·临床病理报告·

少见的IgG4相关性垂体炎

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【摘要】 **研究背景** IgG4相关性疾病为新近定义的自身免疫性疾病类型，主要临床特征为多器官受累和血清IgG4水平升高。可发生于垂体，且部分患者表现为孤立性鞍区肿物和(或)垂体柄增粗，由于缺乏特征性影像学表现，若无血清IgG4水平异常之证据，术前明确诊断困难且易误诊为垂体腺瘤。**方法与结果** 男性患者，47岁，临床主要表现为四肢乏力、性功能减退；血清睾酮、皮质醇、卵泡刺激素和黄体生成素均低于正常值范围。头部MRI显示鞍内、鞍上巨大肿物，增强后病灶均匀强化。临床拟诊为垂体腺瘤，手术大部分切除。光学显微镜观察肿物主要为腺垂体，腺泡萎缩、数目减少，间质内可见大量淋巴浆细胞浸润，伴广泛性纤维组织增生、玻璃样变，未见明确的垂体腺瘤结构；边缘可见多灶性合体样细胞巢团，但胞核异型性不明显。免疫组织化学染色，淋巴浆细胞并非肿瘤性单克隆性增生，但IgG4阳性浆细胞数目＞30个/高倍视野且$IgG4^+/IgG^+$＞40%。合体样细胞巢团波形蛋白、上皮膜抗原和孕激素受体表达阳性；血清IgG4为2.93 g/L。明确诊断为IgG4相关性垂体炎伴鞍区脑膜反应。术后予泼尼松35 mg/d持续治疗2周，减至30 mg/d维持治疗，临床症状明显改善，血清IgG4降至正常水平，鞍区肿物体积明显缩小。**结论** IgG4相关性垂体炎缺乏特征性影像学表现，其组织学与非特异性炎症性病变相似，术前明确诊断和鉴别诊断困难。血清IgG4水平升高是明确诊断的重要线索和依据。

【关键词】 免疫球蛋白G； 垂体； 自身免疫疾病； 病理学； 免疫组织化学

Unusual IgG4 - related hypophysitis: one case report and analysis of clinicopathological characteristics

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【**Abstract**】 **Background** Immunoglobulin G4 (IgG4) - related disease is a recently characterized autoimmune disease entity marked by elevated serum IgG4 levels and tissue infiltration by IgG4 - positive plasma cells in multiple involved organs. Hypophysitis is a rare inflammatory disorder and IgG4 - related sclerosing disease involving the pituitary alone is especially rare. Imaging studies may reveal a mass lesion in the sellar area or a thickening of pituitary stalk, mimicking a pituitary tumor. Due to its rarity and non-specific appearance in radiological examination, it is a diagnostic challenge for clinicians and histopathologists to differentiate solitary IgG4-related hypophysitis from other pituitary lesions. The aim of this study is to summarize the clinicopathological features of unusual IgG4-related hypophysitis and discuss the differential diagnosis of histologically similar inflammatory lesions in pituitary. **Methods** The clinical manifestation of a patient with solitary IgG4-related hypophysitis was presented retrospectively. Resected mass was routinely paraffin - embedded and stained with Hematoxylin and Eosin. Dako EnVision immunohistochemical staining system was used to detect the tumor antigen expressions, including vimentin (Vim), S - 100 protein (S - 100), pan cytokeratin (PCK), epithelial membrane antigen (EMA), CD3, CD20, CD68, CD1a, κ-light chain, λ-light chain and progestrone receptor (PR). **Results** A 47-year-old male patient presented with 1-year history of mild limb weakness and hyposexuality. Laboratory examination revealed hypopituitarism with low levels of serum testosterone, cortisol, luteinizing hormone (LH) and follicle stimulating hormone (FSH), although his serum IgG4 level was high. MRI of the pituitary gland

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revealed a mass lesion in the sellar area with T_1WI mild hyperintense and homogeneous enhancement after gadolinium administration. The patient underwent a transsphenoidal mass resection of the pituitary gland. Histological examination showed bland appearing spindle cell proliferation in the sclerotic background with marked infiltration of lymphocytes, plasma cells, as well as multiple foci of meningothelial-like nodules at the periphery of tissues. Immunohistochemical staining showed that the lymphocytes were positive for CD3 and CD20. Plasma cells were distinct and the number of κ and λ-light chains was the same. There were more than 30 IgG4-positive plasma cells per high power field (HPF), which accounted for greater than 40% of the IgG-positive plasma cells. The meningothelial-like nodules were positive for Vim, EMA and PR, but negative for CD68, S-100 and CD1a. A final histological diagnosis of IgG4-related hypophysitis with meningothelial reaction was made. The patient took prednisolone orally at 35 mg/d for 2 weeks, and the symptoms of limb weakness and hyposexuality showed improvement. The mass lesion of pituitary gland demonstrated a reduction in size. The prednisolone therapy was continued at a dose of 30 mg/d to prevent recurrence of IgG4-related disease. **Conclusions** IgG4-related hypophysitis is a rare disease of central nervous system with good response to corticosteroid treatment. Due to the relative paucity of reported cases and similarities in histological findings, it may be difficult to differentiate IgG4-related disease from other pituitary lesions with prominent inflammatory cell infiltration and stromal fibrosis. Thorough inspection under the microscopy and more importantly elevated serum IgG4 level are necessary for correct diagnosis.

