Euroasia Journal of Mathematics, Engineering, Natural & Medical Sciences
International Indexed and Refereed
ISSN 2667-6702

Contiguous Double Pituitary Adenomas Secreting the Same Hormones

Aynı Hormonu Salgılayan Bitişik Çift Hipofiz Adenomları

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Geliş Tarihi / Received: 28.10.2022
Kabul Tarihi / Accepted: 20.12.2022
Araştırma Makalesi/Research Article
DOI: 10.5281/zenodo.7771205

ABSTRACT

The aim of this study is to investigate the importance of intraoperative observation in the diagnosis of the contiguous double pituitary adenomas secreting the same hormone which cannot be detected as double pituitary adenoma on (CE)-T1W1 magnetic resonance imaging. 400 patients with pituitary adenoma (PA) treated by transsphenoidal surgery (TSS) were investigated retrospectively. During the operation, we saw that the PA consisted of two pieces of two different colors and hardness. Biopsies were taken from these two different regions. Specimens were stained with hematoxylin and eosin staining (H&E). Each pathological section was subjected to immunohistochemical staining with an avidin biotin-peroxidase complex system. The intensity values of both contrast enhancing and non-enhancing region of the PA and normal pituitary were measured on preoperative CE-T1W1 magnetic resonance imaging (MRI). Their clinical data and MRI findings were analyzed. The CDPA secreting the same hormone was diagnosed in 6 patients. 4 (0,1%) patients had prolactinoma, 1 patient (0,25%) had CDPA secreting growth hormone, 1 patient (0,25%) had CDPA secreting ACTH. The prolactinomas were macroadenomas, the others were microadenomas. Immunohistochemical staining of pathological samples taken from two different regions with different morphological features of the PA revealed that these cells were mainly positive for the same hormones. The CDPA secreting the same hormone appeared as hypointense or hyperintences on (CE)-T1W1 MRI. The CDPA secreting the same hormone appeared as PA on (CE)-T1W1 MRI. The CDPA secreting the same hormones is difficult to diagnosis as DPA on CE-T1W1 MRI. Intraoperative detection of color and consistency changes in different parts of the PA is very important in the diagnosis of the CDPA the secreting same hormone.

Keywords: Double pituitary adenoma, transsphenoidal surgery, hormone, magnetic resonance imaging

ÖZET

Bu çalışmanın amacı (CE)-T1W1 magnetic resonance görüntüleme de çift hipofiz adenomu olarak tesbit edilemeyen aynı hormonu salgılayan bitişik çift hipofiz adenonomlarının teşhisinde ameliyat esnasındaki gözlemin önemine işaret etmektir. Transsefenoidal cerrahi ile tedavi edilen 400 hipofiz adenomlu hastalar bu çalışmaya dahil edildi ve sonuçlar geriye dönük olarak incelendi. Operasyon sırasında hipofiz adenomun iki ayrı renge ve sertliğe sahip olduğunu gördük. Biyopsiler bu iki kısımdan ayrı ayrı olarak alındı. Örnekler hematoxylin and eosin (H&E) ile boyandı. Herbir patolojik örnek immunohistokimyasal olarak boyandı. Hipofiz adenomunun contrast tutan ve tutmayan bölgelerinin intensite değerleri operasyon öncesi CE-T1W1 MRI de ölçüldü. Onların klinik bulguları ve MRI bulguları analiz edildi. Aynı hormonu salgılayan bitişik yapıdaki çift hipfiz adenomu 6 hastada teşhis edildi. 4 (0.1%) hastada prolaktinoma, 1 hastada (0.25%) büyüme hormone salgılayan bitişik çift hipofiz adenomu ve bir hastada (0.25%) ACTH salgılayan bitişik çift

