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Follicular Thyroid Carcinoma with Cavernous Sinus Metastasis and Perineural Spread: A Rare Manifestation of Radioiodine-refractory Disease

Kavernöz Sinüs Metastazı ve Perinöral Yayılım Gösteren Foliküler Tiroid Karsinomu: Radyoiyot Tedavisine Dirençli Hastalığın Nadir Bir Belirtisi

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Abstract

Cavernous sinus metastasis from follicular thyroid carcinoma (FTC) is exceedingly rare and typically indicates advanced, radioiodine-refractory disease. We report a 37-year-old man with minimally invasive FTC who was treated with total thyroidectomy, neck dissection, and cumulative radioiodine therapy totaling 720 mCi for persistent iodine-avid disease. Four years later, he developed progressive left-sided palsies of cranial nerves III, IV, and VI. Imaging revealed a cavernous sinus mass with orbital apex extension and perineural spread. Serum thyroglobulin was markedly elevated (>500 ng/mL), whereas diagnostic radioiodine scintigraphy demonstrated no uptake, a finding consistent with dedifferentiated disease. Biopsy confirmed metastatic FTC. The patient received external beam radiotherapy and systemic therapy with lenvatinib; however, the disease progressed, and he died 16 months after the diagnosis of cavernous sinus metastasis. This case highlights the aggressive potential of FTC, the limitations of radioiodine imaging in dedifferentiated disease, and the poor prognosis associated with skull-base metastases despite multimodal therapy.

Keywords: Follicular thyroid cancer, cavernous sinus metastasis, iodine-131 whole-body scintigraphy, ^{18}F-FDG PET/CT

Öz

Foliküler tiroid karsinomundan (FTC) kaynaklanan kavernöz sinüs metastazı son derece nadirdir ve tipik olarak ilerlemiş, radyoiyot tedavisine dirençli hastalığı gösterir. Bu yazıda, minimal invaziv FTC'si olan ve total tiroidektomi, boyun diseksiyonu ve kalıcı iyot tutulumu nedeniyle 720 mCi kümülatif radyoiyot tedavisi uygulanan 37 yaşında bir erkek hastayı bildiriyoruz. Dört yıl sonra, ilerleyici, sol üçüncü, dördüncü ve altıncı kraniyal sinir felçleri gelişti. Görüntülemede, orbital apeks uzantısı olan ve perinöral yayılım gösteren bir kavernöz sinüs kitlesi saptandı. Serum tiroglobulin düzeyi belirgin yüksekti (>500 ng/mL), tanısal radyoiyot sintigrafisi ise dediferansiye hastalıkla uyumlu olarak tutulum göstermedi. Biyopsi, metastatik FTC'yi doğruladı. Hastaya eksternal radyoterapi ve lenvatinib ile sistemik tedavi uygulandı; ancak hastalık ilerledi ve kavernöz sinüs metastazı tanısından 16 ay sonra hayatını kaybetti. Bu olgu, foliküler tiroid kanserinin agresif potansiyelini, dediferansiye hastalıkta radyoiyot görüntülemenin sınırlılıklarını ve çok yönlü tedaviye rağmen kafa tabanı metastazlarıyla ilişkili kötü prognozu vurgulamaktadır.

Anahtar Kelimeler: Foliküler tiroid kanseri, kavernöz sinüs metastazı iyot-131 tüm vücut sintigrafisi, ^{18}F-FDG PET/CT

