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Case Report

Lymphoid Structure Presenting as a Hypermetabolic Adrenal Incidentaloma

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Abstract

Adrenal incidentalomas are a frequent cause for consultation in endocrinology. Current guidelines provide an algorithm for their evaluation to determinate the risk of hormonally active or malignant condition. We report a unique case of benign adrenal incidentaloma in a 53-year-old woman with multiple malignancy criteria on contrast-free computed tomography and [^{18}F]fluorodeoxyglucose positron emission tomography–computed tomography, leading to a left adrenalectomy. Histopathologic analysis showed a 15-mm intra-adrenal lymphoid organ localized in the medulla, without any cellular atypia and organized with a capsule and multiple germinal centers. The surrounding adrenal tissue was unremarkable, and the patient did not develop any inflammatory, infectious, or neoplastic disease during the 2 following years. This is the first described case of a well-organized intra-adrenal ectopic lymphoid organ in the absence of any evident stimulus.

Key Words: ectopic lymphoid organ, adrenal tumor, adrenal incidentaloma

Abbreviations: [^{18}F]FDG-PET/CT, [^{18}F]fluorodeoxyglucose positron emission tomography–computed tomography; AI, adrenal incidentaloma; CT, computed tomography; MRI, magnetic resonance imaging; SUV, standard uptake value.

Introduction

Adrenal incidentalomas (AIs) are defined as asymptomatic adrenal masses bigger than 1 cm, discovered incidentally during imaging performed for unrelated reasons (1). The main goal when such a tumor is discovered is to determine whether it is a hormonally active lesion or a malignant condition. The radiological features of noncontrast computed tomography (CT) or magnetic resonance imaging (MRI) can help to determine whether a lesion is benign. If the nature of the lesion remains undetermined after these examinations, [^{18}F]fluorodeoxyglucose positron emission tomography–CT ([^{18}F]FDG-PET/CT) should be performed (1). A hypermetabolic lesion is suggestive of malignancy. We report here a unique case of benign AI with abnormal radiological features and a hypermetabolic pattern.

Case Presentation

A 53-year-old woman was referred to our department of endocrinology in May 2019 for bilateral AI. She takes pantoprazole 20 mg/day, nebivolol 5 mg/day, and levothyroxine 50 µg/day, and is an active smoker. Her relevant past medical history includes an euthyroid multinodular goiter, polycystic ovary syndrome, and a conization of the cervix.

The lesions were discovered during an MRI of the kidneys (Fig. 1) performed to determine the nature of bilateral renal cysts. MRI revealed 2 adrenal lesions on the left and right with different radiological characteristics. The left adrenal lesion measured 16 × 15.5 mm, and did not enhance on T2-weighted images. Furthermore, there was no loss of signal intensity on out-phase imaging and the contrast media washout was delayed. The right adrenal lesion measured 10 × 17 mm and presented a characteristic pattern of adrenal adenoma with a loss of signal on out-phase imaging. Compared to a CT scan performed in 2015, the left adrenal lesion was not present while the right lesion was stable. Clinical examination revealed weight loss and 2 centimetric lymphadenopathies: one in the right supraclavicular area and the other in the left posterior cervical area.

With this in mind and the fact that the patient is an active smoker, blood and urinary tests were carried out. Urinary metanephrines (52 µg/24 hours [263.65 nmol/day], normal value: 0-320 µg/24 hours [0-1622.43 nmol/day]) and normetanephrines (156 µg/24 hours [790.94 nmol/day], normal value: 0-390 µg/24 hours [0-2128.74 nmol/day]), morning serum cortisol (9.6 µg/dL [26 496 nmol/L], normal value: 7-25 µg/dL [193.2-690 nmol/L]), 17-hydroxyprogesterone (100 ng/dL [3.18 nmol/L], normal value 11-108 ng/dL [0.35-3.43 nmol/L]), and dehydroepiandrosterone-sulfate (162 µg/dL [4.37 nmol/L], normal value 54-400 µg/dL [1.46-10.8 nmol/L]) were normal. Adrenocorticotropin was a bit low (3.80 pg/mL [0.84 pmol/L], normal value: 5-49 pg/mL [1.1-10.78 pmol/L]) and thus a 1-mg overnight dexamethasone suppression test was performed and excluded a cortisol-secreting tumor with a morning serum cortisol level of 1.0 µg/dL [27.59 nmol/L] (normal

