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Case Report

A Rare Case of Primary Adrenal Lymphoma

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Abstract

Adrenal gland incidentaloma (incidental – sudden, accidental) is a mass of the adrenal gland(s), accidentally detected by an instrumental examination conducted for other reasons. The frequency of detection of this pathology based on computer tomography of the abdominal organs is 0.5%–2%. In most cases, the mass is represented by adrenocortical adenomas without hormonal secretion. It is an extremely rare case (less than 1% of all cases) when the adrenal incidentaloma is a primary adrenal lymphoma, which accounts for 1% of all non-Hodgkin lymphomas and 3% of all extranodal lymphomas with a few cases reported in the literature. In our article, we present a case of left adrenal incidentaloma of the adrenal gland, which, during further observation and examination, increased in size, which was the reason for performing laparoscopic adrenalectomy. According to the results of the histological examination, the mass turned out to be diffuse large B-cell lymphoma.

Keywords

adrenal incidentaloma, adrenal lymphoma, laparoscopic adrenalectomy.

INTRODUCTION

Adrenal gland incidentaloma is a mass of the adrenal gland(s), accidentally detected during a noninvasive abdominal imaging technique carried out for reasons unrelated to adrenal diseases.[1] The adrenal incidentalomas are seen in 0.5%–2% of cases of computed tomography (CT) scans of the abdominal cavity.[2] In most cases the masses are represented by adrenocortical adenomas without hormonal secretion. Although 5-25% of incidentalomas increase in size during control studies, the malignancy risk is 1 in 1000 cases.[2]

In extremely rare cases (less than 1% of all cases) incidentalomas may occur as the primary adrenal lymphomas, which accounts for 1% of all non-Hodgkin's lymphomas and 3% of all extranodal lymphomas. There are approximately 120 cases described in the world literature, which are mainly separate clinical observations.[2,3] Both adrenal glands are affected in 70% of cases and the patients are typically males (male/female ratio of 2:1) that are older than 60 years. The first manifestations of the disease are usually associated with adrenal insufficiency. The most common histological variant of the tumor is diffuse large B-cell lymphoma.[3]

In our article, we present a case of a left adrenal incidentaloma, which, during further observation and examination, increased in size thus requiring laparoscopic adrenalectomy. According to the results of the histological examination, the mass turned out to be diffuse large B-cell lymphoma.

CASE REPORT

In October of 2018, a 58-year-old male patient was treated for urolithiasis and ureterolithiasis. Ultrasonography (USG) examination revealed a mass up to 4 cm in diameter of the left adrenal gland with mixed hypoechoic and hyperechoic lesions. Between October 2018 and August 2019, three fine-needle adrenal biopsies were performed; in all cases, atypical cells were not detected. Due to episodic left flank pain, an abdominal USG was performed next in August 2019, which revealed an increase in the size of the mass up to 8×10 cm. Another USG controlled fine-needle biopsy was performed and resulted in 50 ml of brownish fluid. Cytological examination of the fluid revealed no signs of atypia, scanty oxyphilic structureless substance, a large number of red blood cells, single white blood cells and fragments of destroyed cells. The adrenal hormones were within the normal range (cortisol 30.9: normal range 12-35 ng/ml, aldosterone 55.9: normal range 22.1-353 pg/ml, renin 32.3: normal range 4.4-46.1 μMU/ml, metanephrine 46.2: normal range 44-261 mcg/24 hours, normetanephrine 135: normal range 128-484 mcg/24 hours). An abdominal CT with IV contrast demonstrated the presence of a mass in the retroperitoneal space on the left (heterogeneous, with a density of 45-54 Hounsfield units), as well as liver steatosis with an increase in the size of the right lobe ***(Figs 1A, 1B, 1C)****.*

The patient underwent laparoscopic left-sided adrenalectomy under combined anesthesia (endotracheal and intravenous) in September of 2019. The trocars were placed supraumbilical, in the epigastrium along the midline, 10 cm above the navel, pararectally at the level of the navel in the left mesogastrium and left iliac region. During the revision, contouring of the mass was noted below the lower pole of the spleen. The posterior sheet of the peritoneum was dissected along the left lateral canal; further mobilization of the left adrenal gland with the mass was performed using monopolar and bipolar coagulation ***(Fig. 2)****. The mass was removed through the left hypochondrium, through a 10-cm-long incision, followed by an additional revision of the zone where the mass was located and placement of safety drainage.*

