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Langerhans Cell Histiocytosis of Thyroid Gland : A Case Report

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갑상선에 생긴 랑게르한스 세포 조직구증 1예

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= 국문초록 =

랑게르한스 세포 조직구증은 골수에서 유래하는 랑게르한스 세포 조직구의 이상 증식에 의해 발병하는 희귀한 질병으로 알려져 있다. 비록 모든 장기에서 발생 할 수 있으나 갑상선을 침범하는 경우는 매우 드물다. 18세 남자가 5달 전부터 점점 커지는 갑상선 종괴를 주소로 내원하여 세침흡인 세포검사, 총생검, 경부 전산화단층촬영을 시행하였다. 세침흡인 세포검사에서 악성신생물이 의심되었고, 총생검에서 랑게르한스 세포 조직구증으로 나타났다. 경부 전산화단층촬영에서는 우측 갑상선에서 윤곽이 잘 구분되는 저음영의 종괴와 우측 기관 주위 림프절의 종대가 관찰되었다. 갑상선 전절제술과 우측 중앙 선택적 경부 림프절 청소술이 시행되었다. 랑게르한스 세포 조직구증이 갑상선을 침범하는 경우는 드물지만 갑상선 비대가 있는 환자가 뇌하수체 기능부전의 증상이나 뼈와 폐의 침범과 관련된 증상을 호소한다면 갑상선의 랑게르한스 세포 조직구증 침범을 고려해야 한다. 또한, 다른 장기의 랑게르한스 세포 조직구증을 치료한 과거력이 있는 경우는 갑상선 종괴를 감별 진단하는데 있어 랑게르한스 세포 조직구증을 고려해야 한다.

중심 단어 : 랑게르한스 세포 조직구증 · 갑상선.

Introduction

Langerhans cell histiocytosis(LCH) is a monoclonal disease with an unknown etiology which is characterized by abnormal proliferation of the Langerhans cells that originate from bone marrow-derived dendritic cells.[1] LCH has a particular predilection for the hypothalamo-pituitary axis although it can involve almost all organs or systems, and the prognosis varies markedly from a lethal to a mild self-limiting condition.[2] LCH is an uncommon disease with an annual incidence of 4 to 5.4 per million worldwide.[3] Involvement of the thyroid by LCH is very rare, even in extensive cases.[4]

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Case Report

An 18-year-old boy sought medical assistance because of a 5-month history of enlarging mass in the thyroid gland. When he was 15 years old, he experienced polyuria and polydipsia and was diagnosed with central diabetes insipidus due to pituitary LCH. He was treated with radiation therapy(900cGy). Physical examination of the patient revealed an enlarged, diffusely firm, non-tender, non-mobile, and not particularly nodular thyroid gland with mild compressive symptoms. Endocrine evaluation revealed normal levels for thyroxine (free T4 ; 0.87ng/dL), tri-iodothyronine(T3 ; 79.8 ng/dL), and thyroid-stimulating hormone(TSH ; 3. 99μU/mL). Fine-needle

aspiration cytology(FNAC) of the thyroid mass was performed and the initial cytological interpretation suggested malignant tumor. Then a gun biopsy was conducted to get more accurate diagnosis. The tissue was stained with S-100, and the diagnosis was suggested as LCH according to his past medical history. Neck computed tomography(CT) revealed 3× 2.5cm sized, well defined low density mass at right lobe and there were enlarged lymph nodes at the right paratracheal area (Fig. 1).

The patient underwent total thyroidectomy with right central neck dissection. A histological diagnosis of LCH involving the thyroid and lymph nodes was established after careful review of the pathological materials. Proliferated histiocytes were infiltrated in the thyroid gland mixed with scattered eosinophils(Fig. 2), and immunohistochemical studies showed strong positive staining of the Langerhans cells with S-100 and CD1a(Fig. 3).

