

## Letter to the Editor

### Endemic Goiter due to Thyroglobulin Gene Abnormality and Social Ostracism

Dear Sir;

Endemic goiter is clustered occurrences of goiter affecting more than 10% of the population in particular regions. The majority cases are attributed to environmental factors such as iodine deficiency, or food and water containing goiter-causing agents called goitrogens. We report a new type of endemic goiter where the basic abnormality was not due to environment factors, but to thyroglobulin gene abnormality and community isolation through social ostracism. About 40 years ago, Komatsu *et al.* were the first to report a high incidence of goiter (14.5% of 379 inhabitants) in the Omuro community, a remote village in Kochi prefecture, Japan [1] (Fig. 1). Subsequently, Tezuka *et al.* reported an 8.1% goiter incidence in 482 inhabitants. The goiter was not caused by iodine deficiency; histology and electron microscope findings suggested possible thyroid hormone formation defects [2, 3]. Until now, no further studies have been conducted. We recently had the opportunity to observe four families from the Omuro community with huge goiters. The goiters were characteristically marshmallow-like in softness, easily discernable by examiners. All patients were euthyroid with low serum thyroglobulin levels and had high radioiodine uptake without iodine organification defect — characteristic clinical pictures of thyroglobulin gene abnormality. They also had the same homozygous missense thyroglobulin gene mutation, Cys1058Arg, and 18 single-nucleotide polymorphisms in the coding region of the thyroglobulin gene [4]. Therefore, we found thyroglobulin gene mutation to be the cause, which linked to all affected families



Fig. 1. Huge goiter with multiple nodules

due to the founder effect. Why have these incidences been confined to the Omuro community? First, thyroglobulin mutation is inherited in an autosomal recessive fashion. Second, the Omuro people have been isolated from other communities because of geological location and discrimination. Social ostracism and segregation have forced the community to marry solely within the same village. Consanguinity boosts the appearance of the autosomal recessive disease. Considering the high incidences of thyroid cancer with thyroglobulin gene mutations [5], patients with this goiter need total thyroidectomy. This goiter can easily be prevented by avoiding marriage within the same community.

Endemic goiter is still a serious worldwide health problem today, and there may be incidences similar to this that have been overlooked or haven't received proper attention. This report indicates that endemic goiters cannot be solely explained by iodine deficiency. The use of molecular, epidemiological and social studies is required to elucidate the cause of unusual type of endemic goiters.

SHUJI Fukata, AKIRA Hishinuma\*, KANJI Kuma, AKIRA Miyauchi  
AND MASAHIRO Sugawara\*\*

Kuma Hospital, Kobe 650-0011, Japan

\*Department of Clinical Laboratory Medicine, Dokkyo University School of Medicine, Mibu, Tochigi, Japan

\*\*Division of Endocrinology and Metabolism, Molecular Pathology Division, Department of Pathology and Laboratory Medicine, Greater Los Angeles Veteran's Affairs Medical Center and UCLA School of Medicine, USA

### References

1. Komatsu T, Geshi K, Yamaoka M (1964) The study of a locality in education — Research on the actual state of health education in the primary and secondary school of Okitsu in Kochi prefecture —. *Report of academic research in Kochi University* 13: 1–60 (In

- Japanese).
2. Tezuka U, Murakami T, Niki M, Mishiro K, Fujino M, Takeichi O (1970) Congenital goiter found in a district of Omuro, Kochi, Shikoku, Japan: environment and incidence of goiter. *Endocrinol Japon* 17: 289–295.
  3. Tezuka U, Murakami T, Mishiro K, Fujino M, Takeichi O (1971) Congenital goiter found in a district of Omuro, Kochi, Shikoku, Japan: morphological study. *Endocrinol Japon* 18: 281–289.
  4. Hishinuma A, Fukata S, Nishiyama S, Nishi Y, Oh-Ishi M, Murata Y, Ohyama Y, Matsuura N, Kasai K, Harada S, Kitanaka S, Takamatsu J, Kiwaki K, Ohye H, Uruno T, Tomoda C, Tajima T, Kuma K, Miyauchi A, Ieiri T (2006) Haplotype analysis reveals founder effects of thyroglobulin gene mutations C1058R and C1977S in Japan. *J Clin Endocrinol Metab* 91: 3100–3104.
  5. Hishinuma A, Fukata S, Kakudo K, Murata Y, Ieiri T (2005) High incidence of thyroid cancer in long-standing goiters with thyroglobulin mutations. *Thyroid* 15: 1079–1084.