CASE REPORT

Langerhans cell histiocytosis presenting as hypothyroid goitre: a unique presentation

Krishna Chaitanya Marupudi,¹ Suman S Karanth,¹ Joseph Thomas²¹Department of Internal Medicine, Kasturba Medical College, Manipal University, Manipal, Karnataka, India²Department of Medical Oncology, Kasturba Medical College, Manipal, Karnataka, India

Correspondence to

Dr Suman S Karanth,
drsumansk@gmail.com

Accepted 19 November 2014

SUMMARY

Langerhans cell histiocytosis (LCH) is a disease involving the antigen presenting cells, which can range from a single system involvement with an indolent course to a multisystem disease with increased morbidity. We present a rare case of LCH presenting as hypothyroid goitre that was successfully treated as per the LCH III trial protocol with a combination of vinblastine and oral prednisolone. We highlight the need for awareness of this rare presentation of LCH as a painless goitre which is often misdiagnosed as poorly differentiated thyroid carcinoma or overlooked as a benign disease.

BACKGROUND

Langerhans cell histiocytosis (LCH) is a heterogeneous disease involving the antigen presenting cells. It can range from single organ involvement with an indolent course, to a multisystem involvement carrying greater morbidity and mortality.¹ While involvement of organs such as bones, skin, lungs, central nervous system and lymph nodes are well documented, the involvement of the thyroid gland is very rare.² We present a rare case of LCH presenting as a hypothyroid goitre, and the diagnostic challenges and treatment protocol in management of this disease.

CASE PRESENTATION

A 33-year-old Indian man presented to us with a painless swelling in the neck for 3 months. In addition, he reported of constipation and weight gain. He did not suffer from fever or have any compressive symptoms. He developed a painful ulcerative lesion over his hard palate.

On examination, a diffusely enlarged, firm and non-tender multinodular goitre was palpable. The rest of the physical examination was unremarkable.

INVESTIGATIONS

Laboratory investigations revealed elevated thyroid-stimulating hormone (TSH) of 100 U/L with low T3 and T4 levels. The patient tested negative for antithyroglobulin antibodies. Blood tests for antithyroid peroxidase, antismooth antibodies and antiparietal antibodies were negative. Ultrasound of the neck showed an enlarged thyroid gland with multiple nodules, the largest being 3.0×1.2 cm in size. Fine-needle aspiration of the thyroid nodule revealed oval cells with grooved and lobulated nucleoli consistent with Langerhans histiocytes, against a background of lymphocytes and eosinophils (figures 1 and 2). Wedge biopsy of the ulcerative lesion on the hard palate revealed a similar

Figure 1 Cells are admixed with focal aggregates of lymphocytes, plasma cells, abundant eosinophils and histiocytes (H&E ×40).

picture. Immunohistochemistry on the biopsy specimen showed positivity to S-100 protein as well as CD1a (figure 3). Contrast-enhanced CT imaging of the brain, head and neck, thorax, abdomen and pelvis were normal. A bone scan performed did not reveal any bony involvement.

DIFFERENTIAL DIAGNOSIS

Multisystem LCH without risk organ involvement.

TREATMENT

The patient was classified as multisystem LCH without risk organ involvement and started on LCH protocol III comprising of vinblastine and oral prednisolone for a duration of 6 weeks. He did not suffer from neutropenia and its complications.

Figure 2 Langerhans cells with deeply grooved 'coffee bean' nuclei.

CrossMark

To cite: Marupudi KC, Karanth SS, Thomas J. *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2014-206760

Figure 3 Immunohistochemistry revealing CD1a positive Langerhans cells (IHC $\times 20$).

OUTCOME AND FOLLOW-UP

Following chemotherapy, we noticed a regression in the size of thyroid swelling as well as healing of the palatal ulcer. The TSH levels were 16.9 U/L postchemotherapy. At follow-up, positron emission tomography of the whole body demonstrated a complete remission of the disease.

DISCUSSION

LCH has been classified as a single system or multisystem disease based on the sites of involvement of disease. Single system LCH typically involves one of the following organs, namely, bone, skin, lymph nodes, lungs or central nervous system. Multisystem disease is identified when two or more organs or systems are involved, with or without the involvement of risk organs, which include the haematopoietic system, liver and spleen.³ Our patient had a palatal ulcer in addition to diffuse thyroidal enlargement and thus was classified as multisystem LCH without risk organ involvement. LCH has a florid clinical picture ranging from skin rash, interstitial lung disease, lytic bone lesions and presentation as tumours. The posterior pituitary involvement in the form of central diabetes insipidus is the commonest endocrine presentation of LCH.^{4 5} Thyroid involvement is extremely rare with 59% of cases mentioned in the literature presenting as diffuse thyroid enlargement and 25.8% presenting as nodular thyroid involvement. Most of the documented cases presented with euthyroid status (40.9%) with only 19.7% presenting as hypothyroidism.⁶ Our patient presented with diffuse painless enlargement and symptomatic hypothyroidism. Thyroid involvement is more common in the adult population and is known to have an indolent course.