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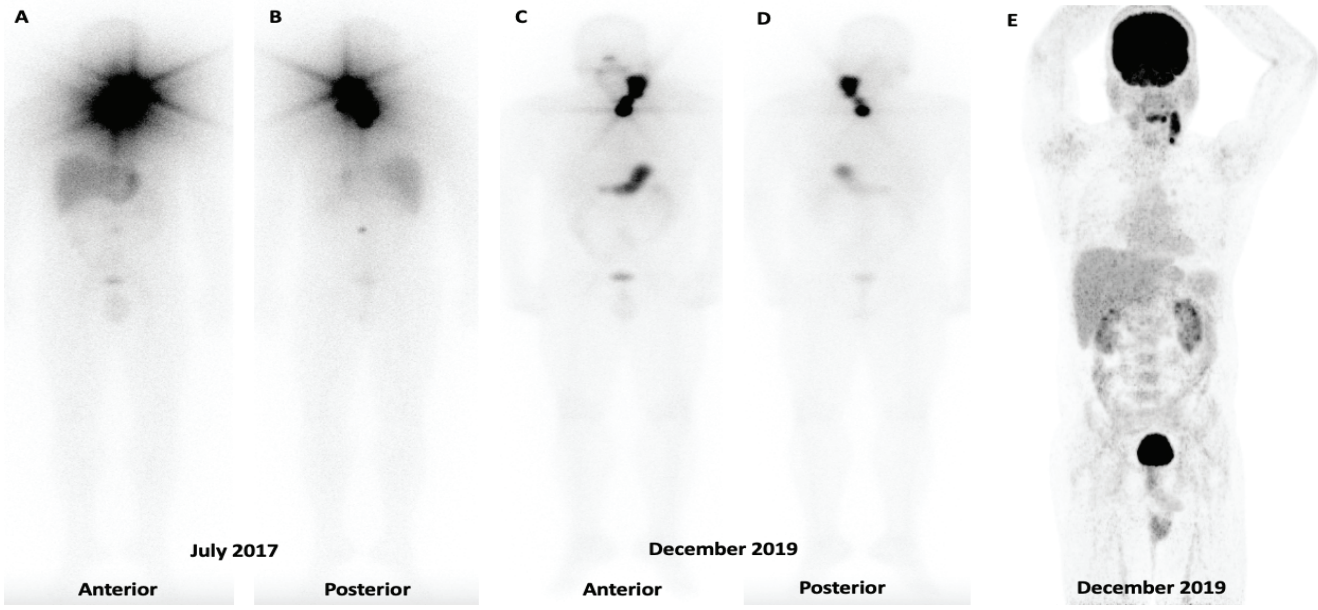

Figure 1. A 37-year-old man with minimally invasive follicular thyroid carcinoma (FTC) presented with a left thyroid nodule and underwent hemithyroidectomy, followed by completion thyroidectomy and left cervical lymph node dissection, which confirmed metastatic disease (pT3aN1bM0). He subsequently received multiple courses of adjuvant radioiodine therapy (a cumulative dose of 720 mCi) for persistent iodine-avid disease in the thyroid bed, cervical region, and upper mediastinum (A, B). Despite repeated treatment, serial imaging demonstrated residual disease (C, D), and stimulated serum thyroglobulin levels progressively rose to >500 ng/mL, indicating ongoing tumor activity. ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography demonstrated metabolically active left cervical lymphadenopathy (E), which was followed by locoregional recurrence requiring further surgical resection.

