German Pituitary Tumor Registry

In 1996, the German Registry of Pituitary Tumors was founded by the Pituitary Section of the German Society of Endocrinology as a reference center for collection and consultant pathohistological studies of pituitary tumors.

The collection comprises a total of 16,283 cases up until the end of 2018. Of these cases, 12,673 originated from surgical and 3,610 from autopsy material. All specimens were fixed in formalin and embedded in paraffin. The sections were stained with H&E stain and PAS. Monoclonal (prolactin, TSH, FSH, LH, and alpha subunit) or polyclonal (GH and ACTH) antibodies were used to detect pituitary hormones in the lesions. Since 2017, antibodies against the transcription factors Pit-1, T-Pit, and SF-1 has been used in difficult cases. The criteria of the The 2017 World Health Organization classification of tumors of the pituitary gland have been basic principles for classification since 2018 (Osamura et al. 2017). For differentiation of other sellar tumors, such as meningiomas, chordomas, or metastases, the use of additional antibodies was necessary. For these cases, it was possible to use a broad antibody spectrum. Autopsy pituitaries were generally studied by H&E and PAS sections. If any lesions were demonstrated in these specimens, additional immunostaining was performed.

Multiple tumorous lesions with more than one pituitary neuroendocrine tumor (PitNET) respectively adenoma make up 1.4% (232 cases) in our collection. Within the selected cases, synchronous multiple pituitary neuroendocrine tumors (PitNETs) account for 17.3%, PANCH cases (pituitary neuroendocrine tumor with neuronal choristoma) for 14.7%, PitNETs and posterior lobe tumors for 2.2%, PitNETs and metastases for 5.2%, PitNETs and mesenchymal tumors for 2.6%, PitNETs and cysts for 52.2%, and PitNETs and primary inflammation for 6.0%. The mean patient age was 53.8 years, with a standard deviation of 18.5 years. A total of 55.3% of the patients were female and 44.7% were male. From 1990 to 2018, there was a continuous increase in the number of multiple tumorous lesions.

From the studies, Schöning et al. concluded that considering possible tumorous double lesions during surgeries and in preoperative X-ray analyses is recommended [1)].

Inflammatory pituitary lesions account for 1.8% of all specimens from the German Pituitary Tumor Registry. They occur in 0.5% of the autoptical specimens and in 2.2% of the surgical cases. Women are significantly more often affected than men and are often younger when first diagnosed. In general, primary and secondary inflammation can be distinguished, with secondary types occurring more frequently (75.1%) than idiopathic inflammatory lesions (15.4%). In primary inflammation, the lymphocytic type is more common (88.5%) than the granulomatous type of hypophysitis (11.5%). The most common causes of secondary inflammation are Rathke's cleft cysts (48.6%), followed by tumors (17.4%) such as craniopharyngioma (9.1%), and adenoma (5.5%) or germinoma (2.0%). More causes are tumor-like lesions (7.1%) such as xanthogranuloma (3.5%) or Langerhans histiocytosis (3.5%), abscesses (5.5%), generalized infections (5.1%), spread inflammations (4.7%) and previous surgeries (4.0%). In 1.6% of all specimens, the reason for the inflammation remains unclear. The described classification of hypophysitis is important for specific treatment planning after surgery [2)].

Searching the data bank of the German Pituitary Tumor Registry 12 double pituitary neuroendocrine tumors with diverse lineage were identified among 3654 adenomas and 6 hypophyseal carcinomas diagnosed between 2012 and 2020. The double adenomas were investigated immunohistochemically for the expression of hormones and lineage markers. In addition, chromosomal gains and losses as well as global DNA methylation profiles were assessed, whenever sufficient material was available (n = 8 PA).

In accordance with the literature, combinations of GH/prolactin/TSH-FSH/LH adenoma (4/12), GH/prolactin/TSH-ACTH adenoma (3/12), and ACTH-FSH/LH adenoma (3/12) were observed. Further, two out of 12 cases showed a combination of a GH/prolactin/TSH adenoma with a null-cell adenoma. Different expression patterns of hormones were confirmed by different expression of transcription factors in 11/12 patients. Finally, multiple lesions that were molecularly analyzed in 4 patients displayed distinct copy number changes and global methylation patterns.

The data confirm and extend the knowledge on multiple PAs and suggest that such lesions may originate from distinct cell types [3)].

Between 1996 and 2020, 12,565 cases were enrolled in the German Registry of Pituitary Tumors including 10,084 PitNETs (10,067 adenomas and 19 carcinomas obtained surgically and 193 adenomas diagnosed at autopsy) as well as 69 spindle cell tumors of the neurohypophysis (64 surgical specimens and 5 autopsies). In six patients (1 post-mortem and 5 surgical specimens), PitNETs, as well as posterior lobe tumors, were found in the specimens. Two of the PitNETs were sparsely granulated prolactin-producing tumors, combined in one case with a granular cell tumor and in one case with a pituicytoma. One of the PitNETs revealed that the autopsy was a sparsely granulated GH tumor combined with a neurohypophyseal granular cell tumor. Two PitNETs were null cell adenomas combined with a pituicytoma and a spindle cell oncocytoma, respectively. Further, one Crooke cell tumor was combined with a spindle cell oncocytoma. In five cases, the PitNETs were larger than the posterior lobe tumors and accounted for the clinical symptoms. Previously, four cases of co-existing pituitary anterior and posterior lobe tumors were described in the literature, comprising two ACTH PitNETs, one gonadotrophic PitNET and one null cell PitNET, each in combination with a pituicytoma. PitNETs and concomitant granular cell tumor or spindle cell oncocytoma, as observed in our cohort, have not been reported before [4)].

The first 10 years of this registry based on 4122 cases were reported by Saeger et al. The data supplement former collections of the years 1970-1995 with 3480 surgically removed tumors or lesions of the pituitary region. The cases were studied using histology, immunostainings, and in some cases also molecular pathology or electron microscopy. The adenomas were classified according to the current World Health Organization classification in the version of 2004. From 1996 on 3489 adenomas (84.6%), 5 pituitary carcinomas (0.12%), 133 craniopharyngiomas (3.2%), 39 meningiomas (0.94%), 25 metastases (0.6%), 22 chordomas (0.5%), 115 cystic non-neoplastic lesions (2.8%), and 46 inflammatory lesions (1.1%, 248 other lesions or normal tissue (6.0%)) were collected by us. The adenomas (100%) were classified into densely granulated GH cell adenomas (9.2%), sparsely granulated GH cell adenomas (6.3%), sparsely granulated prolactin (PRL) cell adenomas (8.9%), densely granulated PRL cell adenomas (0.3%), mixed GH/PRL cell adenomas (5.2%), mammosomatotropic adenomas (1.1%), acidophilic stem cell adenomas (0.2%), densely granulated

ACTH cell adenomas (7.2%), sparsely granulated ACTH cell adenomas (7.9%), Crooke cell adenomas (0.03%), TSH cell adenomas (1.5%), FSH/LH cell adenomas (24.8%), null cell adenomas (19.3%), null cell adenoma, oncocytic variant (5.8%), and plurihormonal adenomas (1.3%). Following the WHO classification of 2004, the new entity 'atypical adenoma' was found in 12 cases in 2005. Various prognostic parameters and clinical implications are discussed [5)]

1)
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