Paragangliomas: A Four-Decade Experience in a Academic Center

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Objective: Latin American reports on pheochromocytomas and paragangliomas (PPGL) are scarce. Recent studies have shown changes in both clinical presentation and management of these patients. We aimed to assess the main characteristics of PPGL patients in a single academic center over the last four decades. Experimental design: Cohort study. Patients and methods: Demographic, clinical, biochemical, genetic and perioperative data from 105 PPGL patients were retrospectively and prospectively collected over the 1980–2019 period. Patients were categorized into four groups (14 patients in the 1st, 25 patients in the 2nd, 27 patients in the 3th and 39 patients in the 4th decade) according to the date of diagnosis. **Results:** The mean age at diagnosis was 46±19 years, and the tumor size was 5.3±2.2 cm, female gender was 63%, bilateral tumor of 15%, paragangliomas 9% and metastatic disease in 15%. The aforementioned parameters remained stable across the four decades. During the study period we observed significant increases in doxazosin dosing (2.7±2.6 mg vs. 8.0±4.5 p<0.003) and laparoscopic procedures (28% vs. 84% p<0.001) along with a decrease in the length of hospital stay (10.0±8.9 vs. 3.8±1.7 days p=0.007). Among the 24 genetic tests performed, we identified 59% germline mutations. The most frequent mutations were RET (18%) and SDHX (18%), followed by VHL (14%), MAX (5%) and NF1 (4%). Notably, in the last decade we observed a dramatic increase in the proportion of incidental PPGL diagnosis (0% vs. 53% p<0.001) and genetic testing analyses (0 vs. 19 p<0.001). When comparing incidental diagnosis (n=25) versus clinically suspicious cases(n=50), incidentalomas had fewer adrenergic symptoms (38 vs. 62%; p<0.001), and lower rates of hypertension (64 vs. 80%; p=0.01), hypertension crises (28 vs. 44%; p=0.02), functionality (79 vs. 100%; p=0.01) and total catecholamines and/or metanephrine levels (8.4 vs. 12.5 fold above the upper normal limit; p=0.04). **Conclusions:** The implementation of a multidisciplinary program increased diagnosis and genetic testing and also optimized anesthesia and surgical procedure, translating into a notorious improvement in perioperative outcomes. In addition, we observed a change in the clinical presentation of PPGL in recent decades with a
marked increase in incidental cases, which highlights the importance of early diagnosis and treatment.

Adrenal

ADRENAL – CLINICAL RESEARCH STUDIES

Clinical and Pathological Features of Metastatic Adrenocortical Carcinoma

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Introduction: Adrenocortical carcinoma (AAC) is a rare and aggressive disease, associated with a poor prognosis. Surgery with complete resection (R0) remains the only curative treatment. However, even after complete resection, most patients present with distant metastatic disease. The aim of this study is to determine clinical and pathological features of metastatic disease in AAC. **Materials and methods:** Retrospective cohort study in 34 patients with AAC followed in our centre since 1991 until 2019. Selected patients with metastatic disease (n=21) and without metastatic disease (=13). Descriptive and comparative data analyses. Statistics: SPSS®v.23, with the variables: age, sex, clinical signs and symptoms, hormonal activity, imaging and pathological characteristics, surgical procedure, postoperative adjuvant treatments and overall survival. **Results:** 27 (79%) female and 7 (21%) male patients were included in our study, with a median age of 50 ± 13 years at the time of diagnosis. 21 patients (61,2%) presented with metastatic disease (38% of witch at the time of diagnosis) representing the metastatic disease group. 13 (38,8%) patients had no metastases until the collected data (group without metastatic disease). In the comparative analyses between the two groups, patients with metastatic disease had significantly more laparotomy procedures (71,2% n=15 *vs* 15,4% n=2; p<0,05), bigger tumours (≥ 12cm) (52,4% n=11 *vs* 23% n=3; p<0,05) and higher Ki67 (34,18% *vs* 1%, p<0,05). Postoperatively, the metastatic group had higher LDH (LDH at 6 months) (582 ± 502 *vs* 181 ± 47; p<0,05) and lower overall survival (months) (22,9 ± 4,69 *vs* 237,16 ± 44,42; p<0,05). Patients with metastatic disease had more constitutional symptoms (weight loss and asthenia) (33,3% n = 7 *vs* 15,4% n = 2; p = 0.092) and incomplete surgical recessions (R1/R2) (42,8% n = 9 *vs* 15,4% n = 2; p=0.18), however, without statistical significance. There were no differences regarding: age, sex, hormonal activity, imaging characteristics and post-surgical medical treatment. **Conclusion:** In this study, the adrenocortical carcinoma metastasis rate was 61,2% with an overall survival of 23 months in the metastatic group. Laparotomy surgeries, tumour size ≥12cm and higher KI67 are features significantly associated with metastatic disease in adrenocortical carcinoma. Constitutional symptoms and incomplete surgical recessions are more common in metastatic patients, however without statistical significance, in this cohort.