CLINICAL IMAGE

Adult multisystem Langerhans cell histiocytosis

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A 31-year-old man was found to have a 1 cm × 1 cm subcutaneous nodule on the neck 8 months ago. The nodule was hard in texture, nontender, and easily movable. Three months ago, the patient underwent neck magnetic resonance imaging (MRI) that showed diffuse enlargement of the bilateral submandibular glands and thyroid. Multiple nodules were observed in the left parotid gland and bilateral external auditory canal. The patient received no treatment. Two months later, the nodule enlarged to approximately 10 cm × 10 cm. Laboratory tests showed a reduced level of free thyroxine (10.3 pmol/l; reference range [RR], 12–22 pmol/l) and a rise in thyroid-stimulating hormone level (7.33 μU/ml; RR, 0.27–4.2 μU/ml). Elevated levels were observed for white blood cells (13.2×10^9/l; RR, 3.5–9.5×10^9/l), neutrophils (10.68×10^9/l; RR, RR, 1.8–6.3×10^9/l), monocytes (0.8×10^9/l; RR, 0.1–0.6×10^9/l), and eosinophils (0.85×10^9/l; RR, 0.02–0.52×10^9/l), while lymphocyte count was below the normal value at 0.84×10^9/l (RR, 1.1–3.2×10^9/l). There was an increase in alanine aminotransferase, aspartate aminotransferase, and notably γ-glutamyl transferase protein levels. The patient reported a progressive rise in water intake and urine output within the last 5 years, albeit without precise quantification. Additionally, the patient used to smoke for 2 years, consuming an average of 20 cigarettes per week. However, he has successfully quit smoking for over 3 months. The patient had no documented history of substance abuse, alcohol consumption, or exposure to hazardous substances. He underwent ultrasound-guided needle biopsy of the neck mass, which showed lymphocyte and eosinophil infiltration in the tissue, along with multinucleated giant cell reaction (FIGURE 1A). Immunohistochemistry showed positive staining for CD1a (FIGURE 1B), langerin, S100, and cyclin D1, suggesting the presence of Langerhans cell histiocytosis (LCH). Molecular examination of the tissue sample indicated the absence of *BRAF* V600E mutation, and no mutations in the mitogen-activated protein kinase / extracellular-signal-regulated kinase pathway were detected. The patient underwent ^{18}F-fluorodeoxyglucose positron emission tomography / computed tomography (^{18}F-FDG PET/CT), which revealed marked enlargement of the bilateral submandibular glands and thyroid, with increased FDG uptake (maximum standardized uptake value [SUV_{max}], 20.8). Multiple nodules with high FDG uptake (SUV_{max}, 15.1) were detected in the left parotid gland, subcutaneous tissue, mediastinum and neck lymph nodes, and external auditory canal (FIGURE 1C–1E). The lungs showed multiple ground-glass opacities with mildly increased FDG uptake (SUV_{max}, 1.8) and multiple localized air spaces (FIGURE 1F). The liver exhibited nonuniform FDG uptake (SUV_{max}, 4.8; FIGURE 1G). The patient underwent contrast-enhanced MRI of the neck and brain for follow-up. The MRI scan revealed significant enlargement of both submandibular glands and the thyroid, as well as mild enlargement of both external auditory canal nodules and left parotid gland nodules (Supplementary material, *Figure S1*). Additionally, the brain MRI showed multiple punctate-enhancing lesions in the pons and numerous nodules on the scalp (Supplementary material, *Figure S2A*). However, no abnormalities were found in the pituitary gland (Supplementary material, *Figure S2B*). Chest CT revealed multiple cystic lucent areas in the lungs and patchy hypodense lesions in the liver (Supplementary material, *Figure S2C* and *S2D*). The patient did not undergo further liver imaging, nor were pulmonary function or echocardiographic examinations conducted. Laryngoscopy revealed slight thickening and white appearance of the anterior vocal cords. Neither blood gas analysis nor bone marrow biopsy were performed. The patient received a combination of vindesine and