【Key words】 Immunoglobulin G; Pituitary gland; Autoimmune diseases; Pathology; Immunohistochemistry

IgG4相关性疾病(IgG4-RD)是新近定义的自身免疫性疾病类型,该名称最早于2001年由Hamano等[1]用于描述1例硬化性胰腺炎(SP)病例,该例患者因血清IgG4水平显著升高而备受关注。但随后的研究发现,此类患者胰腺以外的其他器官如胆管、涎腺、眼眶、淋巴结、后腹膜、纵隔、软组织及神经系统均存在相似的病变[2-3],且具有共同的组织学特点,即间质广泛纤维化、弥漫性淋巴浆细胞浸润伴闭塞性静脉炎,以及血清IgG4水平显著升高。因此,2010–2012年召开的一系列国际会议达成共识,接受这一新的疾病类型并正式确定其命名[4-6]。自2004年首例IgG4相关性垂体炎病例[7]报道以来,至今已相继报道约30例,目前国内尚无相关报道。现有的临床资料表明,IgG4相关性垂体炎主要表现为垂体功能减退和尿崩症,而影像学则显示为鞍区肿物或垂体柄增厚,易被误诊为垂体腺瘤;组织学检查可见大量淋巴浆细胞浸润,极易误诊为垂体非特异性炎症或鞍区富淋巴浆细胞型脑膜瘤。鉴于此类病变临床鲜见且诊断较为困难,我们报告的1例典型IgG4相关性垂体炎患者,由于其特殊的临床、影像和组织学表现,曾在术前、术中快速冰冻病理和术后组织病理检查中误诊为富淋巴浆细胞型脑膜瘤。本文回顾该例患者诊断与治疗经过,复习文献中IgG4相关性疾病之临床表现、影像学和组织学特点,对此类临床少见的垂体病变进行分析,以期提高对该病的诊断与鉴别诊断能力。

病历摘要

患者 男性,47岁。主因四肢乏力、性功能减退1年余,于2013年10月8日入院。患者1年前开始出现四肢乏力、性功能减退,未引起重视,此后临床症状与体征逐渐加重,于2013年9月末至我院就诊,头部MRI显示鞍区占位性病变,临床拟诊为垂体腺瘤。患者自发病以来,无发热、耳鸣、眩晕、记忆力减退和步态不稳等症状与体征。

既往史、个人史及家族史 全身状况尚佳,可正常工作、生活。否认肝炎、结核病等传染病史,否认手术史、外伤史、输血史,否认食物、药物过敏史,预防接种史不详。无疫区、疫水、特殊化学物品或放射线接触史。父母健康,无家族遗传性疾病病史,家族中无类似疾病。

体格检查 患者体温36.3 ℃,心率68次/min,呼吸15次/min,血压138/85 mm Hg(1 mm Hg = 0.133 kPa)。神志清楚,语言流利。全身皮肤和黏膜无紫绀、黄染,全身浅表淋巴结未触及、无肿大。自觉四肢乏力,但肢体无畸形,肌力、肌张力正常。双侧视野检查显示生理盲点扩大,颞侧视野光敏感度局部下降,双眼视力正常。神经系统检查第Ⅰ、Ⅱ、Ⅲ、Ⅴ、Ⅶ、Ⅷ、Ⅸ、Ⅺ和Ⅻ对脑神经未见阳性体征。无颈项强直,脑膜刺激征阴性,腱反射阳性,病理征未引出。

辅助检查 实验室检查:血常规、凝血功能试

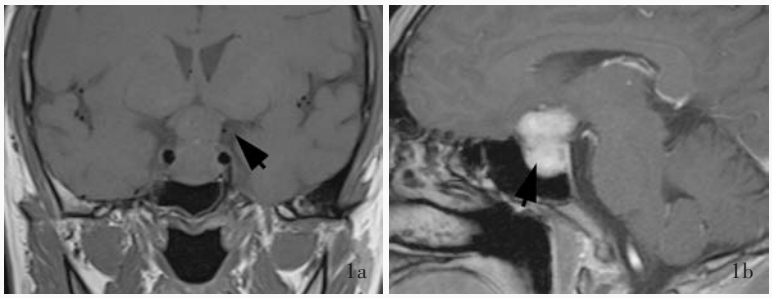

图1 术前头部MRI检查所见 1a 冠状位T_1WI显示鞍区和鞍上边界清楚的肿物呈稍高信号(箭头所示) 1b 矢状位增强T_1WI显示,病灶呈均匀强化(箭头所示)

