Changes in percentage of lymphocyte subsets after ^{131}I treatment in patients with differentiated thyroid cancer

LUO Quan-Yong, CHEN Li-Bo, YU Yong-Li, LU Han-Kui, ZHU Rui-Sen

(Department of Nuclear Medicine, Shanghai Sixth People's Hospital, Shanghai Jiaotong University, Shanghai 200233)

Abstract To monitor the extent and the duration of lymphocyte subset changes in patients with thyroid carcinoma undergoing therapeutic ^{131}I administration, the percentage of lymphocyte subsets were serially analyzed before and after ^{131}I treatment. In patients who received 1850 MBq of ^{131}I for ablation of thyroid remnants, only for NK cells and B cells showed a significant reduction. In patients received 3700 MBq of ^{131}I for treatment of local lymph node metastases, NK cells, B cells and CD4+ were found decreased. In patients received 7400 MBq of ^{131}I for treatment of distant metastases, NK cells, B cells and CD4+ and CD8+ were all affected. However, there is no significant reduction compared to the baseline in the percentage of all lymphocyte subsets three months after ^{131}I treatment. The results show that the sensitivity of lymphocytes to ^{131}I internal radiation depends upon lymphocyte phenotype and ^{131}I activity. The immunosuppression effects are temporary and reversible.

Key words Differentiated thyroid cancer, Lymphocyte subsets, Iodine-131, Radiation therapy, Radionuclide

CLC numbers R736.1, R817.5

1 Introduction

Radioiodine therapy is widely used in the treatment of thyroid cancer and toxic goitres. Literature about the effects on the lymphocyte subset modifications in cancer patients undergoing iodine-131 treatment is scarce.[1-3] Changes largely similar to those observed after external radiation therapy for cancer were reported in patients with toxic or atoxic nodular goitre receiving from one to three doses of 300–550 MBq of ^{131}I. At 6 weeks after ^{131}I therapy there was a small but statistically significant increase of the frequency of T cells. This was essentially due to an increased proportion of CD4 T cells. ^{131}I treatment also decreased the capacity of lymphocytes to secrete immunoglobulins (Ig).[4] It is suggested that blood lymphocytes passing through the continuously irradiated gland are damaged mainly by beta-rays from ^{131}I.

Changes in lymphocyte subsets in patients with thyroid carcinoma who received ^{131}I for diagnostic and therapeutic purposes were evaluated.[4,5] The aim of this study was to monitor the extent and the duration of lymphocyte subset changes in patients with thyroid carcinoma undergoing therapeutic ^{131}I administration.

2 Experimental

One hundred and two patients with thyroid carcinoma after total or near total thyroidectomy were entered in the study. There were 33 women and 69 men, with an age range of 24—72 years (mean ± SD: 43 ± 6). Pathological diagnosis found papillary carcinoma in 61 and follicular carcinoma in 41 patients. Patients were divided into three groups. Group A patients received 1850 MBq of ^{131}I for ablation of thyroid remnants, while group B patients received 3700 MBq of ^{131}I for treatment of local lymph node metastases and group C received 7400 MBq of ^{131}I for treatment of distant metastases. All patients were prepared either by waiting 30 days after their surgical thyroidectomy (group A) or by discontinuing L-thyroxine for 30 days prior to ^{131}I administration (group B and group C). All patients were asked to follow a standard low-iodine diet beginning 10 days before the ^{131}I administration. L-thyroxine was resumed after radioiodine administration.

Supported by the Science and Technology Development Fund of Shanghai (No: 024119053)

Received date: 2005-01-21

Serum free triiodothyronine (T3) and thyroxine (T4), thyroid-stimulating hormone (TSH), thyroglobulin (Tg), and the percentage of B (CD19) and T (CD3) lymphocytes, NK cells, subsets CD4, CD8 in peripheral blood were serially analyzed 1 day before ^{131}I administration and 7 days, 1 month, 3 months after iodine administration. Ten euthyroid volunteers served as a control group for lymphocyte subset values. Patients underwent a complete clinical examination on the days when blood samples were drawn. In particular they were carefully evaluated for any sign of infection.

3 Results and discussion

3.1 Lymphocyte subsets

Comparing the baseline lymphocyte subsets of the whole patient group (A+B+C) with the control group, only NK cells showed significantly higher levels in patients than in controls ((19.6±4.1)% vs (15.8±3.4)%, $P<0.05$). Among group A, B, C, only the percentage of NK cells in group C was markedly higher than group A and group B before the administration of ^{131}I.

NK activity has previously been reported to increase in the postoperative period in patients with colon carcinoma.[6] Whether the hypothyroid state or the cancer condition may be related to an increase in NK cells is controversial as conflicting data have been reported in the literature,[7] and little is known about the relationship between thyroid hormones and NK cells in humans.[8-10]

In group A, significant changes after radioiodine administration were observed only for NK cells and B cells, which showed a significant reduction 7 days after ^{131}I treatment (Table 1).

In group B, a decrease in the percentage of NK cells at days 7, 30 was observed, while a significant decrease in the percentage of B cells was only observed at day 7. Among T cells, a reduction in the CD4+/CD8+ ratio resulting from CD4+ decrease at day 30 was observed (Table 2).

In group C, patients showed a decrease in the percentage of NK cells and B cells at days 7, 30. Among T cells, a marked reduction in the CD4+/CD8+ ratio resulting from CD4+ decrease and CD8+ increase at day 30 was observed (Table 3).