The aetiology of LCH is still under investigation with no conclusive evidence, however, the role of immunological dysfunction in the genesis of the disease is being favoured.⁷ The diagnosis of LCH is based on histological and immunohistochemical study of the involved tissue. The initial work up in this case was an ultrasound of the neck and fine-needle aspiration of the thyroid swelling. The palatal ulcer was also biopsied. The histological diagnosis was established by the presence of oval grooved cells with lobulated nucleoli suggestive of histiocytes interspersed in the background of lymphocytes and eosinophils. Immunohistochemistry was positive for S-100 and CD1a, which is not only diagnostic for LCH, but helps in distinguishing it from other histiocytic lesions.⁸

For treatment, surgery is preferred in cases of solitary thyroid involvement. In cases of multisystem involvement, systemic therapy is preferred. We treated our patient as per the LCH-III trial protocol, which suggests therapy with prednisolone and

vinblastine to be effective with a minimal side effect profile. Patients with multisystem disease with or without risk organ involvement, who respond to initial therapy, have an overall better chance of survival.^{9–11}

We highlight this rare presentation of LCH, especially as it is often misdiagnosed as poorly differentiated thyroid carcinoma or overlooked as a benign disease. Although controversies still exist regarding treatment regimens, our patient experienced complete remission of the disease using the LCH-III protocol.

Learning points

- ▶ Langerhans cell histiocytosis (LCH) is a heterogeneous disease involving antigen presenting cells.
- ▶ LCH has been classified as either a single system or multisystem disease based on the sites of involvement of disease.
- ▶ Immunohistochemistry positivity for S-100 and CD1a is not only diagnostic for LCH, but helps in distinguishing it from other histiocytic lesions.
- ▶ In case of an antibody negative hypothyroid goitre, fine-needle aspiration cytology helps in diagnosing a rare infiltrative aetiology and should be performed.
- ▶ LCH presenting as a hypothyroid goitre is extremely rare. Awareness among clinicians is important as it is often misdiagnosed as poorly differentiated thyroid carcinoma or overlooked as a benign disease.

Contributors KCM, SSK and JT were involved in the concept, design, definition of intellectual content and literature search. SSK and KCM were, in addition, involved in the preparation, editing and review of the manuscript. JT and KCM were involved in clinical care of the patient.

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

- 1 Philip M, Allen C, Gerson P, *et al.* Comparison of FDG-PET scans to conventional radiography and bone scans in management of Langerhans cell histiocytosis. *Pediatr Blood Cancer* 2009;52:97–101.
- 2 Lollar K, Farrag TY, Cao D, *et al.* Langerhans cell histiocytosis of the thyroid gland. *Am J Otolaryngol* 2008;29:201–4.
- 3 Minkov M. Multisystem Langerhans cell histiocytosis in children: current treatment and future directions. *Paediatr Drugs* 2011;13:75–86.
- 4 Behrens RJ, Levi AW, Westra WH, *et al.* Langerhans cell histiocytosis of the thyroid: a report of two cases and review of literature. *Thyroid* 2001;11:697–705.
- 5 Hand J. Polyuria and tuberculosis. *Arch Pediatr* 1893;10:673–5.
- 6 Patten DK, Wani Z, Tolley N. Solitary Langerhan histiocytosis of the thyroid gland: a case report and literature review. *Head and Neck Pathol* 2012;6:279–89.
- 7 Egeler RM, Favara BE, van Meurs M, *et al.* Differential in situ cytokine profiles of Langerhans-like cells and T cells in Langerhans cell histiocytosis: abundant expression of cytokines relevant to disease and treatment. *Blood* 1999;94:4195–201.
- 8 Seiji M, Shimao K, Fitzpatrick TB, *et al.* The site of biosynthesis of mammalian tyrosinase. *J Invest Dermatol* 1961;37:359–68.
- 9 Gadner H, Heitger A, Grois N, *et al.* Treatment strategy for disseminated Langerhans cell histiocytosis. DAL HX-83 Study Group. *Med Pediatr Oncol* 1994;23:72–80.
- 10 McClain KL. Drug therapy for the treatment of Langerhans cell histiocytosis. *Expert Opin Pharmacother* 2005;6:2435–41.
- 11 Gadner H, Grois N, Potschger U, *et al.* Improved outcome in multisystem Langerhans cell histiocytosis is associated with therapy intensification. *Blood* 2008;111:2556–62.

Copyright 2014 BMJ Publishing Group. All rights reserved. For permission to reuse any of this content visit <http://group.bmj.com/group/rights-licensing/permissions>.
BMJ Case Report Fellows may re-use this article for personal use and teaching without any further permission.

Become a Fellow of BMJ Case Reports today and you can:

- ▶ Submit as many cases as you like
- ▶ Enjoy fast sympathetic peer review and rapid publication of accepted articles
- ▶ Access all the published articles
- ▶ Re-use any of the published material for personal use and teaching without further permission

For information on Institutional Fellowships contact consortiasales@bmjgroup.com

Visit casereports.bmj.com for more articles like this and to become a Fellow