Figure 1 Preoperative MRI findings. Coronal T_1WI demonstrated a well-circumscribed lesion located in the sellar and suprasellar area with slight hyperintensity (arrow indicates, Panel 1a). Sagittal enhanced T_1WI revealed that the lesion was homogeneous enhancement after gadolinium administration (arrow indicates, Panel 1b).

验、乙型肝炎五项和感染四项均呈阴性。血清肿瘤学标志物甲胎蛋白(AFP)、癌胚抗原(CEA)均于正常水平。血清睾酮0.10 ng/ml[(1.58~8.77) ng/ml]、皮质醇为9 μg/L[(29~194) μg/L]、卵泡刺激素(FSH)0.82 IU/L [(1~8) IU/L]、黄体生成素(LH)0.22 IU/L[(2~12) IU/L],游离T_4为8.67 pmol/L[(9.01~19.05) pmol/L]、T_4 51.77 nmol/L[(62.68~150.80) nmol/L];其他激素如生长激素(GH)、雌二醇、泌乳素(PRL)、孕酮等均正常。影像学检查:胸部X线检查未见异常,腹部和盆腔B超检查未见淋巴结肿大。头部MRI可见鞍内、鞍上巨大实性肿物,边界清楚,大小约为29 mm×20 mm,T_1WI呈等信号、T_2WI呈高信号,增强后病灶明显均匀强化;鞍底下塌,肿物从鞍内向鞍上生长、呈"束腰征",双侧海绵窦和颈内动脉受压移位,垂体柄稍左偏,脑实质和脑室形态正常(图1)。临床拟诊为垂体腺瘤。

诊断与治疗经过 入院后1周于气管插管全身麻醉下经鼻蝶入路行鞍区占位性病变切除术。术中可见肿物呈黄白色,质地中等,血供稍丰富,无明显包膜,遂行快速冰冻病理检查。光学显微镜下可见送检的小块组织为腺垂体,其内腺泡萎缩,间质内大量慢性炎性细胞浸润,以淋巴浆细胞为主,未见呈肿瘤性增生的垂体腺瘤结构(图2)。故考虑为淋巴细胞性垂体炎(LYH)可能。手术大部分切除肿物,行组织病理学检查。(1)大体标本观察:手术切除标本为不规则破碎组织块,约1.50 cm×1.00 cm×0.50 cm大小,呈灰红色、质地中等、无包膜。经体积分数为10%中性甲醛溶液固定、石蜡包埋,切片后行常规HE染色和免疫组织化学染色。(2)HE染色:光学显微镜观察,送检的组织标本主要为腺垂体成分,但腺泡明显萎缩,数目减少,间质弥漫性慢性炎性细胞浸润,以淋巴浆细胞为主,并可见散在分布的嗜酸性粒细胞,未见明显的淋巴滤泡形成。间质纤维组织增生并玻璃样变,形态温和的梭形细胞呈编织状排列,未见典型漩涡状结构(stroiform)。在增生的纤维组织和淋巴浆细胞边缘尚可见多灶性上皮样细胞巢团,呈合体细胞样,胞核形态温和、异型性不明显、未见核分裂象(图3a~3c)。间质中无血管内皮细胞肾小球样增生,未见出血坏死灶。(3)免疫组织化学染色:采用EnVision二步法检测试剂盒(丹麦Dako公司)进行免疫组织化学染色。检测抗体为腺垂体激素(生长激素、泌乳素、促甲状腺素、促肾上腺皮质激素、卵泡刺激素和黄体生成素)、波形蛋白(Vim)、广谱细胞角蛋白(PCK)、上皮膜抗原(EMA)、CD3、CD20、CD1a、CD68、免疫球蛋白κ(Igκ)和免疫球蛋白λ(Igλ)、S-100蛋白(S-100)、孕激素受体(PR),分别购自美国Santa Cruz公司和丹麦Dako公司。结果显示,萎缩的腺垂体腺泡不同程度地表达腺垂体激素;在组织中浸润的淋巴细胞CD3和CD20呈不同程度阳性,不支持肿瘤性单克隆性增生;浆细胞表达Igκ和Igλ,且无明显差异,不支持浆细胞性肿瘤;送检组织内S-100蛋白和CD1α表达阴性,不支持朗格汉斯细胞组织细胞增生症(LCH)和Rosai-Dorfman病(RDD);多灶性合体细胞巢团Vim、EMA、PR表达阳性(图3d~3f),其他检测指标均呈阴性,提示该细胞团巢为脑膜上皮细胞。根据脑膜上皮细胞增生和广泛性淋巴浆细胞浸润之特点,组织病理学诊断为:(鞍区)富淋巴浆细胞型脑膜瘤(WHO Ⅰ级)。