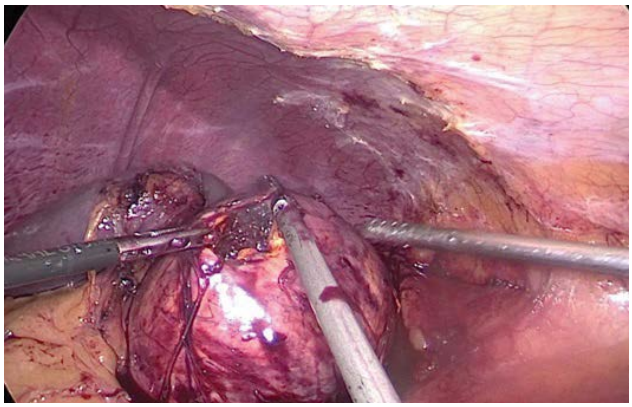

Figure 2. Laparoscopic intraoperative image of the mass.

The incisions were sutured in layers. The postoperative specimen is shown in ***Figs 3, 4****.*

Histological analysis revealed diffuse infiltration of atypical large lymphocytes having oval to round or irregular cleaved vesicular nuclei, conspicuous one or several nucleoli and frequent mitotic figures. The results of an immunohistochemical examination showed that tumor cells did not express CD10, glypican-3, cytokeratin 20, cytokeratin 7, Inhibin alpha, S100, CD56, synaptophysin, and Mart-1 (Melan A). There was a positive diffuse reaction with CD45, Ki 67 52%; immunophenotype of tumor proliferate CD20 + (diffuse), MuM1 + (diffuse 80%), BCL-2 + (diffuse 70%); Bcl-6 (-). Therefore, the morphological picture and immunophenotype corresponded to diffuse large B-cell lymphoma, DLBCL, Bcl-2 +.

The postoperative period was uneventful, the control drainage was removed on the second day and the patient was discharged in satisfactory condition 3 days after operation. The LDH levels were normal (155 [normal range 135-225 U/L]) and the patient did not report any "B"- symptoms. The patient completed six courses of R-CHOP-21 chemotherapy (rituximab, cyclophosphamide, hydroxidaunorubicin, Oncovin, prednisone) and no radiation therapy. The control PET CT scan in 2020 showed no evidence for relapse.

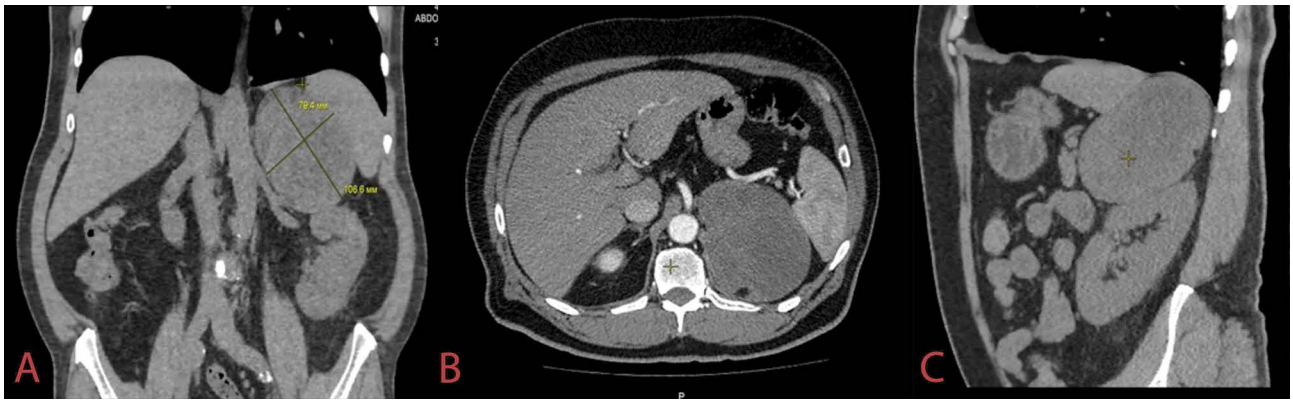

Figure 1. A. CT of the abdominal cavity (frontal plane); **B.** CT of the abdominal cavity (axial plane); **C.** CT of the abdominal cavity (sagittal plane).