hipofiz adenomu teşhis edildi. Prolaktinomalar makroadenomdu , diğerleri ise mikroadenomdu. Hipofiz adenomunun iki farklı bölgesinden alınan örneklerin patolojik immunohistokimyasal boyanması bu hücrelerin aynı hormona pozitif olduğunu ortaya çıkardı. Aynı hormone salgılayan bitişik çift hipofiz adenomları CE-T1W1 MRI de hipointens veya hiperintens olarak görüldü. Aynı hormone salgılayan bitişik çift hipofiz adenomlarını CE-T1W1 MRI de çift bitişik hipofiz adenomu olarak teşhis etmek güçtür. Hipofiz adenomunun farklı kısımlarındaki renk ve sertlik değişikliklerinin ameliyat esnasında tesbit edilmesi, aynı hormonu salgılayan bitişik çift hipofiz adenomlarının teşhisinde önemlidir.

Anahtar Kelimeler: Çift pituitary adenom, transsphenoidal cerrahi, hormon, magnetic resonance görüntüleme

INTRODUCTION

Double pituitary adenoma (DPA) are the adenomas with different types and localization which consist of secreting and/or non-secreting tumors and are a rare occurrence (Andrioli, 2010; Meij, 2000; Mendola, 2014; Ratliff, 2000; Rosai, 1993:2446-59; Sano, 1999).

PAs were classified according to size (micro, macro and giant) and type of hormones secreted. The pituitary gland releases prolactin (PRL), growth hormone (GH), follicle stimulating hormone (FSH)/luteinizan hormone (LH), adrenocortical hormone (ACTH) and thyroid stimulating hormone (TSH).15-30% of PAs are non-functioning pitutary adenoma (NSPA) (Chanson, 2015; Terano, 1993; Trouillas, 1995; (Sathyakumar, 2020).

The vast majority of the PAs are monoclonal tumors which have hormone immunoreactivity and ultrastructural features of known adenohypophysial cell types (Cochran, 2009; Rosai, 1993). Plurihormonal tumors produce two or more hormones which differ in immunoreactivity and biological effects (Rasul, 2014; Sano, 1999).

DPAs are the tumors with presence of two different celluler components of the same type of tumor at different locations in the sella (Kim, 2004; Mendola, 2014) and are rare in the surgical specimens showing two distinct components (Mehta, 2015; Meij, 2000; (Ratliff and Oldfield, 2000). The DPAs which recognized by pathologists were classified as clearly separated and contiguous (Andrioli, 2010; Steiner, 1992).

PAs have a nested architecture with large groups of cells surrounded by incomplete reticulin network. They may show papillary, diffuse, sinusoidal architecture (Cochran, 2009) and display two distinct morphological patterns of cytoplasmic hormone-containing secretory granules, namely the densely (DG) and sparsely granulated (SG) PA subtype (Buurman, 2006; Cochran, 2009; Larkin, 2013; Rosai, 1993), It is unknown whether these morphological variants reflect distinct pathophysiological entities at the molecular level. Adenomas secreting GH have DG and SG and both subtypes and are clinically active (Rosai, 1993: 2446-59). Macroprolactinomas usually have harbored densely-granulated cells, while microprolactinomas have sparsely-granulated cells (Rosai, 1993:2446-59). Prolactinomas show diffuse or trabecular growth patterns (Rosai, 1993:2446-2459). Gonadotroph adenomas usually manifest a sheet-like, solid arhitecture, but may have sinusoidal patterns secondary to diffuse fibrosis (Rosai, 1993:2446-2459). Adenomas secreting ACTH have a nested architecture with large groups of cells surrounded by incomplete reticulin network and show sinusoidal and diffuse pattern. Adenomas secreting TSH usually have large infiltrative masses with fibrosis and atypia, and have solid and sinusoidal pattern (Rosai, 1993:2446-59). Most of the nonfunctioning adenomas have solid sheets and sinusoidal or pseudopapillae pattern (Cochran, 2009:1028-30).

MATERIAL AND METHODS

400 patients with PA operated by TSS were investigated retrospectively. All patients had no presence of underlying genetic syndromes which may be associated with a higher chance of double or multiple pituitary adenomas (Luk, 2010) and collision sellar lesions.

