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CASE IMAGE

Incidental Langerhans cell histiocytosis associated with metastatic neuroendocrine tumor in the adult liver

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Abstract

This is an unusual adult case of a metastatic well-differentiated neuroendocrine tumor with incidentally discovered subtle involvement of Langerhans cell histiocytosis (LCH), a clonal proliferation of Langerhans cells. It is important to recognize that LCH can often co-exist with other malignancies (solid > hematologic).

KEYWORDS

BRAF mutation, langerhans cell histiocytosis (LCH), liver, *MAP2K1* mutation, neuroendocrine tumor (NET)

A 38-year-old man with pancreatic well-differentiated neuroendocrine tumor (WD-NET) underwent resection and chemotherapy. Two months later, CT showed multiple liver lesions but no lesions in any other site. A liver biopsy demonstrated metastatic WD-NET with an intimately admixed proliferation of smaller cells containing scant cytoplasm and elongated nuclei with nuclear grooves (Figure 1A–E). Unlike the WD-NET, the small cells were negative for synaptophysin and chromogranin and positive for CD1a, langerin, and S100, confirming the diagnosis of Langerhans cell histiocytosis (LCH) (Figure 1D–H). Capture-based DNA sequencing of the liver biopsy revealed a *BRAF* p.V600E mutation and a *TSC2* p.E159* mutation, both at subclonal mutant allele frequencies. BRAF V600E immunohistochemistry was positive only in the LCH (Figure 1I), consistent with the subclonal allele frequency. Furthermore, LCH are known to harbor frequent mutations in *BRAF* p.V600E or *MAP2K1*, but not in *TSC2*.[1–3] Pancreatic WD-NET, on the contrary, demonstrate frequent mutations in *MEN1*, *DAXX*, *ATRX*, and *TSC2*, but not in *BRAF*.[4–6]

This is an unusual case of metastatic WD-NET with co-existing LCH, highlighting that adult LCH often co-occurs with other malignancies.[1–3] The patient received peptide receptor radionuclide therapy for WD-NET (LCH not treated) and has been alive >1 year post-biopsy.