术后患者一般情况稳定,实验室相关激素检查:血清睾酮0.15 ng/ml、皮质醇8 μg/L、卵泡刺激素0.97 IU/L、黄体生成素0.21 IU/L。临床考虑为全垂体功能减退症,予以泼尼松20 mg(1次/d),以及左甲状素钠片75 μg(1次/d)和十一酸睾酮胶丸80 mg(2次/d)替代治疗。术后1月余复查,主诉多尿(4~5 L/d)伴右眼视物模糊。头部MRI可见鞍内、鞍上肿物,边界清楚,大小约为21 mm×22 mm×22 mm,T_1WI呈等至低信号、T_2WI呈稍高信号;增强后病灶

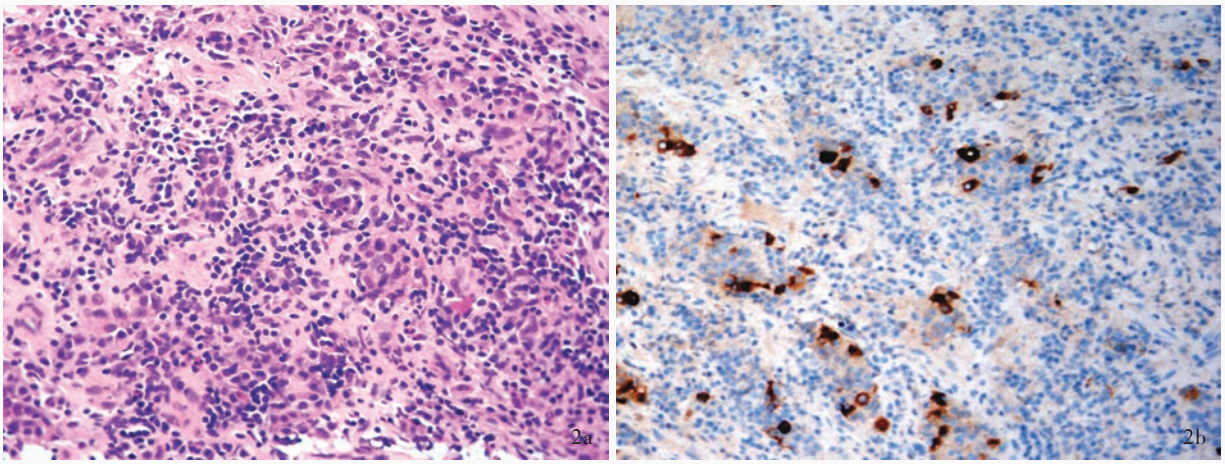

图2 术中快速冰冻病理检查所见 ×200 2a 萎缩的腺垂体腺泡和间质内大量淋巴浆细胞浸润 HE染色 2b 腺垂体腺泡表达GH 免疫组织化学染色(EnVision二步法)

Figure 2 Intraoperative histopathological findings. ×200 Under the microscopy, there were numerous infiltration of lymphocytes and plasma cells in the stroma of adenohypophysis with atrophic pituitary acini (Panel 2a). HE staining The atrophic pituitary acini demonstrated immuno-positive for GH (Panel 2b). Immunohistochemical staining (EnVision)

明显强化,视交叉受压上移(图4a)。根据患者临床和影像学表现,考虑为脑膜瘤复发,要求复查术后组织学切片,发现病变组织中有较丰富的浆细胞,补充行免疫组织化学IgG和IgG4染色,同时建议临床行血清免疫球蛋白检测。结果显示,血清IgG4 2.93 g/L(< 2 g/L)、IgA 2.09 g/L[(1.45 ~ 3.45) g/L]、IgM 1.86 g/L[(0.92 ~ 2.04) g/L]、IgG 14.90 g/L[(10.13 ~ 15.13) g/L]。免疫组织化学染色,IgG4阳性细胞数目 > 30个/高倍视野(× 400)、$IgG4^+/IgG^+$ > 40%(图4b)。根据上述结果,最终修正组织病理学诊断为:IgG4相关性垂体炎伴鞍区脑膜反应。

明确诊断后予泼尼松35 mg(1次/d)口服治疗,2周后患者视力基本恢复,多尿症状减轻,遂减少泼尼松剂量至20 mg(1次/d),治疗2周后再次出现右眼视物模糊,尤以休息不充分时明显,又增加泼尼松剂量并持续维持于30 mg(1次/d)。目前患者性功能正常,四肢乏力症状消失,视力模糊和多尿症状明显改善。术后6个月,复查血清IgG4 2.02 g/L,接近正常值范围。2014年4月复查MRI显示鞍区肿物体积明显缩小。目前仍予泼尼松30 mg(1次/d)口服维持治疗,并持续随访。