Following surgery, positron emission tomography scan and CT scans of the chest and abdomen were done, which revealed soft tissue density at the anterior mediastinum, bony destruction of manubrium and focal increase of fluorodeoxy glucose uptake in the L4 spinal body. Subsequently, he received 1,000 cGy to his anterior mediastinum and 1,000cGy to his L4 spinal body and a chemotherapy regimen of vinblastine and prednisolone was given for 2 weeks. He has been alive for 3 years postoperatively. At present, he is well without signs of recurrence and with no proven evidence of systemic disease.

Discussion

LCH can develop in many organ systems and present in a variety of ways. Seventy-five percent of patients have various skin involvements, and lung involvements affect 25% of patients. The most common endocrinological manifestation of LCH is associated with posterior pituitary involvement pre-

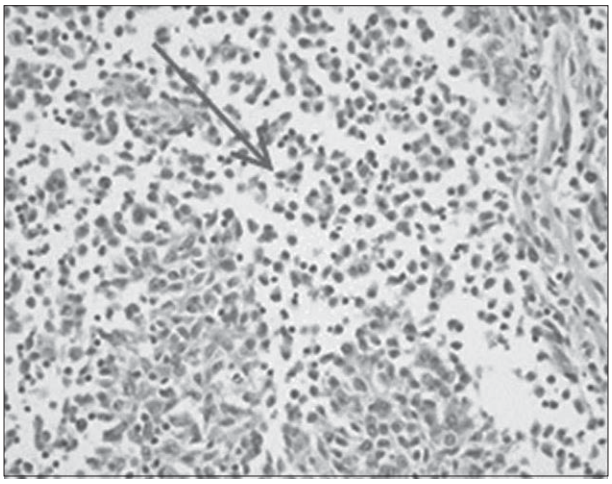

Fig. 2. Infiltrating cells are histiocytes mixed with scattered eosinophils. Histiocytes showed nuclear grooves(arrow)(H&E, 400×).

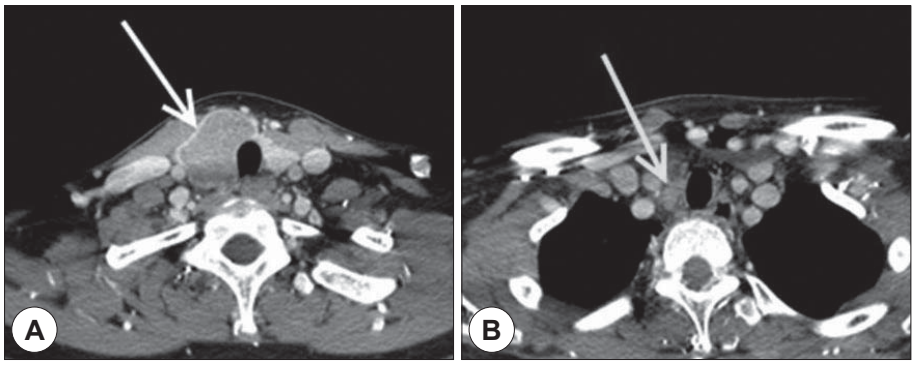

Fig. 1. A : Axial-enhanced CT scan reveals a well defined low density mass at right lobe & isthmus of thyroid gland(arrow). B : CT scan shows lymph node enlargement at right paratracheal area(arrow).

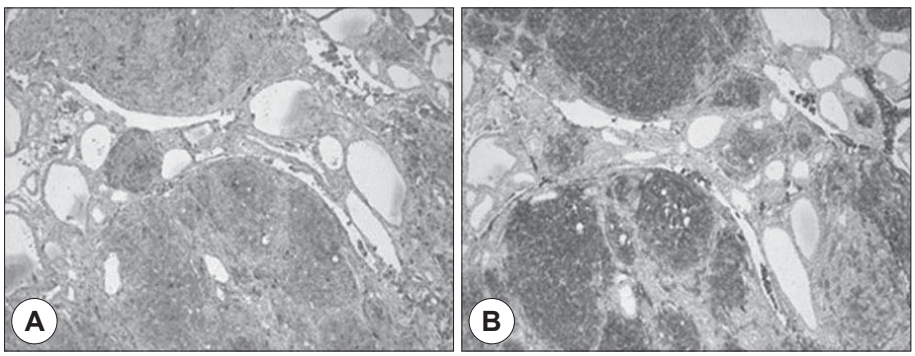

Fig. 3. A : Photomicrography showing cytoplasmic staining of Langerhans cells with S-100 protein(100×). B : Diffuse membrane staining of histiocytes with CD1a monoclonal antibody(100×).