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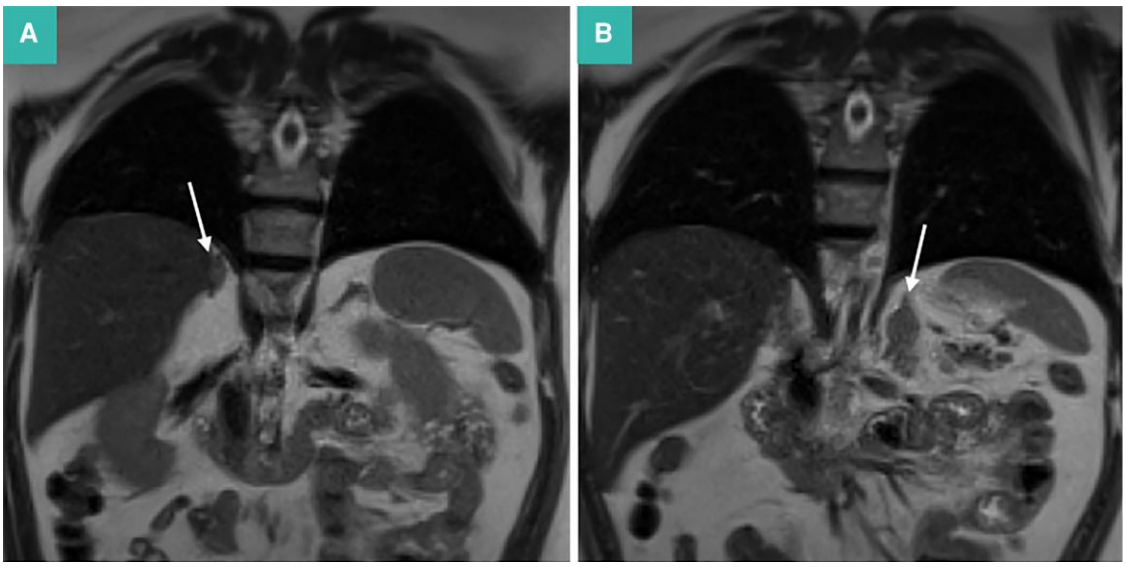

Figure 1. T2-weighted magnetic resonance imaging of the kidneys showing A, right, and B, left adrenal incidentalomas, measuring 10 × 17 mm and 16 × 15.5 mm, respectively.

value: < 1.8 µg/dL; < 49.66 nmol/L). The aldosterone-to-renin ratio was slightly high but aldosterone level (21.2 ng/dL [0.58 nmol/L], normal value 3.5-30 ng/dL [0.10-0.83 nmol/L]) was normal. This was explained by the fact that the assay was performed under β-blockers, which can reduce renin (1 pg/mL [0.02 pmol/L], normal value 3-33 pg/mL [0.07-0.78 pmol/L]) and artificially increase the ratio.

Due to medical history of goiter, thyroid investigation was also carried out, including normal dosing of thyrotropin (1.25 IU/L, normal value 0.46-4.68 IU/L) and tetraiodothyronine (16.3 pmol/L, normal value 10-28.2 pmol/L). Echographic assessment showed stable subcentimetric nodules when compared to previous exams, categorized as thyroid imaging reporting and data system (TI-RADS) 2 and 4a, not meeting fine-needle aspiration criteria.

Diagnostic Assessment

An abdominal contrast-free CT (Fig. 2A and 2B) was performed 2 months after the diagnostic MRI. The CT revealed a growing, round, homogenous left adrenal lesion (arrow) (20 × 15 mm) with a density of 43 Hounsfield units (HU).

Due to the rapid progression of the lesion and the atypical radiological features, a [^{18}F]FDG-PET/CT was carried out (Fig. 2C and 2D) and showed a hypermetabolic lesion with a standard uptake value (SUV) max of 7.2 and an adrenal/liver SUV ratio of 1.95. This advocated for malignancy. There was no other suspect lesion; in particular, subcentimetric clinical cervical lymphadenopathies were nonhypermetabolic.

Treatment

A laparoscopic left adrenalectomy was performed. Histopathologic analysis (Fig. 3) with hematoxylin and eosin staining of the resected left adrenal (Fig. 3A and 3B) showed a 15-mm intra-adrenal lymphoid organ localized in the medulla. There were numerous big germinal centers and no cellular atypia. The surrounding adrenal tissue showed good corticomedullary differentiation, with no specific lesions.