讨 论

尽管,IgG4相关性疾病是新近定义的自身免疫性疾病类型,但其历史可追溯至20世纪60年代。1961年,Sarles等[8]首次提出自身免疫反应导致的慢性胰腺炎;1995年,日本学者Yoshida等[9]将一类具有胰腺导管狭窄、无痛性阻塞性黄疸和对激素治疗反应敏感的胰腺病变命名为自身免疫性胰腺炎(AIP);2001年,Hamano等[1]首次发现部分硬化性胰腺炎(sclerosing pancreatitis)患者血清IgG4水平显著升高、组织中IgG4阳性浆细胞数目明显增多,遂将此类自身免疫性胰腺炎之亚型称为IgG4相关性硬化性胰腺炎(IgG4 - related sclerosing pancreatitis)。然而,随着此后其他器官和系统的类似病变相继报道,IgG4相关性疾病方被正式提出并确定为新的疾病类型[4-6]。根据多次国际会议所达成的共识,IgG4相关性疾病具备下述临床和组织学表现:(1)临床可观察到肿物形成。(2)病变组织内存在广泛性淋巴浆细胞浸润、纤维化和闭塞性静脉炎形成。(3)血清IgG4水平升高(> 1.35 g/L)且组织内IgG4阳性浆细胞数目增加。并根据具体情况分为确诊(definite)、疑似(probable)、可能(possible)和排除(denial)等不同诊断层次[5]。

累及中枢神经系统的IgG4相关性疾病较为少见,但文献报道的病例多集中发生于垂体。迄今仅约30例IgG4相关性垂体炎见诸文献报道[10]。其中多数为男性且年龄较大(平均64.70岁),常见症状为垂体功能减退和尿崩症,但也有个别患者完全缺乏垂体功能减退的表现[11];均有血清IgG4水平升高和垂体肿物的特点,大多数患者可伴多器官受累(多伴胰腺病变),或伴脑膜炎、副鼻窦炎症状[10,12]。

