Abstract citation ID: bvac150.1008

Neuroendocrinology and Pituitary

ODP298

Are there identifiable differences in pituitary adenoma width, extension, invasion, or cystic degeneration in subclinical compared to clinical pituitary apoplexy patients?

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Background: Pituitary apoplexy [PA] is defined as an infarction, haemorrhage, or both within the pituitary gland, and can be life threatening. (Onesti 1990) Typically, it presents with sudden onset headache, visual changes, loss of consciousness and potentially life-threatening panhypopituitarism. If so, it is defined as a 'clinical' PA. In absence of these symptoms, it is defined as a 'subclinical' PA. (Kim 2009) Subclinical PA occurs more frequently than clinical PA. (Kim 2009; Möller-Goede 2011; Liu 2010; Cinar 2013) The rationale for this is still unclear. Tumour size, site of invasion, and cystic degeneration are all risk factors for apoplexy. (Biousse 2001;Boellis 2014)It is important to understand whether these factors differ between these groups to understand why subclinical apoplexy is more common, and to improve prevention and treatment. **Aim:** To identify whether underlying pituitary adenoma tumour size (width mm), site of invasion, or presence of cystic degeneration differed between clinical and subclinical populations with pituitary apoplexy (PA). Study design: This is a quantitative retrospective cohort study of patients attending Macquarie University Endocrinology Clinic and Macquarie Medical Imaging between 2011-2021. **Methods:** Clinical and subclinical patients were divided based on the acuity of their presentation (clinical = sudden onset headache, nausea, vomiting, visual changes, subclinical = gradual onset, or lack of symptoms). Adenomas > 10mm were classified as macroadenomas and <10mm were microadenomas. Age, gender, presence of suprasellar extension, intrasellar invasion, lateral invasion, and cystic change were identified from neurosurgeon and neuroradiologist cross-reporting on MRI. **Results:** 18 patients were

included in the study aged between 19 years to 85 years with 13 females and 5 males. 55.6% presented subclinical and 44.4% clinically. 15 (83%) had macroadenomas and 3 (16%) had microadenomas. There were no significant differences in age, gender, width of adenoma, site of invasion, or presence of cystic degeneration between the two cohorts. However, the data supported previous literature which suggests that clinical pituitary apoplexy patients tend to have marginally larger adenomas and are more commonly associated with cystic degeneration. **Conclusions:** Overall, this study highlights potential differences in tumour size and presence of cystic degeneration between subclinical and clinical apoplexy patients. However, further research is required with a larger cohort to determine the significance of these differences. The critical demarcation of the underlying pathology between patients experiencing subclinical versus clinical PA is not yet clear in the literature to date. When haemorrhage is secondary to an underlying lesion, regrowth of the pituitary tumour years after an episode may occur, and patients may require long-term clinical and imaging surveillance. Therefore, the importance of these research findings is that it may allow for increased predictability and prevention of pituitary apoplexy, which can be a life-threatening event.

Presentation: No date and time listed