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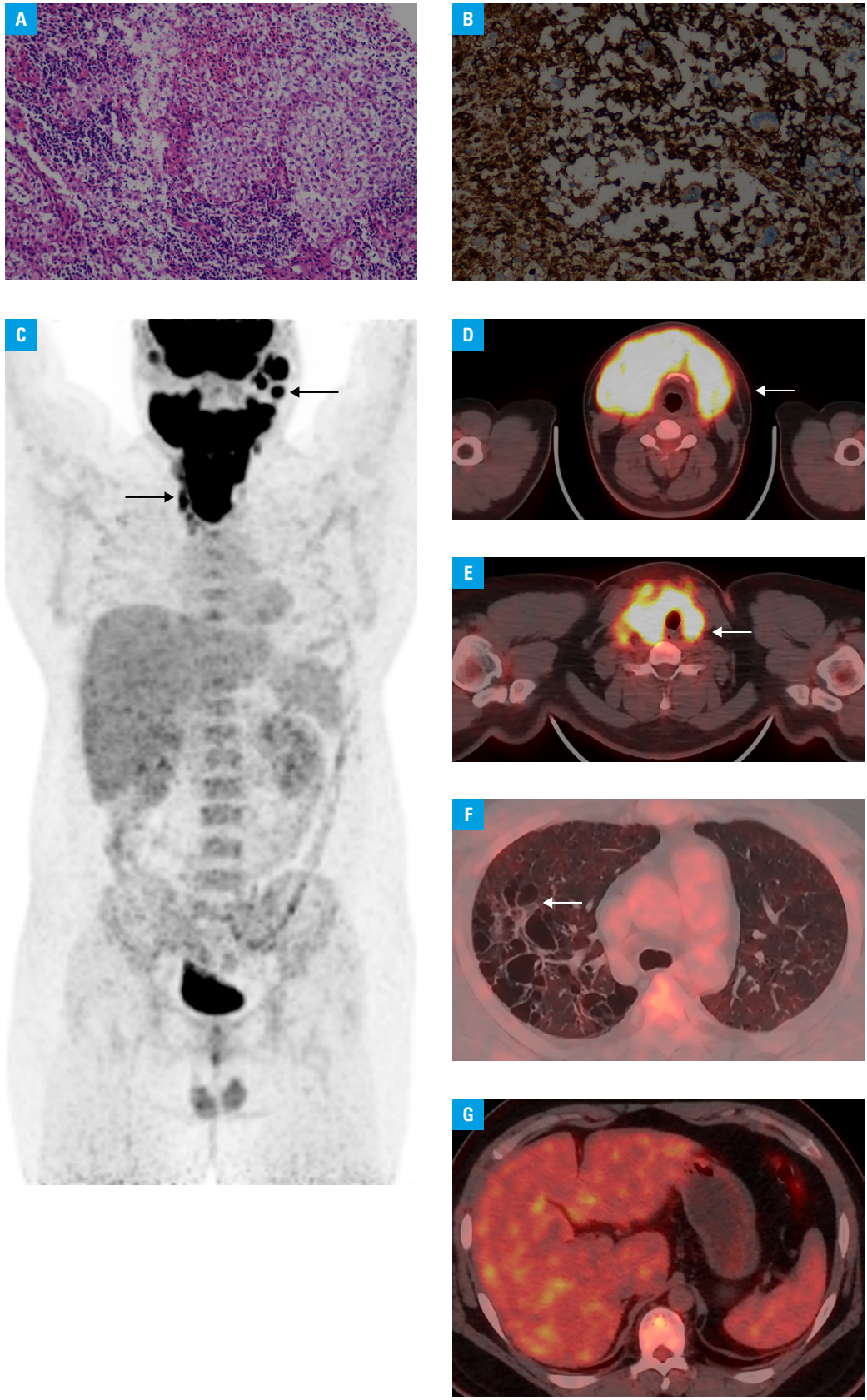

FIGURE 1 **A** – histopathologic examination showing lymphocyte and eosinophil infiltration within the tissue, accompanied by notable multinucleated giant cell reaction (hematoxylin and eosin [HE] staning, magnification × 200); **B** – immunohistochemical analysis revealing positive staining for CD1a (magnification × 200); **C**–**E** – multiple soft tissue density nodules with significantly elevated ^{18}F-fluorodeoxyglucose (FDG) uptake identified in the left parotid gland, subcutaneous tissue, thyroid, neck lymph nodes, and the external auditory canal (**C** – arrows show nodules in the left paroid gland and right neck lymph nodes; **D** – arrow shows enlarged submandibular gland; **E** – arrow shows enlarged thyroid); **F** – the lungs exhibiting multiple ground-glass opacities, mildly increased FDG uptake, and numerous localized air spaces (arrow indicates Langerhans cell histiocytosis in the right lung) **G** – the liver displaying diffuse, slightly low-density nodules with nonuniform FDG uptake

prednisone acetate, alongside symptomatic supportive therapy.

LCH is the most common type of histiocytic disorder, characterized by abnormal function, differentiation, and proliferation of mononuclear phagocyte system cells. LCH primarily impacts the pediatric population, with peak occurrence at the age between 1 and 3 years. Its prevalence among adults is much lower, estimated to range from 1 to 1.5 cases per million individuals on an annual basis.[1-3] LCH can involve almost any organ, and multisystem involvement is more common than single lesions. The most commonly affected organs are the bones, skin, pituitary gland, liver, lungs, lymph nodes, and central nervous system.[1] Involvement of the salivary glands and thyroid is rare. Research indicates a 10.1% incidence rate of thyroid involvement in adult LCH. Of the patients with thyroid involvement, 81.5% initially presented with diabetes insipidus, and 51.9% reported neck swelling or a mass. As compared with those without thyroid involvement, the patients with affected thyroid more often showed instances of pituitary gland (88.6% vs 53.4%), liver (45.7% vs 20.7%), and lymph node (54.3% vs 31.6%) involvement, but less often bone involvement (45.7% vs 72%). Cases involving both the submandibular glands and the external auditory canal are exceedingly rare.[4,5]

SUPPLEMENTARY MATERIAL

Supplementary material is available at www.mp.pl/paim.

ARTICLE INFORMATION

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