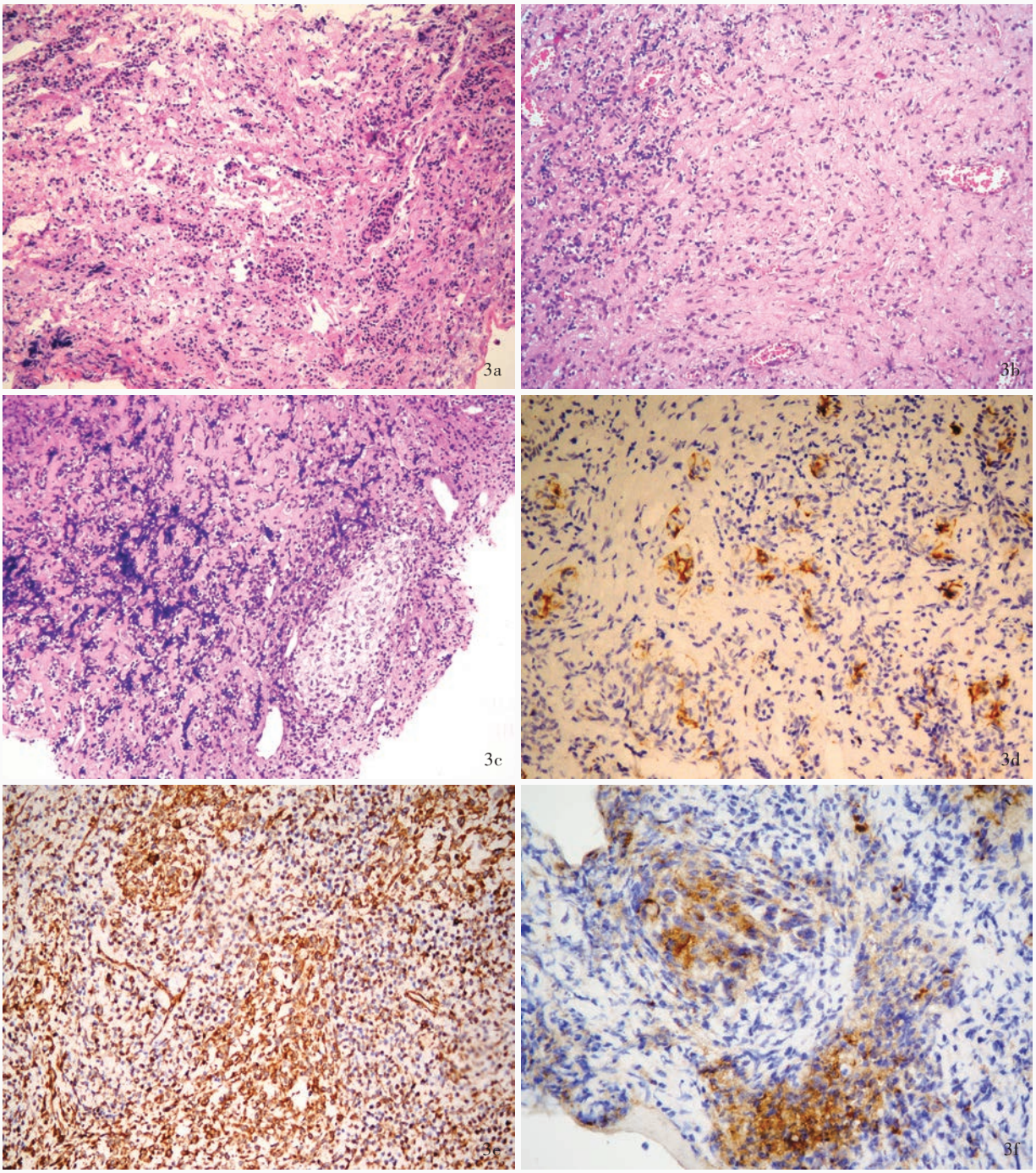

图3 术后组织病理学检查光学显微镜观察所见 ×200 3a 腺垂体腺泡萎缩、数目减少，并有大量淋巴浆细胞浸润 HE染色 3b 间质内广泛性纤维组织增生和玻璃样变 HE染色 3c 增生纤维组织内可见多灶性上皮样合体细胞巢团，胞核无明显异型性 HE染色 3d 残留的腺垂体腺泡表达PRL 免疫组织化学染色（EnVision二步法） 3e 上皮样合体细胞巢团表达Vim 免疫组织化学染色（EnVision二步法） 3f 上皮样合体细胞巢团表达EMA 免疫组织化学染色（EnVision二步法）

Figure 3 Postoperative optical microsopy findings. × 200 There were numerous infiltration of lymphocytes and plasma cells in adenohypophysis. The pituitary acini were obsereved to be atrophic and decreased in quantity (Panel 3a). HE staining There was dense fibrous changes demonstrated in the lesion (Panel 3b). HE staining Multiple foci of epithelioid syncytial cell nodules could be found at the periphery of lesion, which were resemble to meningothelial nodules (Panel 3c). HE staining The residual atrophic pituitary acini were positive for PRL (Panel 3d). Immunohistochemical staining (EnVision) The epithelioid syncytial cells were positive for Vim (Panel 3e) and EMA (Panel 3f). Immunohistochemical staining (EnVision)

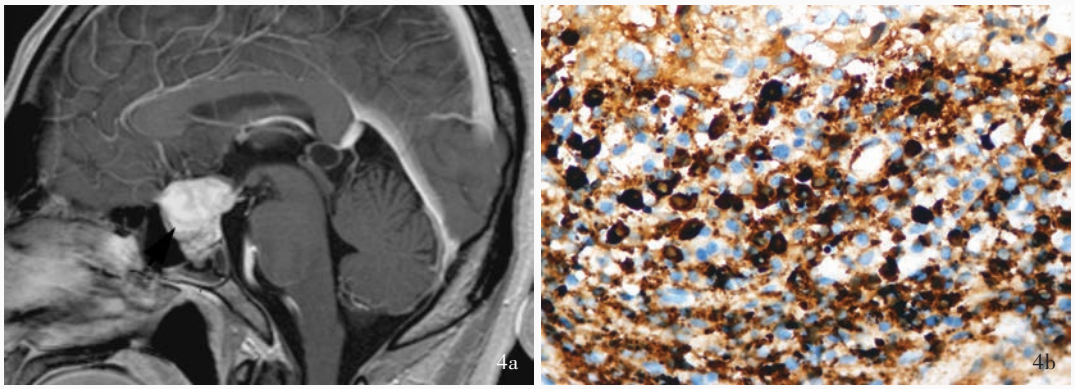

图4 术后1个月复查MRI和补充组织病理学检查所见 4a 矢状位增强T_1WI显示，鞍区、鞍上病灶呈均匀强化，体积无明显缩小（箭头所示） 4b 光学显微镜观察显示，垂体病灶IgG4阳性细胞数目＞30个/高倍视野 免疫组织化学染色（EnVision二步法） ×400

