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Long-term Survival over 28 Years of a Patient with Metastatic Adrenal Cortical Carcinoma – Case Report

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Abstract. *Adrenal cortical carcinoma (ACC) is a rare and highly malignant tumour with up to 70% of the patients diagnosed at an advanced clinical stage, up to 40% presenting with metastases. Even after complete surgical excision, up to 80% of the patients show locoregional recurrence or metastases. We report a case of a 62-year-old woman with a non-functional ACC of the left adrenal gland (T_2 N_0 M_0 classified as stage II). After the initial resection, 3 operations for metastasis of the contralateral adrenal gland and 4 operations for metastasis of the lungs were carried out, allowing survival for more than 28 years with a good quality of life. This case report emphasises the need for careful clinical and radiographic follow-up. A repeat surgical approach should be adopted whenever possible providing long-term survival over decades.*

Adrenal cortical carcinoma (ACC) is a rare and highly malignant tumour with a worldwide annual incidence of approximately 0.5-2 cases per million, accounting for 0.2% of all cancer-related deaths (1, 2). Due to the rarity of ACC and the impossibility of direct clinical examination of the adrenal glands, the diagnosis is often delayed and the patients may be at an advanced stages of disease connected with poor prognosis. With respect to the ability, quantity and quality of hormone production, ACC can be distinguished between functioning and non-functioning tumours. Functioning tumours can be detected more easily by endocrine symptoms, whereas small non-functioning tumours have to reach a large size and local invasiveness to cause symptoms. The mainstay of therapy is still the radical surgical resection of the tumour and adjacent organs. Even after complete and radical surgical excision locoregional relapse or distant metastases are common, with most of the patients dying within one year without further treatment. We present a case of non-functional adrenocortical carcinoma with long-term survival over 28 years, in spite of recurrent metastatic disease in the contralateral adrenal gland and the lungs. The patient was treated by 8 sequential reoperations and is, 9 months after the last operation, free of disease.

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Case Report

The history of the 62-year-old female patient started 28 years previously when she presented with pain and a palpable mass of the left flank. After excluding the presence of metastatic disease by imaging procedures, a total left adrenalectomy and splenectomy *via* a transabdominal transperitoneal approach was carried out with a complete margin-negative resection. Intraoperatively no visceral metastases were seen. The histopathological examination revealed a non-functional adrenal cortical carcinoma, weighting 1091 g, with a maximum diameter of 17 cm, composed of polygonal cells whose cytoplasma were eosinophilic and vacuolized with extensive areas of necrosis and intratumoral haemorrhages. No tumour cell invasion into the surrounding tissue and no metastasis could be seen at the time of the diagnosis (T_2 N_0 M_0 according to stage II, using the staging system by MacFarlane and modified by Sullivan *et al.* (3, 4)).

After four years of disease-free survival, a lesion of the contralateral adrenal gland was found during follow-up. The lesion was resected by subtotal adrenalectomy, saving a part of the right adrenal gland. Histopathological examination showed a metastasis of the contralateral gland (Figure 1).

Thirteen years after the initial operation and nine years of disease-free survival, metastasis of both lungs could be evaluated during follow-up. Two of the metastasis of the left lung were resected. Histological examination confirmed the suspicion of metastasis of ACC. Postoperatively chemotherapy using mitotane was administered. The chemotherapy was stopped after 15 months because of acute adrenal insufficiency.