Masson trichrome staining (Fig. 3C) suggested the presence of a capsule (arrow). On immunohistochemistry, the organization of B cells (CD20+/CD3-) and T cells (CD20−/CD3+) was normal (Fig. 3D and 3E). CD68 staining revealed a preserved macrophage population (Fig. 3F).

Outcome and Follow-up

During the 2-year postoperative follow-up, the patient did not develop any problems, especially no sign of inflammatory, infectious, or neoplastic disease, and the cervical lymphadenopathies resolved a few weeks after surgery. No further follow-up imaging was performed in the absence of evidence of underlying disease.

Discussion

The frequency of AI is increasing with age, advancements in technology, and increased imaging frequency. A prospective radiological study reported a prevalence around 0.9% of AI on abdominal CT. According to these authors, the prevalence rises up to 4.6% on 3801 randomly reevaluated CT scans, highlighting the underreporting of adrenal lesions (2).

In an Italian multicentric retrospective study (3) including 1004 cases of AI of which 380 underwent adrenalectomy, the common causes identified were cortical adenomas (52%), cortical carcinomas (12%), pheochromocytomas (11%), and myelolipomas (8%). Cystic lesions, ganglioneuromas, and metastases were less frequent etiologies (3), while angiosarcomas, primary adrenal lymphomas, regenerative hepatic nodule, or extramedullary hematopoiesis were extremely rare (4, 5). Some infectious diseases like tuberculosis, histoplasmosis, blastomycosis, or cryptococcosis can also increase the size of the adrenal glands, as well as granulomatous diseases like Castleman disease (6).

Diagnosing AI can be challenging due to the wide diversity of etiologies, severity, and prognosis. The first objective is to determine which lesions are suspected of malignancy. According to the new 2023 guidelines from the European Society of Endocrinology (1), it is recommended to perform