The intensity values of both contrast enhancing and non enchanging region of the PA and normal pituitary were measured on CE-T1W1 MRI.

During the operation, we observed that the PA consisted of two pieces of two different colors and hardness. One of these two regions was yellow-white in color and of medium hardness, and the other was gray-purple in color and soft in consistency. Biopsies were taken from these two different regions. Specimens were stained with hematoxylin and eosin staining (H&E) and were examined under an optical microscope. Subsequently, each pathological section was subjected to immunohistochemical staining with an avidin biotin-peroxidase complex system.

The PAs were classified according to granulation pattern (sparsely and densely), consistency (soft and moderate hard) and nested architecture with large groups of cells surrounded by incomplete reticulin network (papillary, diffuse, sinusoidal).

STATISTICAL ANALYSIS

One-way analysis of variance and Tukey-HSD tests were used for evaluation of intensity values. A value of $p < 0.05$ was considered as significant.

RESULTS

The CDPA secreting the same hormone was diagnosed in 6 patients. 4 patients (%75) were female and 2 patients (%25) were male. The age of patients was between 18 and 61 years old (mean, 50 ± 20 years).

4 patients with the CDPA secreting the same hormone (0,1%) had prolactinoma, 1 patient(0,25%) had the CDPA secreting growth hormone. 1 patient (0,25%) had the CDPA secreting ACTH. Prolactinomas were macroadenomas, the others were microadenomas.

Immunohistochemical staining of the six CDPA revealed that the cells were mainly positive for the same hormones.

The CDPA secreting the same hormone were seen as hypointence or hyperintence on (CE)-T1W1 MRI, but sometimes hypointence and hyperintence areas were seen together.

The prevalence of the CDPA secreting the same hormone in this study was 1.5%.

The part of PA which has gray-purple in color and has soft consistency appeared as hypointense and hyperintense on CE-W1 T1 MRI (Figure 1). The part of PA which has gray-purple in color and has soft consistency appeared as hypointense and hyperintense on CE-W1 T1 MRI (Figure 2).

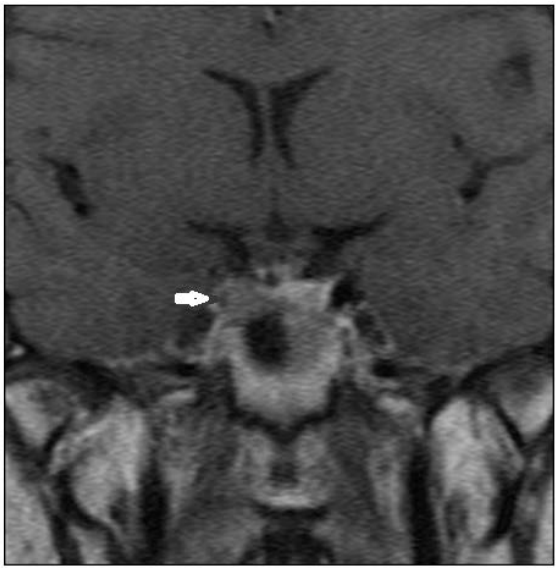

Figure 1. PA showing hypointense area on coronal CE-T1W1 MRI (white arrow)

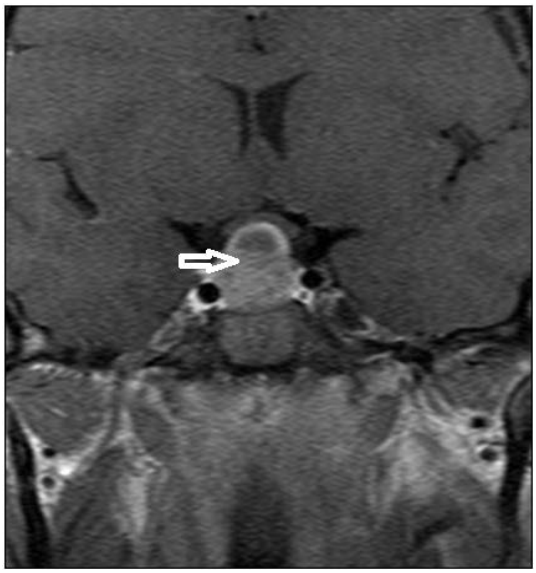

Figure 2. PA showing as hyperintense area with hypointense area on coronal CE-T1W1 MRI (white arrow)