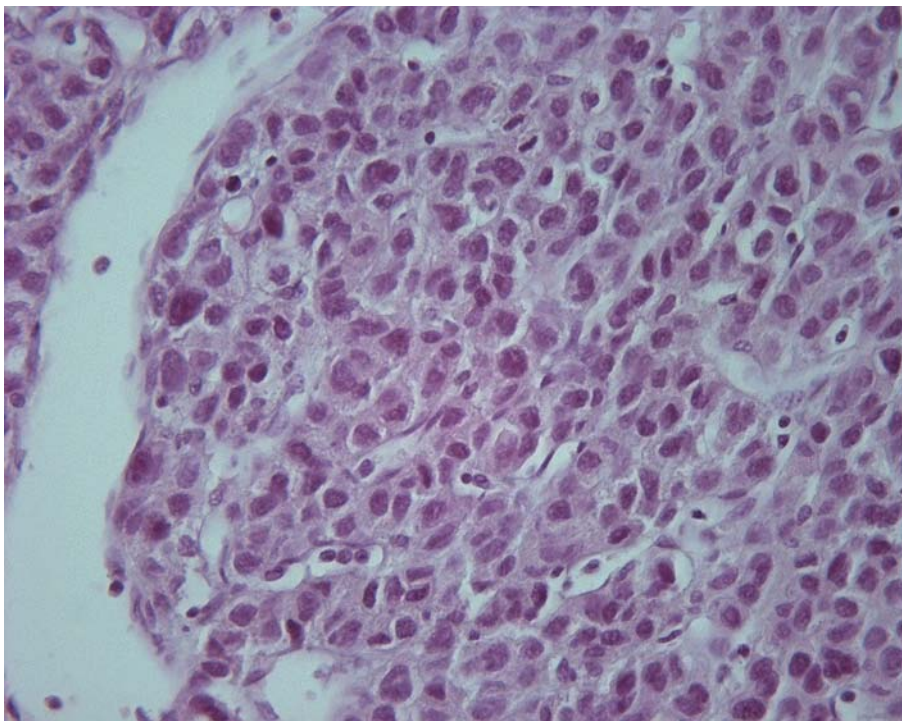

Figure 1. *Histopathological specimen of the metastasis of the right adrenal gland four years after the first operation (Hematoxylin/Eosin; 1:40).*

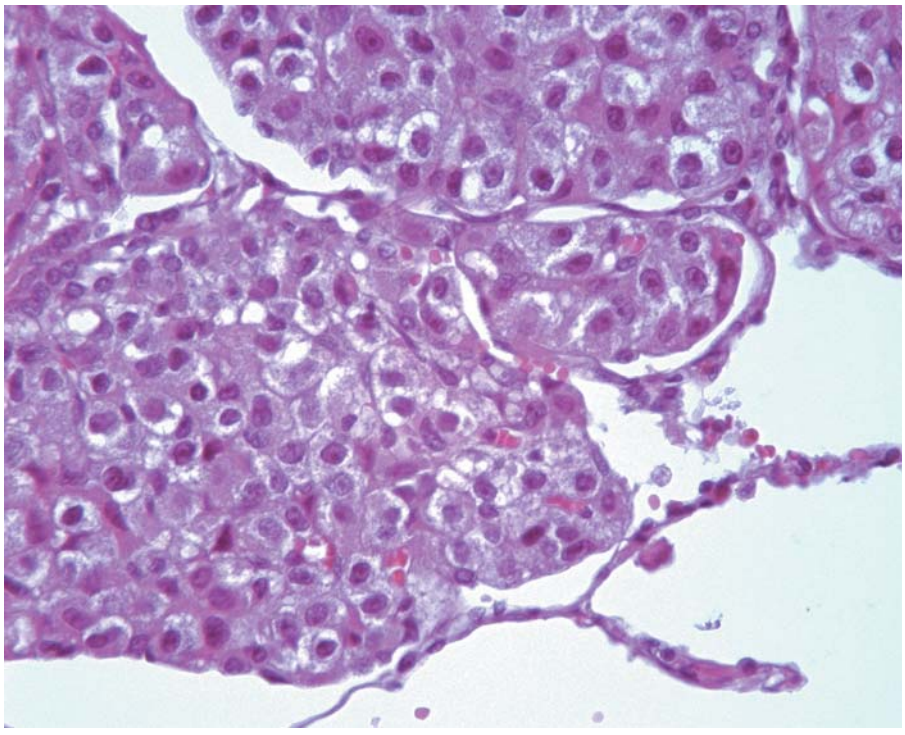

Figure 2. *Histopathological specimen of the metastasis of the left lung 24 years after the first operation (Hematoxylin/Eosin; 1:40).*

Seven years after the third operation, a new lesion in the right adrenal gland was seen during follow-up. The right adrenal gland was resected completely showing metastasis of the right adrenal gland.