Table 1 Changes in lymphocyte subsets after 1.75GBq ^{131}I treatment in group A ($x\pm s$, $n=8$)

Time	NK cell (%)	B cell (%)	T cell (%)	CD4+ (%)	CD8+ (%)	CD4+/CD8+
1 day before treatment	18.3±2.3	11.2±2.1	65.1±6.7	36.2±4.6	28.4±4.9	1.3±0.4
7 days after treatment	12.8±1.9, $P<0.05$	8.2±1.6, $P<0.05$	71.2±7.3	43.6±3.8	30.4±5.6	1.4±0.3
1 month after treatment	17.3±2.4	10.9±1.5	68.6±5.9	40.7±3.5	28.5±4.2	1.5±0.5
3 months after treatment	20.1±2.6	10.1±2.1	66.3±5.5	37.6±4.6	30.1±4.8	1.3±0.2

Table 2 Changes in lymphocyte subsets after 3.7GBq ^{131}I treatment in group B ($x\pm s$, $n=43$)

Time	NK cell (%)	B cell (%)	T cell (%)	CD4+ (%)	CD8+ (%)	CD4+/CD8+
1 day before treatment	19.5±2.6	13.2±1.3	65.2±7.3	39.2±4.3	27.4±3.7	1.4±0.5
7 days after treatment	11.2±2.1 $P<0.01$	9.6±2.4 $P<0.05$	73.3±7.8	40.4±4.7	32.3±4.3	1.3±0.2
1 month after treatment	12.5±2.5 $P<0.05$	13.7±3.0	69.8±5.7	30.1±2.9 $P<0.05$	37.5±4.6	0.8±0.3 $P<0.05$
3 months after treatment	18.8±3.2	11.6±2.1	66.4±6.4	36.4±3.5	30.3±4.1	1.2±0.4

Table 3 Changes in lymphocyte subsets after 7.4GBq ^{131}I treatment in group C ($x\pm s$, $n=51$)

Time	NK cell (%)	B cell (%)	T cell (%)	CD4+ (%)	CD8+ (%)	CD4+/CD8+
1 day before treatment	24.3±2.6	12.1±2.0	60.6±5.3	35.6±4.2	26.1±2.5	1.4±0.4
7 days after treatment	16.7±2.8 $P<0.05$	9.5±1.3 $P<0.05$	67.0±6.2	36.4±4.7	30.8±4.3	1.2±0.1
1 month after treatment	17.2±3.4 $P<0.05$	9.2±1.8 $P<0.05$	68.1±7.5	25.1±3.6 $P<0.01$	40.6±4.4 $P<0.05$	0.6±0.2 $P<0.01$
3 months after treatment	21.1±3.2	12.6±2.3	62.2±4.6	32.1±3.9	30.2±3.4	1.1±0.3

NK cells and B lymphocytes were the most radiosensitive cells. The NK cells reduction was observed in each group, even if at different times. This finding indicates that even relatively low therapeutic ^{131}I activity may affect the NK subset. NK cells are involved in the immune response against viral and tumor antigens. Despite convincing evidence from animal studies, the role of NK cells in the immunological surveillance against cancer in humans is not clearly defined. As NK cells are involved in the immune response against tumor cells, their reduction by ^{131}I radiation therapy may pose additional risks for patients with thyroid cancers who undergo repeated radioiodine treatments. B-cell lymphopenia was marked and becoming evident early after irradiation. These results are in line with what is known about lymphocyte behavior after exposure to external ionizing radiation.[11-13] T cells are more radioresistant than B cells.

In all patients there are no significant reduction compared to the baseline in the percentage of B and T lymphocytes, NK cells, subsets CD4, CD8 and CD4+/CD8+ ratios three months after ^{131}I treatment.

3.2 Hormonal status and clinical evaluation

Mean values of FT4, FT3 and TSH did not differ significantly between the three groups throughout the study. No signs or symptoms of infection were recorded in all patients at the scheduled follow-up examination time. The changes observed in lymphocyte subsets did not have any clinical impact.

4 Conclusion

In DTC patients, the sensitivity of lymphocytes to the effects of iodine-131 internal radiation largely depends upon lymphocyte phenotype and ^{131}I activity. NK cells and B lymphocytes seem to be the most radiosensitive cells. At higher ^{131}I activity B and T lymphocytes, NK cells, subsets CD4, CD8 are all affected. However, these changes do not result in clinically relevant immunosuppression. The immunosuppression effects caused by ^{131}I are generally temporary and reversible.

Acknowledgment

The authors wish to thank Ms. XIN Li-Jun and Ms. DING Ying for their kindly cooperation in this work.

References

1 Leeper R. Thyroid Today, 1982, **4**: 1-6
2 Van Nostrand D, Neutze J, Atkins F. J Nucl Med, 1986, **27**: 1519-1527
3 Blomgren H, Petrini B, Wasserman J, *et al.* Int J Radiat Oncol Biol Phys, 1987, **13**: 209-215
4 Bushnell D L, Boles M A, Kaufman G E, *et al.* J Nucl Med, 1992, **33**: 2214-2221
5 Tofani A, Sciuto R, Cioffi R P, *et al.* Eur J Nucl Med, 1999, **26**: 824-829
6 Tartter P I, Martinelli G, Steinberg B, *et al.* Cancer Detect Prev, 1986, **9**: 359-364
7 Brittenden J, Heys S D, Ross J, *et al.* Cancer, 1996, **77**: 1226-1243
8 Ohashi H, Itoh M. Endocr Regul, 1994, **28**: 117-123
9 Corrales J J, Orfao A, Mirrales J M, *et al.* Hormon Metab Res, 1994, **26**: 104-108
10 Kasuga Y, Kobayashi S, Fujimori M, *et al.* Eur J Surg, 1998, **164**: 173-178
11 Anderson R E, Williams W L. Am J Pathol, 1977, **89**: 367-378
12 Anderson R E, Warner N L. Adv Immunol, 1976, **24**: 215-235
13 Anderson R E, Lefkovits I, Troup G M. Contemp Top Immunobiol, 1980, **11**: 245-274