The part of PA which has white-yellow in color and has moderate hard consistency appeared as hyperintense and hypointense on CE-W1 T1 MRI (Figure 3). Prolactinomas had densely and sparsely pattern or granulation pattern (Figure 4 A-B).

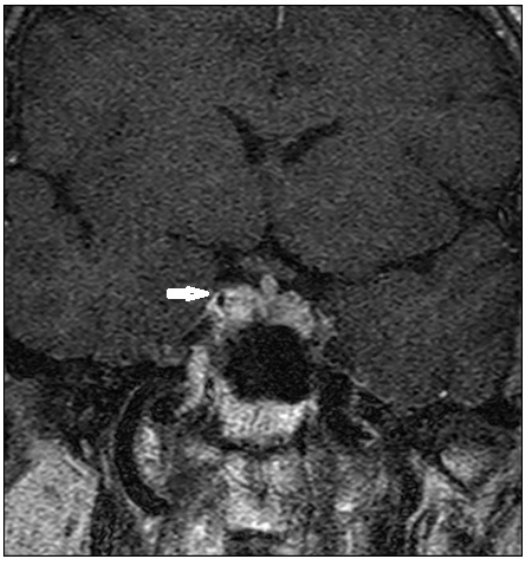

Figure 3. PA showing as hyperintense area coronal CE-T1W1 MRI (white arrow)

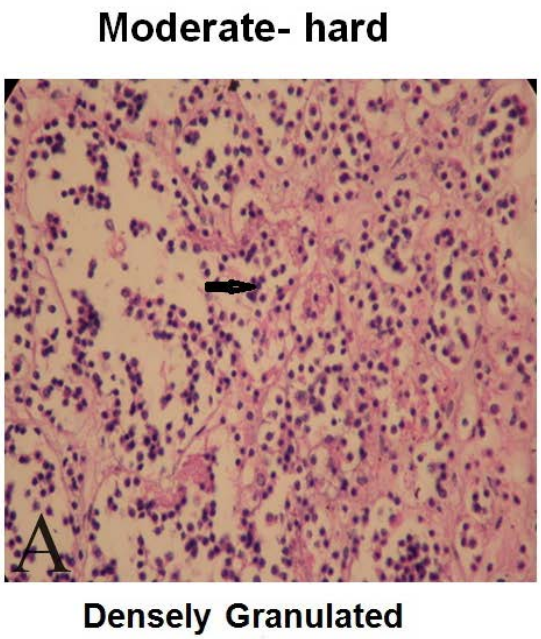

Figure 4A: PA which has moderate hard consistency showing densely granulated pattern (H&E stained; Magnification X40). Densely granulated adenomas consist of monomorphic cells that are eosinophilic on H&E stain (black arrow).

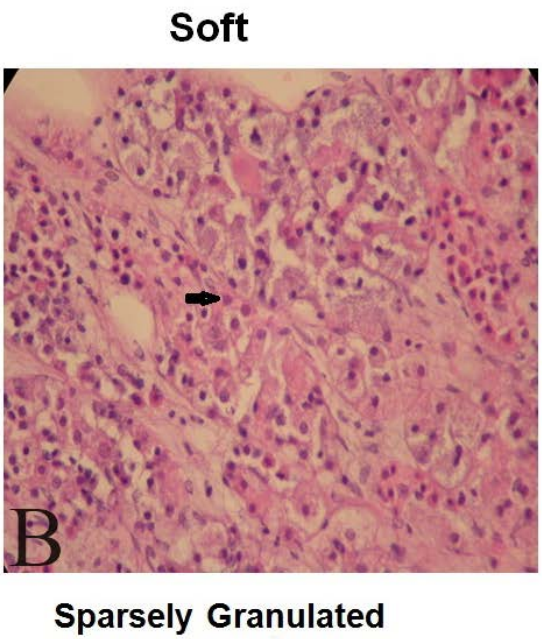

Figure 4B: PA which has soft consistency showing sparsely granulated pattern (H&E stained; Magnification X40). Sparsely granulated adenomas consist of monomorphic cells that are eosinophilic on H&E stain (black arrow)