senting as diabetes insipidus. However, hypothalamic-pituitary axis disturbance and anterior pituitary deficiency resulting in secondary or tertiary hypothyroidism are rare for unclear reasons. Lytic bone lesions, bone marrow involvement or hepatosplenomegaly are also frequent manifestations.[5)]

LCH involving the thyroid gland is relatively more common in adults compared to children and has a relatively indolent course. Most common clinical features are diffuse or nodular thyroid enlargements which are rubbery, non-tender and immobile.[6,7)] Primary hypo-thyroidism in patients with LCH can be seen because of thyroid damage due to histiocytic infiltration. Patients can be euthyroid initially, as in our case, however hypo-thyroidism usually develops over time as the tissue damage progresses.[6,8)] On imaging examinations, CT usually reveals enlarged thyroid with low-density areas in it and thyroid ultrasound shows hypoechoic thyroid masses. Cold nodules can be obtained with thyroid isotope scan and hypermetabolic activity in the neck with fluolodeoxyglucose positive emission tomography.[9)] Because not only the physical signs but also the thyroid hormone status, antithyroid antibodies and imaging findings may be similar, thyroid involvement of LCH can be indistinguishable from other thyroid disorders presenting with goiter such as thyroid carcinoma or autoimmune thyroiditis.

Although non-specific findings can be seen, ultrasonography and FNAC are the first-line modalities for the workup of LCH with thyroid involvement.[8,10)] Large histiocytes with abundant cytoplasm interspersed in a background of lymphocytes and eosinophils are the typical presentation of LCH on FNAC.[6)] However, Langerhans cells can be misinterpreted as some other cell type such as atypical follicular epithelial cells when LCH is not considered in the differential diagnosis. In the thyroid gland, LCH can be mistaken for poorly differentiated carcinoma on histology even after thyroid resection,[11)] and can also be misinterpreted as papillary carcinoma on fine-needle aspiration.[12)] In difficult cases, the usage of appropriate immunohistochemical stains will settle the issue because LCH cells do not stain for cytokeratin and thyroglobulin antibodies but are S-100 and CD1a positive. Strong and diffuse positive stain for CD1a and S-100 are characteristic features.[13)] On an ultrastructure level, Birbeck or Langerhans granules, which represent invaginations of plasma membrane are typically identified in LCH cells.[13)]

The treatment of LCH is determined by the clinical extent and progression of the disease.[6)] Multisystem involvement, vital organ dysfunction, young age and disease unresponsive to treatment suggest an unfavorable outcome.[14)] Localized lesions may regress spontaneously over time. Therefore, conservative treatments such as observation, topical steroid, radiation or local excision are recommended in localized disease.[14)] For disseminated or aggressive disease, many chemotherapeutic regimens have been tried including glucocorticoids, vinblastine, etoposide, cyclophosphamide, cyclohexyl-chlorethyl-nitrosourea, methotrexate and doxorubicin.[14)] Monoclonal anti-CD1a radioreactive antibodies[14)] and thalidomide[15)] are additional possible treatments.

The role of surgery in patients with LCH of the thyroid is still controversial and no specific guidelines exist regarding management. Surgical excision is favored in cases with isolated thyroid involvement, whereas aggressive systemic therapy is reserved for cases exhibiting disseminated disease.

In conclusion, LCH is a rare disease that can involve many organs. Although the thyroid gland is rarely involved, it should be considered when the patients with thyroid enlargements complain symptoms of posterior or anterior pituitary dysfunction or symptoms related to bone or pulmonary involvement. Moreover, in patients with a history of LCH involvement of other locations, it should always be included in the differential diagnosis of thyroid mass.

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