Three years after the fourth operation, the metastasis of the left lung were resected. One year later the metastasis of the left and of the right lung were resected (Figure 2).

After the sixth operation, all metastasis had been resected completely. Two years after the sixth operation a new tumour in the region of the former right adrenal gland was seen. The lesion was resected and a cholecystectomy was carried out simultaneously. Histopathological examination showed a metastasis of the ACC in the former region of the right adrenal gland. Two years after the seventh operation, a new pulmonary metastasis of the left lung was found and successfully resected.

All histological specimens were evaluated in the same department and were compared again after every operation, showing metastasis of the initial tumour. All eight operations were well tolerated by the patient without any complications. Nine months after the last operation there is no radiological or clinical evidence of tumour progression.

Discussion

Non-functioning ACC's can be seen in 30 to 60% of the patients (5-12). Unspecific abdominal discomfort or pain as a result of rapid growth, significant tumour size or local invasion is the major symptom in patients with this tumour entity (5, 8, 9, 11-14). Up to 70% of the patients with ACC are diagnosed at an advanced clinical stage of disease (5-13, 15-18). In 40% of the patients simultaneous existence of metastases can be seen with lung and liver being the most frequent sites (5, 6, 8, 9, 11-15, 19-22). The only potentially curative treatment is the complete surgical resection of the tumour, the lymph nodes and any adjacent organ, involving a transabdominal approach which facilitates the maximum exposure necessary for complete resection (11-14, 22, 23). After complete and curative resection, the 5-year survival is about 42-57% whereas untreated patients have a very poor prognosis with a mean survival of only 3-6 months. Patients with incomplete resection have a mean survival of less than 12 months with a 5-year survival rate of 0-9% (6, 8, 11, 13, 15, 18, 20). This demonstrates the impact of a complete margin-negative surgical resection on the survival.

Another factor influencing survival is the stage of disease. Patients at a lower stage of the disease have an improved survival. The overall 5-year survival for all patients independent of the stage of disease is 19-38%, for patients at stage I or II 43-78%, for patients at stage III 21-27% and for patients at stage IV only approximately 0-10% (4, 6, 8-11, 13, 15, 17-21, 24, 25). An incomplete resection and the presence of metastases are the most unfavourable prognostic factors (4, 6, 8, 11, 13, 15, 17, 19, 20). However, the 5-year survival is not equivalent to cure of disease, because even after complete surgical excision in 23-80% of the operated patients, locoregional recurrence or the development of metastases occur with a mean disease-free interval of 12-22 months (6, 8-10, 12, 15, 17, 18).

In case of locoregional recurrence, re-operation with complete resection is connected with a mean survival of 42 - 56 months and a 5-year survival rate of 27-57%, whereas medical treatment with various chemotherapeutic agents is connected with a mean survival of only 16-19 months and a 5-year survival rate of 0-8% (6, 8, 11, 15, 18). This emphasises the impact of surgery on locoregional recurrence or development of distant metastasis. A repeat surgical approach should be adopted among the patients with potentially resectable lesions whenever possible. Additionally, reoperation provides excellent palliation in symptomatic tumours. By multiple re-operation, long-term survival over decades can be achieved as was shown in our case (26, 27). To our knowledge this report presents the longest survival of metastatic adrenal cortical carcinoma in the world.

In conclusion, the high rate of recurrent disease, even in patients with a curative resection, emphasises the necessity for careful clinical and radiographic follow-up to discover locoregional recurrence or development of distant metastasis. Reoperation in patients with potentially resectable lesions should be performed whenever possible. A low stage and a complete margin-negative resection of the primary tumour, but also of the locoregional recurrence or the metastasis, provides prolonged disease-free survival.

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