The CDPA secreting ACTH had a nested architecture with large groups of cells surrounded by incomplete reticulin network and showed diffuse pattern and sinusoidal pattern (Figure 5A-B).

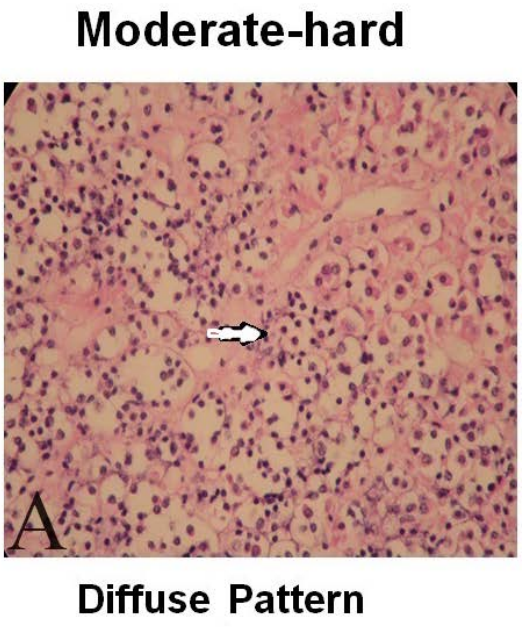

Figure 5A. PA which has moderate hard consistency showing diffuse pattern (H&E stained; Magnification X40). The pituitary tumour exhibits diffuse strong positivity. Pituitary adenoma is characterized by a monomorphic expansion of usually one cell type with lack of reticulin network among neoplastic cells. The growth pattern is diffuse (white arrow).

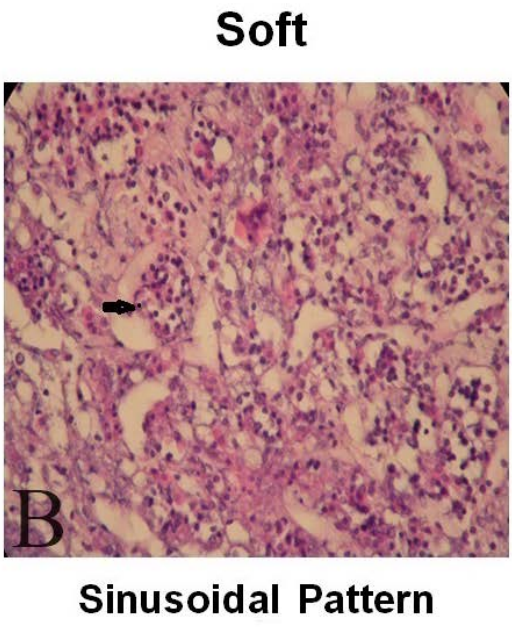

Figure 5B. PA which has soft consistency showing sinusoidal pattern (H&E stained; Magnification X40). Pituitary adenoma is characterized by a monomorphic expansion of usually one cell type with lack of reticulin network among neoplastic cells. The growth pattern is sinusoidal (black arrow)

The CDPA secreting the growth hormone had diffuse pattern and papillary pattern (Figure 6A-B).