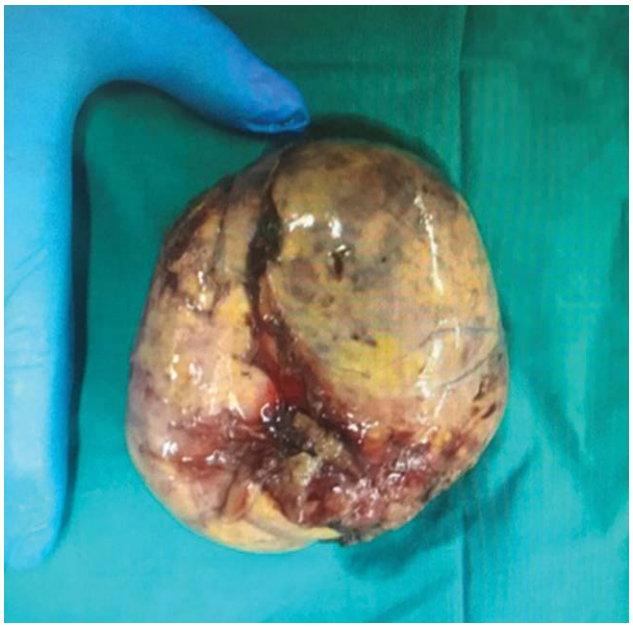

Figure 3. Postoperative specimen of the adrenal gland's mass.

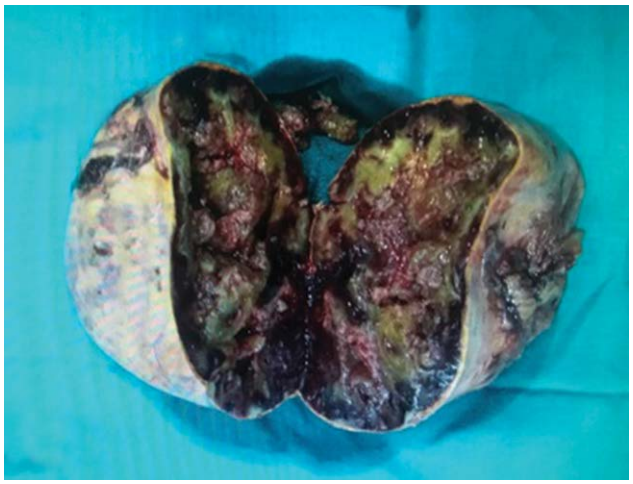

Figure 4. Postoperative specimen of the adrenal gland's mass (sliced).

DISCUSSION

Adrenal masses have different nature: adenomas (36%–94%), hyperplasia (7%–17%), carcinomas (1.2%–11%) of the adrenocortical layer; pheochromocytomas (1.2%–23%), ganglioneuromas (up to 6%), ganglioneuroblastomas (less than 1%) of the cerebral layer; metastases (up to 24% of cases of metastases of cancer of the lungs, breast, kidneys, melanoma, less often the intestine), inflammatory etiology (amyloidosis), infectious diseases (tuberculosis, histoplasmosis, cryptococosis) and others (myelolipomas, lymphomas, liposarcomas, angiomyolipomas, hamartomas, fibromas, teratomas, cysts).[2,4]

Primary adrenal lymphoma is a malignant proliferative disease with a unilateral or bilateral localization in the adrenal gland, which probably originates from the hematopoietic tissue inherent to the adrenal gland.[5] Secondary adrenal involvement in the lymphoproliferative processes is frequent (in up to 24% of all cases).[6] However, primary localization in the adrenal gland is extremely rare (in 1% of all non-Hodgkin lymphomas and 3% of all extranodal lymphomas).[2,3] Diagnosis of the disease is associated with a number of difficulties, since the clinical picture is often scarce. Moreover, early detection of pathology significantly increases the chances of complete remission, which must be taken into account when choosing treatment tactics in patients with a morphologically unconfirmed diagnosis of adrenal incidentaloma. Fine needle or core biopsy can be performed for differential diagnosis, but they are often uninformative. Due to the lack of management protocols for patients with primary adrenal lymphomas, preference is given to standard chemotherapy regimens recommended for the treatment of non-Hodgkin's lymphomas, surgery and hormone replacement therapy.[7]

The immunohistochemical examination revealed diffuse large B-cell lymphoma with diffuse expression of MUM 1 (+), which indicates plasmablastic cell differentiation of the process and is associated with a more aggressive clinical course, shorter survival in the R-CHOP treated group.[8] However, the current case demonstrates early surgical management followed by 6 courses of R-CHOP chemotherapy and no relapse based on the latest PET CT scan.

