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The local spread of pheochromocytoma after adrenalectomy with a rupture of the tumor capsule at the time of the surgery

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Abstract: Introduction: We present a case of a 29-year-old patient treated due to fully symptomatic pheochromocytoma of the right adrenal gland.

Case presentation: Patient was operated on and an open right-sided adrenalectomy was performed. At the time of the surgery, a rupture of the tumor capsule occurred. Five years post-operatively, a recurrence of the symptoms of chromaffin-cell tumor was noted. After the exact localization of the multiple recurrences, the patient was reoperated on.

Conclusion: The case of pheochromocytoma is presented due to the possibility of chromaffin-cell seeding into the peritoneum, with no signs of distal metastases so far.

Keywords: pheochromocytoma, malignant pheochromocytoma, metastases of pheochromocytoma

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1 Introduction

We present here the case of an unfortunate spread of chromaffin cells within the operating area after the accidental damage of the pheochromocytoma capsule during the surgery. This case is interesting as there are no similar cases described in the literature. The following search strategy for similar cases in papers written in English within the time period of 2000-2015, using PubMed and EMBASE was used: (Pheochromocytoma) AND ((Neoplasmatic Metastasis) OR (Neoplasm Recurrence, Local)).

In our 30-year single-center experience of treating pheochromocytomas, we have not encountered any other cases of the local spread of chromaffin cells after the primary surgery due to the pheochromocytoma of adrenal glands.

2 Presentation of the case

In March 2007, a 29-year-old female was admitted to the internal medicine clinic due to paroxysmal episodes of hypertension, headaches, palpitation, chest pain and general malaise that had been present for a month. In diagnostic imaging, a 60 mm tumor of the right adrenal gland was visualized (Figure 1). In laboratory tests, concentrations of metoxycatecholamines in urine in three consecutive analyses were as follows: 2145,8; 1645,8; and 2146,8 ug/day. No significant increase in serum concentration of catecholamines was noted. Concentrations of tumor markers were as follows: AFP 1,5ng/ml, CEA 0,5ng/ml, Ca 19-9 14,5U/ml, and Ca-125 17,8u/ml. The patient was diagnosed with pheochromocytoma and scheduled for surgery. During the perioperative period, she was administered 10 mg of dibenziran daily and metoprolol 25 mg twice a day in order to control tachycardia. After approximately three weeks of pharmacological preparation, she

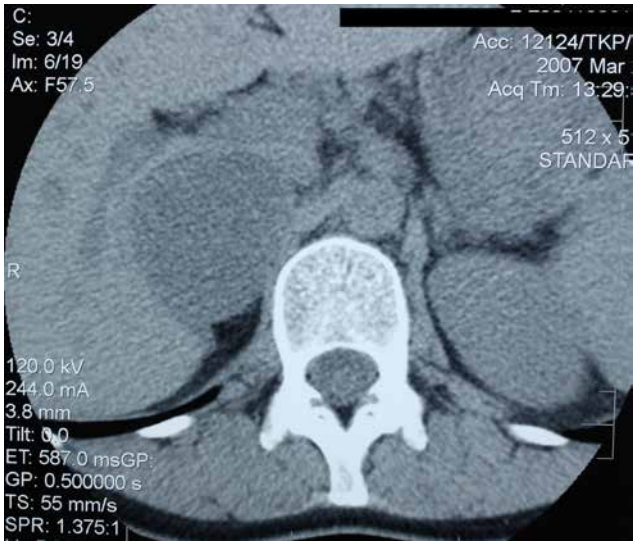

Figure 1: Preoperative CT scan from 2007. Tumor of the right adrenal gland, 67x48 mm in dimension and of 30 Hounsfield units density.

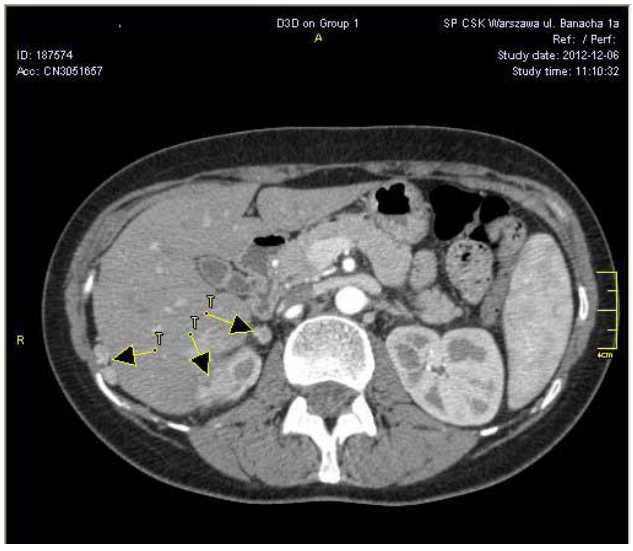

Figure 2: CT scan from 2012. Numerous nodules in sub hepatic region and in the post-operative area.