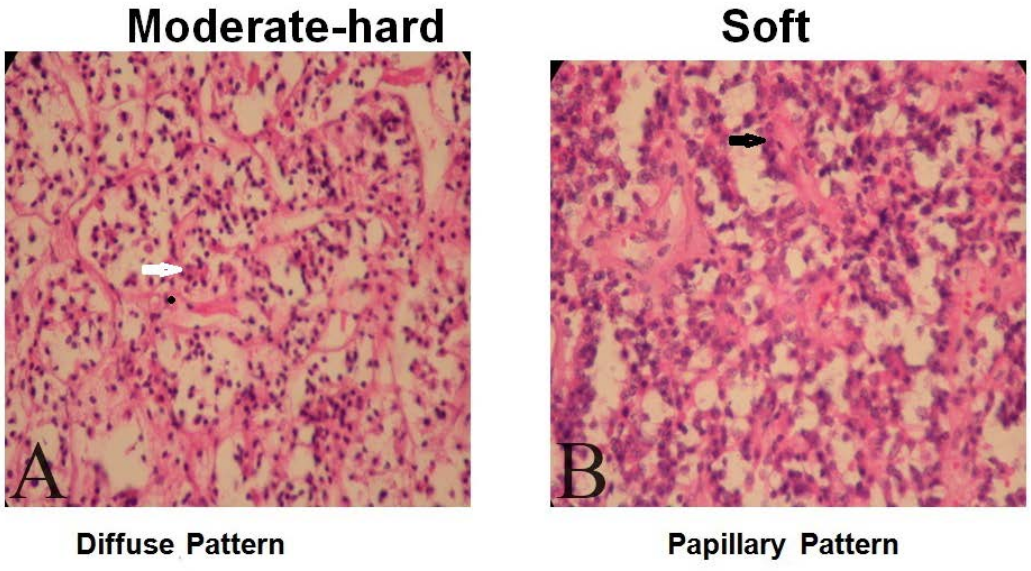

Figure 6A. PA which has moderate hard consistency showing diffuse pattern (H&E stained; Magnification X40). Pituitary adenoma is characterized by a monomorphic expansion of usually one cell type with lack of reticulin network among neoplastic cells. The growth pattern is diffuse (white arrow)

Figure 6B. PA which has soft consistency showing papillary pattern (H&E stained; Magnification X40). Pituitary adenoma is characterized by a monomorphic expansion of usually one cell type with lack of reticulin network among neoplastic cells. The growth pattern is papillary (black arrow).

The average tissue intensity levels of the the 400 patients on CE T1-W1 MRI and standart deviations are shown in Figure 7.

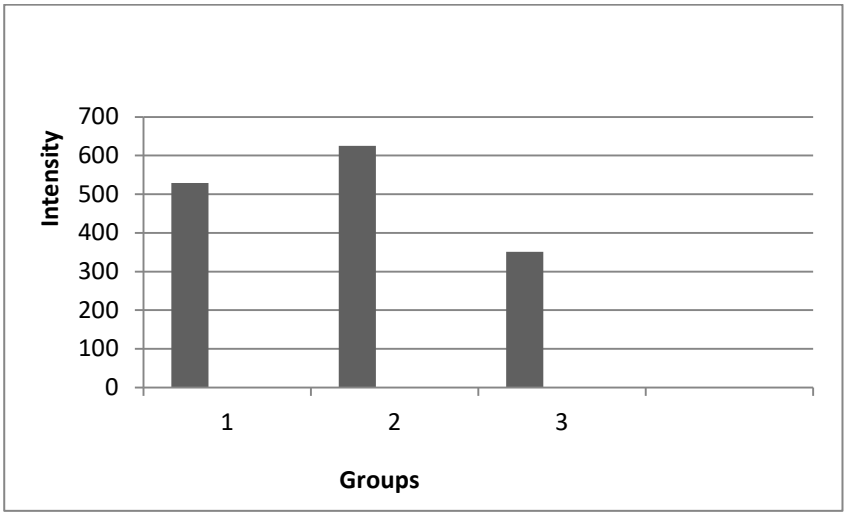

Figure 7. Tissue intensity levels of groups: Group1: normal pituitary glands, Group 2: hiperintensity areas of the PA, Group 3: hipointensity areas of the PA. Each column and vertical bar represent the mean±SD of PA. *p <0,05 is significant.