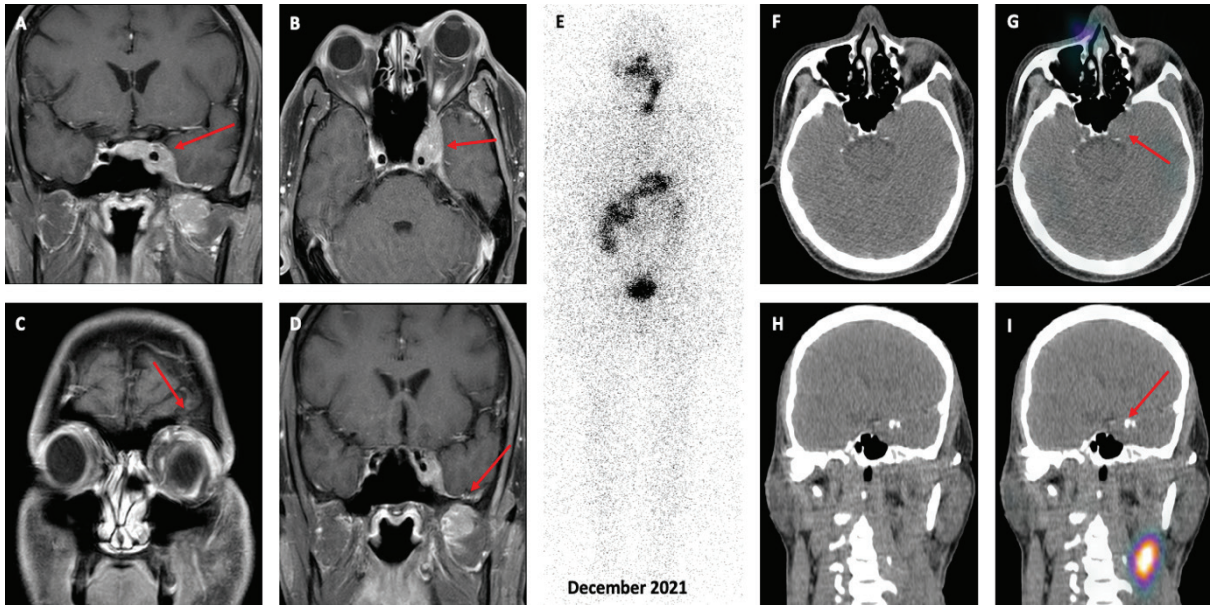

Figure 2. Four years after initial diagnosis, the patient developed progressive left-sided ptosis and ophthalmoplegia, corresponding to palsies of cranial nerves III, IV, and VI. Contrast-enhanced computed tomography (CT) and T1-weighted magnetic resonance imaging revealed an enhancing mass centered in the left cavernous sinus (A, B), measuring approximately 3.6 cm and extending into the orbital apex (C). Perineural spread was present along the mandibular and auriculotemporal nerves, with involvement of the deep lobe of the parotid gland, pterygopalatine fossa, and adjacent masticator space (D). Diagnostic iodine-131 whole-body scintigraphy (E) and SPECT/CT (F-I), performed following recombinant thyroid-stimulating hormone stimulation, demonstrated no abnormal uptake in the cavernous sinus region, confirming loss of iodine avidity.