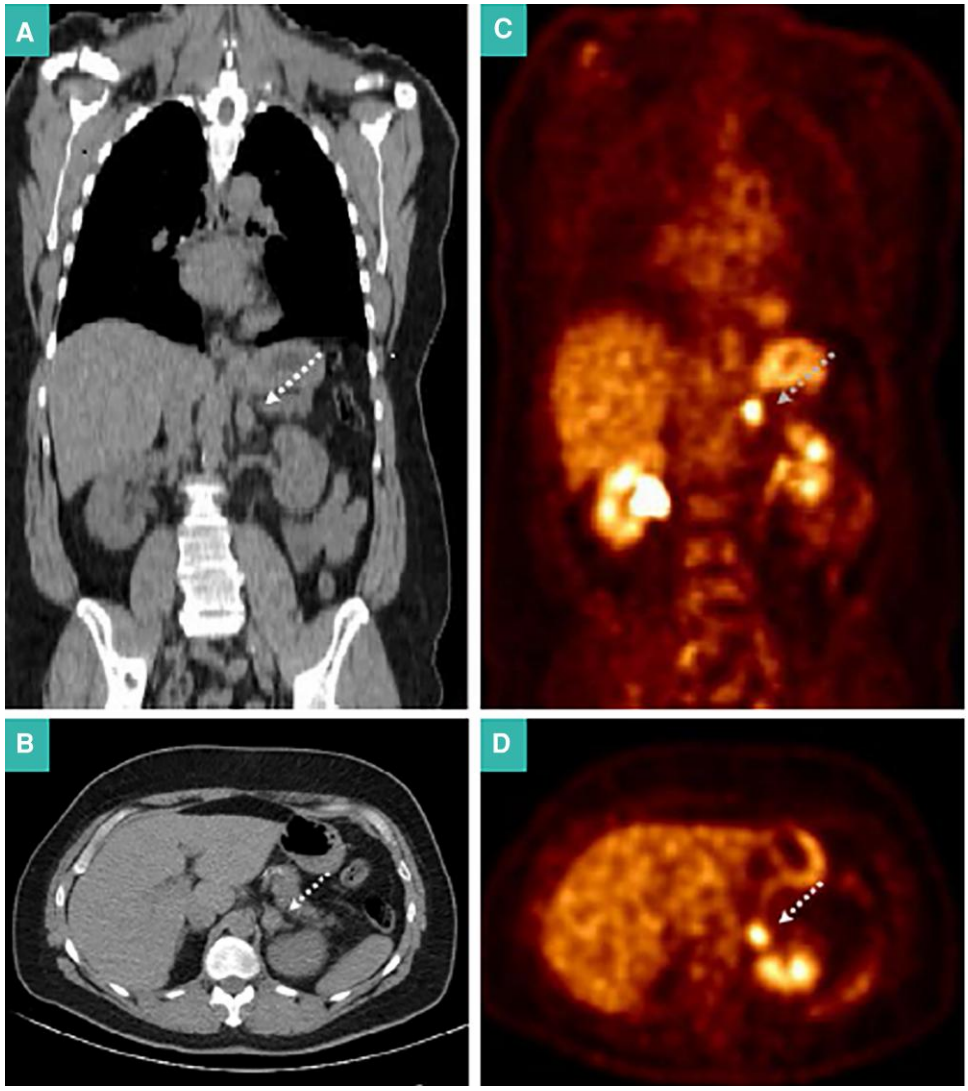

Figure 2. [^{18}F]fluorodeoxyglucose positron emission tomography–computed tomography ([^{18}F]FDG-PET/CT). Arrow showing the suspicious adrenal lesion on A and B, contrast-free abdominal CT, and C and D, after [^{18}F]FDG injection.

a noncontrast CT scan first. If the adrenal mass has an unenhanced density greater than 20 HU, surgery should be considered. Prior to surgery, further evaluation by thoracic CT scan or [^{18}F]FDG-PET/CT is suggested. The second objective is to rule out a hormonally active tumor based on clinical and biological signs.

According to these latest recommendations, the role of [^{18}F]FDG-PET/CT in the work-up is becoming increasingly important. The first interesting information is the SUV_{max}: the higher it is, the more the tumor is suspected of malignancy, with a sensitivity ranging from 86.7% to 100% (1). A second useful indicator is the adrenal-to-liver ratio ($SUV_{max\ tumor}$/$SUV_{max\ liver}$) as a predictor of adrenal carcinoma, with a sensitivity ranging from 85.1% to 100% (1). Using a cutoff of 1.5 in 2 independent cohorts, sensitivity, specificity, and negative predictive value were 86.7%, 86.1%, and 96.9%, respectively (7), and in the second one 90%, 92.6%, and 98% (8). This excellent negative predictive value allows us to exclude an adrenal carcinoma in case of a normal adrenal-to-liver ratio. In case of suspected malignancy, this examination also has the advantage of detecting possible metastases.

In the case we report, due to an elevated adrenal to liver SUV ratio, the hypermetabolic status of our lymphoid incidentaloma raised the question of a lymphoproliferative disorder. Primary adrenal lymphoma is a rare entity with fewer than 200 cases reported up to 2013 (9). This entity is bilateral in 70% of cases and its main subtypes are diffuse large B-cell lymphoma and peripheral T-cell lymphoma, which account for 78% and 7% of cases, respectively (9). In our case, this hypothesis was definitively ruled out by the absence of cellular atypia and normal immunohistochemistry.

The only publication reporting a benign intra-adrenal lymphoid structure describes an isolated lymphoid follicle, also located in the medulla (10). In contrast to our case, the lesion was discovered by the pathologist and was located adjacent to a pheochromocytoma in a multiple endocrine neoplasia type 2 (MEN 2) patient. We report a larger lymphoid structure, organized in multiple germinal centers in a healthy and unremarkable microenvironment. This structure mimics a secondary or a tertiary lymphoid organ. Secondary lymphoid organs include lymph nodes, the spleen, and mucosa-associated lymphoid tissue. Tertiary lymphoid organs are