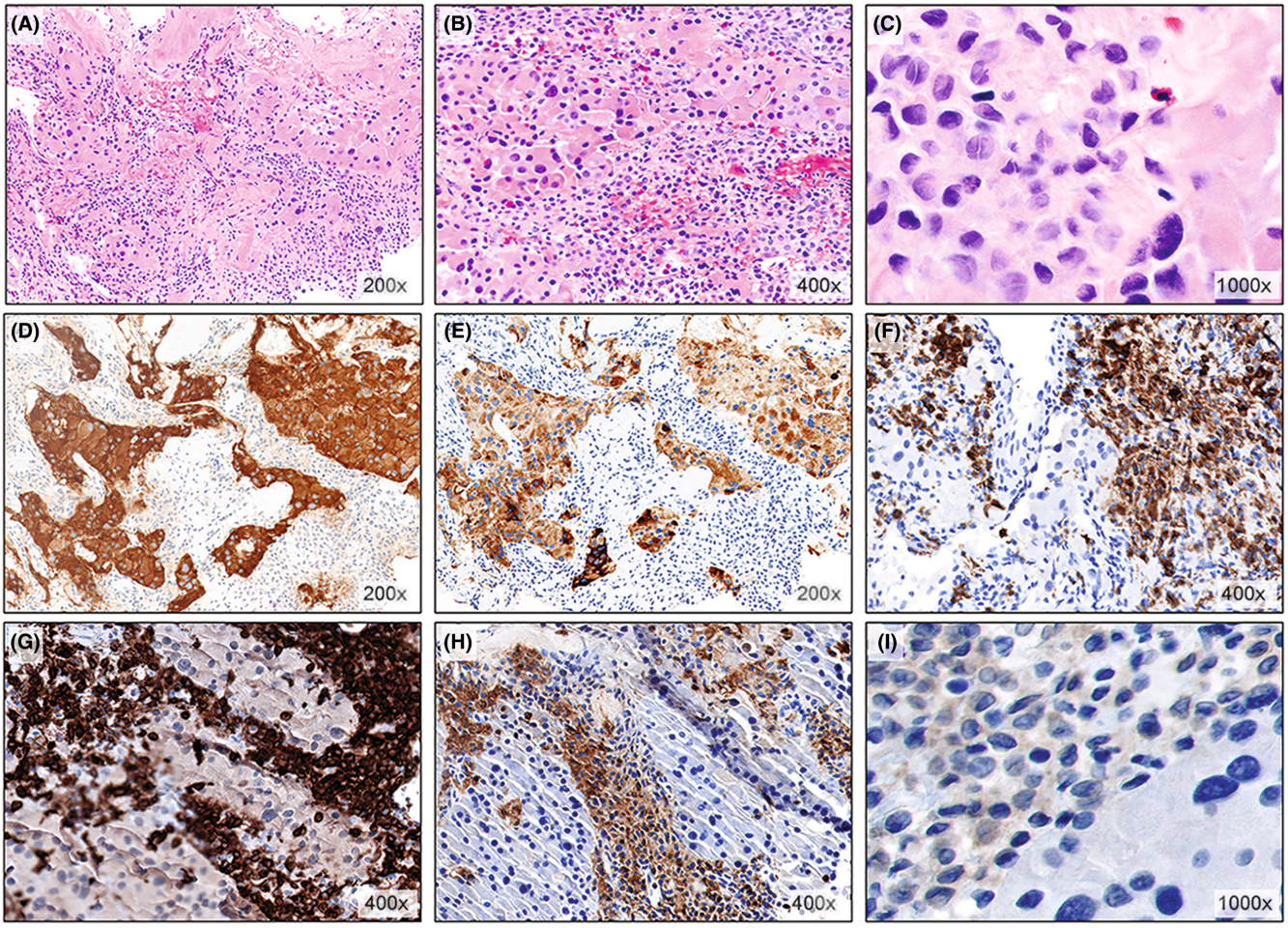

FIGURE 1 Panel (A) (H&E, 200x) and Panel (B) (H&E, 400x) In this liver biopsy, there is a hepatoid metastatic well-differentiated neuroendocrine tumor (WD-NET) with large ovoid nuclei, fine chromatin, and eosinophilic cytoplasm with admixed smaller Langerhans cells. Panel (C) A higher magnification (H&E, 1000x) shows the atypical Langerhans cells (left) with smaller nuclei (relative to the neuroendocrine tumor in the lower right corner of the image) and irregular/elongated nuclear contours, indistinct nucleoli, and eosinophilic cytoplasm. Some of the nuclei have grooves/folds typical of Langerhans cells. Scattered eosinophils are also easily identified in the background. Panel (D) The WD-NET component is diffusely positive for synaptophysin immunostain (200x). Panel (E) The WD-NET component is diffusely positive for chromogranin A immunostain (200x). Panel (F) The Langerhans cell histiocytosis (LCH) component is positive for CD1a immunostain (400x). Panel (G) The LCH component is positive for langerin immunostain (400x). Panel (H) The LCH component is positive for S100 immunostain (400x). Panel (I) The LCH component (left) shows positive immunoreactivity for BRAF V600E stain, whereas the WD-NET component (bottom right) is negative for BRAF V600E (1000x)

AUTHOR CONTRIBUTIONS

NMJ and KWW were involved in conceptualization of study as well as manuscript preparation, editing, and proofreading of the final manuscript.

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CONFLICT OF INTEREST STATEMENT

We declare no competing interests.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ETHICAL APPROVAL

The study was approved by the Institutional Review Board for human subjects research at UCSF Medical Center (IRB # 18–25,787).

CONSENT

Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy.

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