Figure 4 MRI and pathological findings one month after surgery. Sagittal enhanced T_1WI revealed that the lesion located in sellar and suprasellar area was homogeneous enhancement, but the size of mass was not decreased obviously (arrow indicates, Panel 4a). Optical microscopy found plasma cells were stained positive by IgG4 immunostaining, and the number of IgG4-positive plasma cells was more than 30 per high power field (Panel 4b). Immunohistochemical staining (EnVision) ×400

由于此类病变临床十分少见，目前尚无明确的诊断标准。2011年，Leporati等[13]曾建议采用以下5项标准进行诊断：（1）垂体组织内可见大量淋巴浆细胞浸润，IgG4阳性细胞数目＞10个/高倍视野。（2）MRI显示鞍区肿物和（或）垂体柄增粗。（3）组织活检证实其他器官存在IgG4阳性病变。（4）血清IgG4水平升高（＞1.40 g/L）。（5）采用激素治疗后垂体肿物体积缩小，临床症状改善。Leporati等[13]认为，单独标准（1）或标准（2）+（3）或标准（2）+（4）+（5）均可作为IgG4相关性垂体炎的明确诊断依据，无需一定经组织病理学检查。在目前所报道的相关病例中，大多数是通过临床和影像学表现获得诊断，不足半数患者经组织病理学检查明确诊断[10]。对于垂体组织中IgG4阳性细胞数目的标准，目前尚存争议。Cheuk和Chan[2]认为，＞30个/高倍视野即具诊断特异性；但Dhall等[14]认为，＞50个/高倍视野才具高度特异性。目前大多数学者认为，IgG4阳性浆细胞数目＞50个/高倍视野且$IgG4^+/IgG^+$＞40%并伴其他组织学表现（如纤维化和静脉炎、淋巴滤泡形成等）方能作为明确诊断依据[4]。

本文患者无论是临床表现还是影像学所见，以及组织病理学检查均符合Leporati等[13]的诊断标准，故明确诊断为IgG4相关性垂体炎。但与既往文献报道有所不同的是：该患者表现为孤立性垂体病变，而不伴其他器官受累症状与体征。与之相类似的孤立性垂体病变目前仅有5例报道[10,15]。因此，当仅有孤立性垂体病变时，应注意鉴别诊断，防止误诊和延误病情。尽管表现为鞍区肿物或垂体柄增粗，但IgG4相关性垂体炎缺乏特异性的MRI表现，部分患者可伴脑膜炎特点，但相似的影像学亦可同时见于垂体腺瘤、结节病、生殖细胞瘤、朗格汉斯细胞组织细胞增生症和结核病[16]，因此，术前实验室检查若无血清IgG4水平升高，单纯凭借MRI表现很难明确诊断，甚至不易考虑到IgG4相关性疾病的鉴别诊断。组织病理学检查，由于广泛性淋巴浆细胞浸润，在无临床资料提示和未发现免疫组织化学标记IgG4阳性细胞前，极易误诊为淋巴细胞性垂体炎。这可能即是该例患者术中行快速冰冻病理诊断时考虑淋巴细胞性垂体炎的原因。值得注意的是：非IgG4相关性垂体炎作为慢性炎症性病变，不论淋巴细胞性、黄色瘤性、肉芽肿性还是坏死性垂体炎，除外其特征性淋巴细胞浸润、泡沫细胞反应、肉芽肿形成和灶性坏死，其垂体组织内广泛性间质纤维化和玻璃样变均不十分显著，而该例患者同时还表现有广泛性间质纤维化和大量淋巴浆细胞浸润，这一组织病理学特点可作为考虑IgG4相关性垂体炎的诊断线索，但明确诊断仍需免疫组织化学标记IgG4阳性浆细胞之证据。该例患者另一特点是，组织内可见多灶性脑膜上皮细胞巢团，此即是导致术后误诊为富淋巴浆细胞型脑膜瘤的重要原因。事实上，鞍区、颅底肿瘤性或非肿瘤性病变导致的邻近硬脑（脊）膜反应并非少见，偶尔也可见

“脑膜尾征”而误诊为脑(脊)膜瘤[17-18],也有因颅内多发性IgG4相关性疾病而误诊为多发性脑膜瘤的个案报道[19]。本文患者虽然影像学并未观察到“脑膜尾征”,但其组织中的脑膜上皮细胞巢团的确给诊断带来了不小困扰,我们甚至认为是鞍区脑膜瘤压迫垂体造成的相关临床症状。此时若获得患者血清IgG4水平升高的实验室资料,则对明确诊断至关重要。因为富淋巴浆细胞型脑膜瘤不伴血清IgG4水平升高,也不具有组织中IgG4阳性浆细胞数目增多的特点。因此,如果是孤立性垂体病变而组织病理学检查显示大量炎性细胞浸润时,应考虑IgG4相关性疾病,从而给病理科医师提供相应的实验室资料,对明确诊断大有帮助。但应明确的是:IgG4相关性疾病主要以多器官受累为特点,当垂体以外其他器官,特别是胰腺、涎腺等部位同时或相继出现病变时,应警惕IgG4相关性垂体炎的可能。此外,当鞍区和垂体病变组织中存在大量炎性细胞浸润时,还应考虑结核病、朗格汉斯细胞组织细胞增生症和临床少见的Rosai-Dorfman病等,但这些疾病较为特殊的组织学构象和免疫组织化学表型使得鉴别诊断并不困难。