The ± intensity levels as mean ± SD of each group are as follows: group 1 (normal pituitary gland) --529±24.5; group 2 (hyperintensity) --625±28.2; group 3 (hypointensity)--351±21.8. There were significant differences (p <0.05) between all groups.

DISCUSSION

Although the clearly separated DPA can be diagnosed on CE-T1W1 MRI, the CDPA secreting the same hormone may not be diagnosed as DPA on CE-T1W1 MRI. Intraoperative detection of color and consistency changes in different parts of the PA is very important in the diagnosis of the CDPA secreting the same hormone.

MRI studies of pituitary have generally been obtained with either signal-limited rapid T1 techniques or unique sequences (Famini, 2011; Ouyang, 2011; Rennert, 2007). Dynamic MRI of pituitary is considered to improve detection of minute pituitary adenoma (Tabarin, 1998), but Tabarin et al. reported no significant differences between diagnostic accuracy of standard and dynamic MRI techniques (Tabarin, 1998). PAs generally have lower contrast enhancement on CE-dynamic T1 W1 imaging than normal pitutary gland but have low and high contrast enhancement on T2 scans (Ouyang, 2011).

Kontogeorgeos et al.reported in their autopsy series that the prevalence of MPA was 8.9% (Kontogeorgos, 1991; Kontogeorgos, 1991). Buurman et al reported in their autopsy series that the prevalence of the MPA was 6%.). Some authors reported that the prevalence rate of the DPA treated surgically was 0.2–1.8% (Karavitaki, 2012;Kontogeorgos, 1992; Rasul, 2014; Ratliff, 2000).

The prevalence of the CDPA secreting the same hormon in this study was 1,5%. Kontogeorgos reported that the prevalence of the DPA in their cases was 0.37–1.64% (Kontogeorgos, 1991; Kontogeorgos, 1992). Larkin et al. reported that the prevalence of DPA in their cases was 0,36% (Larkin S, 2013). But some authors reported that the prevalence of the DPA secreting different hormones was 2.6% (Iacovazzo, 2013; Luk, 2010; Magri, 2014).

The prevalence of the CDPA secreting ACTH in this study was 0,25%. Some authors reported that the DPA secreting ACTH were rare (Andrioli, 2010; Meij, 2000; Mendola, 2014).

The DPA secreting growth hormone are rare. The prevalence of the CDPA secreting growth hormon in this study was 0,25%.

The DPA may appear as hyperintense and hypointense on CE-T1W1 MRI (Magri, 2014) but hypo and hyperintense areas may be seen together (Mehta, 2015).

Isolated separated DPAs are usually easy to diagnose on CE-T1W1 MRI (Larkin, 2013; Mehta, 2015; Meij, 2000; Mendola, 2014; Ratliff, 2000; Rosai, 1993; Sano, 1999), but the CDPA secreting the same hormone can be difficult to diagnose on on CE-T1W1 MRI.

Thodou et al. reported that the recurrence of PA may also represent a metachronous development of two distinct pituitary adenomas (Thodou, 1995).

Some authors reported that there was a histological pseudocapsule around pituitary tumors (Monteith, 2012; Oldfield and Vortmeyer, 2006). Recognition of this surgical capsule contributes to the identification of microadenomas buried in the pituitary gland (Monteith, 2012; Oldfield, 2006). Residual tumors had nodular and combined enhancement on early postoperative dynamic MRI (Rosai, 1993:2446-59; Steiner, 1992). Residual tumors may be a part of the CDPA which overlooked during the TSS.

The diagnosed of the CDPA was decided based on intraoperative observation and pathology results. The incidence rate of the DPA in surgical series is lower than autopsy series. Advances in MRI technology will facilitate the diagnosis of the CDPA secreting the same hormone.

CONCLUSSION

The CDPA secreting the same hormones is difficult to diagnosis as DPA on CE-T1W1 MRI. Intraoperative detection of color and consistency changes in different parts of the PA is very important in the diagnosis of the CDPA the secreting same hormone.

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