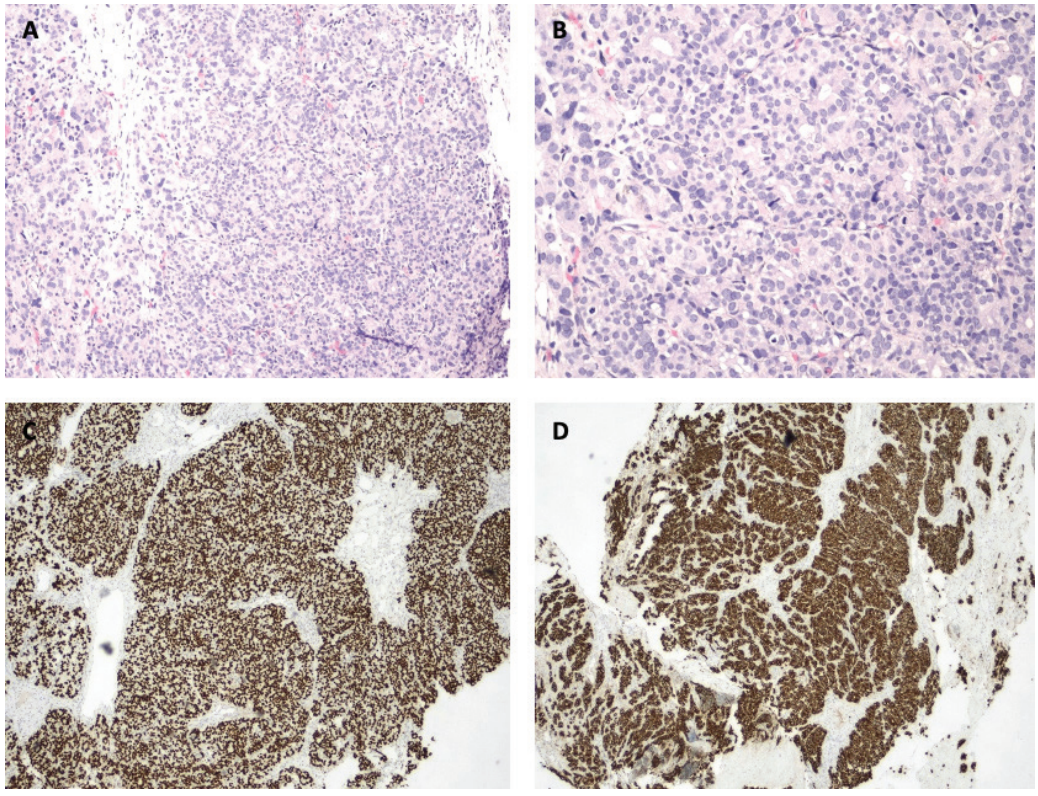

Figure 3. Biopsy demonstrated histopathological and immunohistochemical features of metastatic follicular thyroid carcinoma (FTC). (A) low-power view (x4) showing follicular and nested architecture; (B) high-power view (x20) demonstrating pleomorphic nuclei and mitotic figures; (C) positive nuclear staining for TTF-1; (D) positive cytoplasmic staining for CK7. These findings confirm metastatic FTC and are consistent with radioiodine-refractory disease.

FTC characteristically spreads via hematogenous dissemination, most commonly to the lungs and bones, whereas intracranial metastases are rare (1,2). Cavernous sinus involvement represents an uncommon manifestation of advanced disease and often presents with cranial neuropathies due to its proximity to critical neurovascular structures (3). Tumor spread may occur via the valveless vertebral venous plexus or, less commonly, lymphatic pathways (1). In this case, perineural spread represents an additional route of extension and is associated with aggressive tumor biology and poorer outcomes (4).

Loss of radioactive iodine (RAI) avidity reflects tumor dedifferentiation with reduced sodium-iodide symporter expression, signifying transition to radioiodine-refractory differentiated thyroid carcinoma (RAIR-DTC), which carries a poorer prognosis and limited therapeutic options (5,6). Further RAI therapy is ineffective, and management shifts toward alternative strategies. Given the inoperable skull-base location, external beam radiotherapy was administered for local control, in line with recommendations from the American Head and Neck Society (7). Systemic therapy with lenvatinib was initiated but required modification due to tolerability issues. Despite multimodal treatment, the disease progressed, and the patient died 16 months after diagnosis of cavernous sinus metastasis, reflecting the poor prognosis associated with intracranial involvement in RAIR-DTC (2,6).

This case highlights a delayed aggressive transformation in FTC, emphasizes the recognition of atypical metastatic patterns such as cavernous sinus involvement and perineural spread, and underscores the limitations of radioiodine imaging in dedifferentiated disease.

Ethics

Informed Consent: The patient provided written informed consent.

Footnotes

Authorship Contributions

Surgical and Medical Practices: H.L., M.F.M.R., S.Z.A.H., Concept: H.L., M.F.M.R., Design: H.L., M.F.M.R., Data Collection or Processing: H.L., M.F.M.R., R.G., Analysis or Interpretation: H.L., M.F.M.R., J.J., R.G., S.Z.A.H., Literature Search: H.L., M.F.M.R., J.J., R.G., S.Z.A.H., Writing: H.L., M.F.M.R., J.J., R.G., S.Z.A.H.

Conflict of Interest: No conflicts of interest were declared by the authors.

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