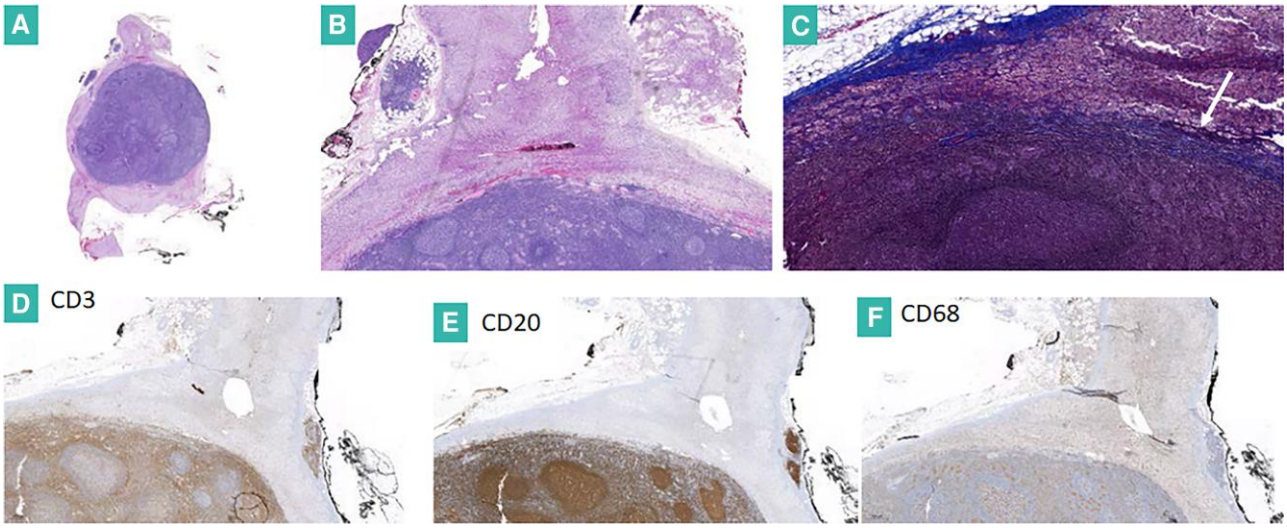

Figure 3. Pathological diagnosis. A and B, Hematoxylin and eosin staining showed a 15-mm intra-adrenal lymphoid organ localized in the medulla. C, Masson trichrome staining suggested the presence of a capsule (arrow). D and E, On immunohistochemistry, the organization of B cells (CD20+/CD3-) and T cells (CD20−/CD3+) was normal. F, CD68 staining revealed a preserved macrophages population.

lymphoid organs that arise in nonlymphoid tissues, in the context of chronic inflammation whatever the cause (infectious, tumoral, inflammatory, or autoimmune disease) (11, 12).

In reviewing the literature, we found some analogies with other cases involving the thyroid gland. For example, a very rare case of pseudolymphoma, also known as reactive lymphoid hyperplasia (13), is described. The nodule was well demarcated but, in contrast with our case, there was no capsule. Other notable differences were the infiltration by lymphocytes and follicles with persistent thyroid tissue within the nodule, and the finding of chronic lymphocytic thyroiditis surrounding the nodule, reflecting an abnormal microenvironment. In another similar case, the patient developed autoimmune thyroiditis and rheumatoid arthritis 2 months after the diagnosis, also pointing to an abnormal autoimmune background (14).

Back to our case, according to these definitions, we are unable to classify our intra-adrenal lymphoid structure as secondary or tertiary. Indeed, the adrenal medulla does not usually contain lymph nodes (secondary lymphoid organ), and we did not find a surrounding tumor or chronic inflammation, even during follow-up, characterizing tertiary lymphoid organs.

Another particularity of our case was the accumulation of radiological features of malignancy, such as a rapid tumor growth, high density on noncontrast CT, high SUV_{max}, and elevated adrenal-to-liver SUV ratio on [^{18}F]FDG-PET/CT. Despite the good sensitivity and specificity of those tools (1), the lesion was finally considered benign.

Learning Points

- We describe the case of a benign adrenal lesion mimicking all aspects of a malignant tumor.
- A lymphoid organ may develop within the adrenal gland.
- An ectopic lymphoid organ can be found in the absence of any evident surrounding tumor or chronic inflammation.

Contributors

All authors made individual contributions to authorship. E.D. was involved in the diagnosis and management of the patient. T.S. was involved in the collection of the data and poster presentation of the case at the Belgian Endocrine Society. M.C.N. was involved in histopathology sectioning and preparation of histology images. X.G. and G.P. wrote the first draft of the manuscript. All authors reviewed and approved the final draft.

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Disclosures

None declared.

Informed Patient Consent for Publication

Signed informed consent obtained directly from the patient.

Data Availability Statement

Original data generated and analyzed during this study are included in this published article.

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