IgG4相关性疾病的发病机制目前尚未阐明,由于电子显微镜下可见病变组织中有免疫复合物沉积,故认为机体对自身抗体的免疫反应是导致病变的重要原因。患者外周血幼稚T细胞数目减少和受累组织记忆T细胞数目增多,也提示病变可能与细胞免疫有关,但具体作用机制尚待进一步阐明[1,3]。IgG4阳性浆细胞数目在受累组织中增多的意义目前仍不十分清楚,这种现象究竟是导致病变发生的始动因素还是单纯作为一种伴随表象,值得深入探讨。IgG4相关性疾病,包括IgG4相关性垂体炎还具有另一特点,即对激素治疗十分敏感,疗效迅速而稳定[4-6]。在已报道的IgG4相关性垂体炎病例中,除1例外[20],均对激素冲击治疗反应良好,但目前尚无文献报道标准的临床应用剂量。对于自身免疫性胰腺炎患者,推荐泼尼松0.60 mg/(kg·d)连续治疗2~4周后,以2.50~5 mg/d维持治疗3年[21];对于部分激素治疗不敏感或复发的患者,可考虑采用利妥昔单抗(rituximab)治疗[22]。对于IgG4相关性垂体炎患者,文献报道的泼尼松剂量为30~60 mg/d,可使肿物迅速缩小,部分疗效不明显者,辅助应用咪唑硫嘌呤(azathioprine)75 mg(2次/d),可取得较好疗效[23]。

由于IgG4相关性垂体炎临床少见,单纯表现为孤立性鞍区和(或)垂体病变时,缺乏特征性影像学表现,术前极易误诊为垂体腺瘤。术后组织病理学检查,又因病变组织内存在广泛性淋巴浆细胞浸润,若不全面仔细观察间质纤维化和玻璃样变,以及闭塞性静脉炎,不易考虑IgG4相关性垂体炎而误诊为非特异性炎症,或因病变所致的鞍底脑膜反应而误诊为富淋巴浆细胞型脑膜瘤。此时,实验室检查提示IgG4水平升高是诊断的重要线索。唯有充分了解此类疾病的临床演变过程、影像学特点和组织病理学表现,方可避免可能出现的诊断陷阱而得出正确的结论。

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·小词典·

中英文对照名词词汇(七)

髓鞘碱性蛋白 myelin basic protein(MBP)
髓鞘少突胶质细胞糖蛋白 myelin oligodendrocyte glycoprotein(MOG)
胎牛血清 fetal bovine serum(FBS)
糖化血红蛋白 glycosylated hemoglobin(HbA1c)
特发性脱髓鞘性视神经炎 idiopathic demyelinating optic neuritis(IDON)
特发性炎性脱髓鞘疾病 idiopathic inflammatory demyelinating disease(IIDD)
天然调节性T细胞 natural regulatory T cell(nTreg)
调节性T细胞 regulatory T cell(Treg)
调节亚单位二肽基肽酶样蛋白 dipeptidyl-peptidase-like protein(DPPX)
同型半胱氨酸 homocysteine(Hcy)
外周血单个核细胞 peripheral blood mononuclear cells(PBMC)
完全前循环梗死 total anterior circulation infarct(TACI)
维A酸相关孤儿受体γt retinoid-related orphan receptor γt(RORγt)
系统性红斑狼疮 systemic lupus erythematosus(SLE)
细胞间黏附分子-1 intercellular adhesion molecule-1(ICAM-1)
B细胞活化因子受体 B cell activating factor receptor(BAFF-R)
细胞外基质 extracellular matrix(EM)
线粒体脑肌病伴高乳酸血症和卒中样发作 mitochondrial encephalopathy with lactic academia and stroke-like episodes(MELAS)
IgG4相关性疾病 IgG4-related diseases(IgG4-RD)
香烟烟雾提取物 cigarette smoke extract(CSE)
3-硝基酪氨酸 3-nitrotyrosine(3-NT)
小动脉病变 small artery disease(SAD)
心源性栓塞 cardioembolism(CE)
信号传导与转录激活因子3 signal transducer and activator of transcription 3(STAT3)
信噪比 signal-to-noise ratio(SNR)
兴奋性氨基酸 excitatory amino acid(EAA)
兴趣区 reagion of interest(ROI)