The chemotherapy usually involves 6 courses of R-CHOP (rituximab, cyclophosphamide, hydroxidaunorubicin, Oncovin, prednisone) followed by monitoring the status on PET scans.[9] Chemotherapy is currently the standard treatment, while the role of radiotherapy and surgery remains unclear. There are about 120 cases reported in the literature of treatment of primary adrenal lymphomas, of which surgical intervention was performed in 17 cases.[2,3,10] The prognosis of the disease is negative: complete remission with R-CHOP chemotherapy is 54.8%, 2-year survival is 68.3%.[3] The prognosis significantly worsens with large tumor size (more than 5 cm), dissemination of the process (more than one extranodal localization), increased LDH, age (over 60), suprarenal insufficiency, stage III-IV disease.[3] Given the ambiguous role of surgical aid in the treatment of primary adrenal lymphoma, laparoscopic approach is the most optimal one due to its low-invasiveness: laparoscopic transperitoneal adrenalectomy for malignant processes has a low risk of postoperative complications (11.5%), a low conversion rate (9.7%), and a high percentage successful resection of education (R0 – 78.8%, R1 – 17.3%).[11] Hormone replacement therapy is indicated after surgery with hydroxycortisone (15 mg/day) and fludrocortisone (0.1 mg/day).[4]

The management of primary adrenal lymphomas is controversial due to the lack of clinical guidelines. Moreover, there are limited large scale studies and the data is mostly presented as case reports. In case of adrenal incidentalomas, the mass is typically followed up with a control scan at 6-12 months, which is based on the principle that adrenal

malignancies are likely to enlarge. The expert panel of European Society of Endocrinology in collaboration with the European Network for the Study of Adrenal Tumors agreed that an increase in more than 20% of the largest tumor diameter together with at least a 5-mm increase of this diameter should be considered as suspicious.[12] Based on our experience, adrenal masses should be evaluated based of USG and CT studies and in case of their enlargement, the mass should be biopsied. Although routine biopsy is not routinely indicated in adrenal masses, it may prove valuable in individual cases and is a low-risk procedure for the patient. When there are still doubts about the nature of the adrenal mass the tumor should be operated. The current management is in favour of minimally invasive techniques at least in centres with a high volume of adrenal surgery.

In the described case we demonstrate surgical treatment for a rapidly growing adrenal mass even with the absence of morphological atypia. This choice decision is augmented by the risk of untimely detection of malignant adrenal gland tumors and the initiation of timely etiotropic therapy. At the same time, modern minimally invasive methods of surgical treatment, in turn, make it possible to favour more aggressive treatment tactics. This is especially important in a controversial situation as it allows extirpation of the mass less traumatically for the patient with subsequent guaranteed morphological verification of the diagnosis and timely initiation of appropriate therapy.

CONCLUSIONS

Primary diffuse large B-cell adrenal lymphoma is an extremely rare pathology that occurs in less than 1% of cases of the adrenal incidental lymphomas and 3% of cases of extranodal lymphomas. In view of the scarce clinical presentation, the diagnosis of this disease is associated with a number of diagnostic and prognostic difficulties. Early detection of pathology significantly increases the chances of complete remission, which must be considered when choosing treatment or observation tactics in patients with a morphologically unconfirmed diagnosis of adrenal incidentaloma. The significant effect of adrenalectomy as the first stage of treatment before starting chemotherapy on the prognosis of patients with primary diffuse large B-cell lymphomas of the adrenal gland remains debatable. However, this is to some degree downgraded by the importance of timely morphological verification.

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Редкий случай первичной лимфомы надпочечников

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Резюме

Инциденталома надпочечника (инцидентный – внезапный, случайный) – это образование надпочечника, случайно установленное инструментальным исследованием, проведённым по другим причинам. Заболеваемость данной патологией по данным компьютерной томографии органов брюшной полости составляет 0.5% -2%. В большинстве случаев образование представлено аденомами коры надпочечников без гормональной секреции. Это чрезвычайно редкий случай (менее 1% всех случаев), когда поражение надпочечников представляет собой первичную лимфому надпочечника, которая составляет 1% всех неходжкинских лимфом и 3% всех экстранодальных лимфом, и только несколько случаев описаны в литература. В нашей статье мы представляем случай поражения левого надпочечника инциденталомой, который при дополнительном наблюдении и обследовании увеличился в размерах, что явилось поводом для выполнения лапароскопической адреналэктомии. По результатам гистологического исследования новообразование оказалось диффузной В-клеточной лимфомой большого размера.

Ключевые слова

инциденталома надпочечника, лимфома надпочечника, лапароскопическая адреналэктомия