered five months after presentation. This dose was calculated on the basis that the thyroid gland size was approximately 15 g.<sup>4</sup> The family felt that the goitre size diminished in the subsequent weeks and she started to gain weight. However she remained biochemically thyrotoxic with a TSH of  $<0.1$  mU/l and free thyroxine of 54.3 pmol/l. A second dose of radioiodine in a dose of 198 MBq was administered 10 months after the initial presentation and she became euthyroid in the subsequent weeks. Propranolol was stopped and thyroxine was commenced in a dose of 25 µg/day. The thyroxine dose was increased to 50 µg/day shortly afterwards because of an increased TSH. Her ophthalmopathy improved in the subsequent months and reassessment by the cardiology team confirmed the clinical impression that the mitral valve prolapse had resolved.

## DISCUSSION

Our patient highlights many of the difficulties and controversies when managing thyrotoxicosis in childhood. She became neutropenic on treatment with carbimazole and then propylthiouracil, and the therapeutic options available at that stage were surgery or radioiodine administration. Beta blockade and the administration of iodine containing compounds can reduce the likelihood of a thyroid crisis at the time of thyroidectomy, but it was felt that radioiodine struck the better balance between safety and efficacy.

Radioiodine is a safe medication in adults but the published experience in childhood with associated long term follow up is relatively small.<sup>4</sup> The link between small doses of ionising radiation and thyroid neoplasia, as evidenced by the Chernobyl accident, may be one reason why paediatricians in Europe do not use radioiodine more readily.<sup>6,7</sup> We suspect that we may have underestimated the size of the thyroid gland and that this is why she remained thyrotoxic after the initial dose of radioiodine. The second dose of radioiodine was intended to be twice the initial amount and was chosen in light of the poor initial response and because of the recognised need to ablate thyroid tissue completely.<sup>4</sup> We intend to monitor this child's progress carefully with regular neck examination and ultrasonography, but believe that the risk of thyroid or other cancer developing following this treatment regimen is remote.

An association between thyroid disease and mitral valve prolapse is well recognised, but has not been described in someone with Graves' disease at such a young age as far as we

are aware.<sup>8,9</sup> It may be a manifestation of the autoimmune process,<sup>10</sup> although it has also been described in children with activating mutations of the TSH receptor.<sup>11</sup> The mitral valve prolapse resolved following treatment, which suggests that thyroid hormone excess may have been a contributory factor in our patient.

In summary, our patient illustrates many of the complexities of thyrotoxicosis in childhood. There is no ideal therapy and all treatment modalities should be discussed with the child and family.

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