CORRESPONDENCE

Deficits in the Management of Patients With Adrenocortical Carcinoma in Germany

by Dr. med. Sarah Johanssen, et al. in volume 50/2010

Statements Cannot Be Substantiated

The Würzburg registry's work has many merits and deserves praise; the number of tumors captured is impressive. However, the authors report alleged deficits in the histopathological reports of adrenocortical tumors without proving these to a satisfactory degree.

- The authors state that for 11% of the cases, the histopathology report contained only insufficient information about resection status (Rx). Rx is a correct description if findings, especially for reasons related to the specimen, do not enable substantiated evaluation of the resection status (for example, a fragmented specimen, tissue sampled by a non-pathologist, missing details on localization, etc). Since this situation is not distinguished from true deficits of the diagnostic report, the current evaluation does not allow for assessing the quality of the histopathological reporting.
- Figure 3 shows the survival of the patients with an Rx status. The graphical representation is not correct because the events of the Rx and R1 curves by far exceed the "n" numbers (16 and 19). The figure does therefore not show an intermediary survival in Rx patients (heterogeneous group).
- The diagnosis reportedly had to be revised in 13% of cases; but plausible evidence is missing. Furthermore it was not shown whether the diagnosis was fundamentally or marginally adapted. In adrenocortical carcinoma, plausible reasons may in individual cases lead to a change in the primary diagnosis without any real errors having been committed. Dignity assessment may be impossible, as may in individual cases the definite differentiation from metastases in an isolated adrenal specimen. Claiming a high rate of misdiagnoses without categorical evaluation of individual cases cannot be justified. Furthermore, individual reference pathologies are insufficient in complex diagnostic studies. The German Society of Pathology rightly asks for expert panels rather than individual experts.
- Demanding reference histology as a default in endocrine-inactive tumors of the adrenal cortex is unjustifiable because this would mean that any incidentaloma of the adrenal cortex would have to be sent out for reference pathology, and many patients would be exposed to worry quite unnecessarily.

A need for improvement should be argued and proved stringently, and studies that postulate deficits should themselves meet particularly stringent quality criteria.

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REFERENCES

1. Johanssen S, Hahner S, Saeger W, et al.: Deficits in the management of patients with adrenocortical carcinoma in Germany. Dtsch Arztebl Int 2010; 107(50): 885–91.

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Conflict of interest statement
The authors declare that no conflict of interest exists.

In Reply:

We thank our correspondents for their interest and are happy to explain the problems with the pathological findings in greater detail:

- In none of the Rx patients was their resection status reported by the pathologist. The classification as Rx was made by the investigators of the German Adrenocortical Carcinoma Registry (Nebennierenkarzinomregister) in cases where the pathology report did not contain information on the resection margin. In another context, Rx is obviously a correct diagnosis—for example, where the tumor capsule was damaged intraoperatively. Patients with a damaged tumor capsule were explicitly excluded from the survival analysis.
- Figure 3 illustrates a Cox regression analysis and is not a Kaplan-Meier figure, as our correspondents seem to assume. Cox regression allows for the calculation of hazard ratios for the respective groups.
- The misdiagnoses concerned metastases of extra-adrenal cancers (n=16), pheochromocytomas (n=2), sarcomas (n=2), and one adrenal adenoma. We are not clear what "marginal" adaptation of the diagnosis refers to—in all cases, treatment with mitotane, for example, would have constituted serious medical mistreatment. Today, the experienced pathologist is usually able to assess the potential malignancy of an adrenal mass and distinguish between primary adrenocortical tumors, adrenal medullary tumors, or metastases. Since most pathologists do not have any experience with the rare adrenal carcinoma they should consult an experienced colleague. We support the demand for expert panels rather than individual experts. The German Society of Pathology should

presently appoint such a panel of competent adrenal pathologists.

- In case of a hormone-inactive incidentaloma, surgery is indicated only if it is suspected to be malignant—in this setting, the pathological results are therefore of utmost importance. The fact that patients still undergo unnecessary surgery is no reason to compromise on the quality of the pathology report.

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1. Johanssen S, Hahner S, Saeger W, et al.: Deficits in the management of patients with adrenocortical carcinoma in Germany. Dtsch Arztebl Int 2010; 107(50): 885–91.

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PD Dr Fassnacht and Professor Allolio are investigators of a study of the pharmacokinetics of mitotane that is being funded by HRA Pharma (France). PD Dr Fassnacht is also the principal investigator and Professor Allolio is the investigator of a study of sunitinib that is funded by Pfizer. PD Dr Fassnacht and Professor Allolio are investigators of a clinical study sponsored by OSI Pharma of OSI-9076 in adrenocortical carcinoma.
Dr Johanssen declares that no conflict of interest exists.