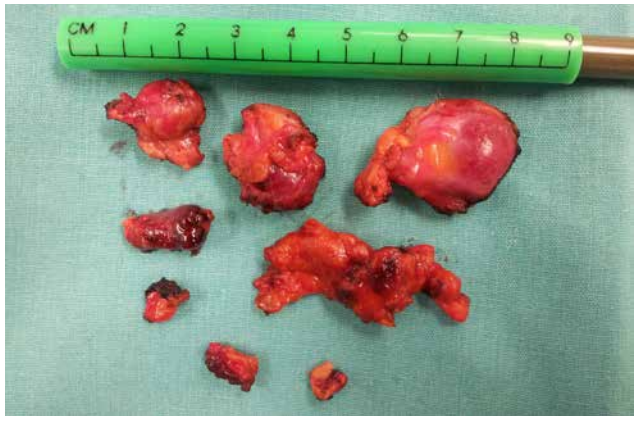

Figure 3: Eight specimens from dissected nodules from peritoneum.

was operated on. A transperitoneal right-sided open adrenalectomy was performed. At the time of the surgery, a rupture of the tumor capsule occurred due to its adhesion to the upper renal pole. No complications were present in the postoperative period. On the fourth day, the patient was transferred to the clinic of internal medicine in order to perform genetic analyses, which revealed no signs of mutation in the RET proto-oncogene, SDHD or SDHC genes. On the seventh day, she was discharged home. The pathological examination report on the tissue removed reads as follows: "an adrenal gland with a tumor of 6 x 6,5 x 4,4 cm in dimension, with a damaged surface, partly decaying in the central area, yellow-greenish in peripheral parts, of pheochromocytoma characteristics, positive for chromogranine (+), positive for synaptophisin (+)".

After 5 years, the patient was readmitted to the internal medicine clinic presenting the same symptoms as previously. As these symptoms can be indicative of a chromaffin-cell tumor, concentrations of metoxycatecholamines in the patient's urine were measured. These concentrations were measured at 2200 ug/d, far above the normal limit.Chromogranine was mildly elevated and reached 97,96ng/ml. The following diagnostic imaging were scheduled: MIBG, PET and CT. This imaging revealed the presence of several tissue foci accumulating marker used in the imaging studies within Morrison's recess and post-tumoral lodge (Figure 2). Overall, there were 8 foci found, with the diameter range from 6-22 mm. Furthermore, cholelithiasis of the gallbladder was revealed. Based on the imaging studies, a thorough mapping of the lesions was performed and the patient qualified for surgery after pharmacological preparation. In January 2013, the patient was operated on. Using the transversal access via previous cicatrix, the peritoneal cavity was opened and 8 lesions were easily localized and dissected with peritoneal fragments and adjacent tissues (Figure 3). After removal of all nodules, a cholecystectomy was performed. All the nodules were sent for pathological examination, which revealed pheochromocytomatic tissue with 1.5% mitotic activity and no other signs of malignancy. On the fifth day after surgery, the patient was discharged home in good general condition. One-month post surgery, the patient's metoxycatecholoamine concentration in daily urine output was analyzed and found to be within normal limits, i.e. 450ug/ml. Due to the possibility of malignancy, patient was scheduled for follow-up in outpatients' clinic.

Ethical approval: The research related to human use has been complied with all the relevant national regulations, institutional policies and in accordance the tenets of the Helsinki Declaration, and has been approved by the authors' institutional review board or equivalent committee.

3 Discussion

Due to the absence of defined features of malignancy of pheochromocytoma, it is difficult to determine the malignant potential of the tumor. The only proven malignant features are the presence of distant metastases, already diagnosed multi-endocrine syndromes or genetic disorders [1,2]. Metastases may be detected in some distant time from the primary surgery, sometimes in ten years' time [3]. The onset of the characteristic symptoms of pheochromocytoma after surgical treatment of an adrenal tumor suggests the existence of distant metastases and their hormonal activity.

In the presented case, a multifocal local recurrence in the area of the primary surgery was visualized in MIBG scintigraphy. This raises the question of whether or not to treat peritoneal spread as distant metastases. However, the presence of chromaffin tissue in an unusual localization fulfills the definition of metastasis. In the available literature, no similar cases have been described previously. Some authors claim that there is a possibility of local spread into the abdominal wall at the time of both open and laparoscopic surgeries. However, this is likely a case of adrenal cortical carcinoma or metastases to the adrenal glands. Distant metastases to lymph nodes and parenchymal organs are more typical for malignant pheochromocytoma. As a consequence of the absence of appropriate diagnostic criteria in primary pathological examination, metastases can be detected 6-7 years after initial surgery to remove a pheochromocytoma[4]. Fully symptomatic syndrome of pheochromocytoma develops in approximately 80% of patients; in the remaining 20% of cases, regardless of their characteristics, asymptomatic or atypical course is observed and final diagnosis is based on the postoperative pathological report [5]. It is mainly a case of group of adrenal tumors called incidentalomas [6,7]. There are no defined consequences of that fact and laparoscopic adrenalectomy is a recognized and recommended method of the treatment, irrespectively of the character of the lesion [4,8]. There are well-established indications for open adrenalectomy, and nowadays it is a supplementary modality to surgical methods for treatment of pheochromocytomas rather than an alternative one. In the diagnosis of abnormalities in adrenal glands, the methods of greatest importance are computed tomography, magnetic resonance, positron emission tomography, MIBG scintigraphy, and ultrasound examination as a screening tool. The imaging modalities may be complementary to each other and in 95% of cases are diagnostically positive in terms of localization and qualitative aspect (9). Based on a common finding that malignant pheochromocytomas account for 5-26% of cases, and in case of paragangliomas up to 36%, the matter of greatest importance in the treatment of such patients is a strict, routine follow-up [4,10].

4 Conclusions

The case of pheochromocytoma is presented due to the possibility of chromaffin-cell seeding into the peritoneum, with no signs of distal metastases so far. In general, the patients operated due to the pheochromocytoma should be followed-up life-long due to the risk of local spread.

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Conflict of interest statement: Authors state no conflict of interest

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