·临床病理报告·

表现为垂体腺瘤卒中的黄色瘤性垂体炎

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【摘要】 **目的** 报告1例黄色瘤性垂体炎病例，总结其临床表现、实验室、影像学和组织病理学特征。**方法与结果** 患者为河北省人民医院2018年7月确诊并治疗的男性黄色瘤性垂体炎病例，临床表现为头痛伴恶心呕吐；头部CT显示鞍区呈软组织密度影，较饱满；MRI显示蝶鞍扩大，鞍内可见一类圆形肿物影。临床考虑为“垂体腺瘤卒中”，于神经内镜下经鼻蝶入路行垂体腺瘤切除术，术后病理学检查，组织细胞呈弥漫性片状浸润，免疫组化染色CD68和波形蛋白呈强阳性，S-100蛋白和CD1α呈阴性，Ki-67抗原标记指数为10%～20%，最终诊断为鞍区黄色瘤性垂体炎。**结论** 黄色瘤性垂体炎临床罕见，症状及影像学表现无特异性，临床诊断极具挑战性，神经内镜活检是诊断与鉴别诊断的“金标准”，伴出血时应注意与垂体腺瘤卒中相鉴别。

【关键词】 自身免疫性垂体炎； 垂体肿瘤； 免疫组织化学； 病理学

Xanthomatous hypophysitis behaving like pituitary adenoma

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【**Abstract**】 **Objective** To report a case of xanthomatous hypophysitis (XH), and summarize its clinical manifestations, laboratory, imaging and histopathological features. **Methods and Results** The patient was a male XH diagnosed and treated by Hebei General Hospital in July 2018. The clinical manifestations were headache with nausea and vomiting. Head CT showed the sella area was dense and full; MRI showed enlargement of the sella and a type of circular mass within the sella. The clinical diagnosis was pituitary adenoma apoplexy, and pituitary adenoma resection was performed through nasal sphenoid approach under neuroendoscopy. The postoperative pathological examination showed the histopathological cells showed flake dense infiltration, the immunohistochemical staining showed strong positive CD68 and vimentin (Vim), and S-100 protein and CD1α were negative, Ki-67 antigen labeling index was 10%-20%, and the final diagnosis was sellar XH. **Conclusions** XH is rare in clinic, and its symptoms and imaging findings are nonspecific, making clinical diagnosis extremely challenging. Neuroendoscopic biopsy pathology is the "gold standard" for diagnosis and differential diagnosis, and attention should be paid to distinguishing pituitary adenoma apoplexy when accompanied by bleeding.

【**Key words**】 Autoimmune hypophysitis; Pituitary neoplasms; Immunohistochemistry; Pathology

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Conflicts of interest: none declared

黄色瘤性垂体炎（XH）是临床罕见的原发性垂体炎，发病机制不明，可能与自身免疫机制有关。根据组织学形态，原发性垂体炎可以分为淋巴细胞性、肉芽肿性、黄色瘤性、坏死性和IgG4相关性垂体炎5种亚型[1]，各亚型的影像学征象极为相似。其中以黄色瘤性垂体炎极为罕见，发病年龄相对年轻，临床表现与其他亚型相似，仅依据临床症状难以区分；其炎症反应不明显，常伴大量出血，应注意与垂体腺瘤卒中相鉴别，垂体激素改变主要为促性腺激素（GTH）和生长激素（GH）水平降低或催乳素

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(PRL)水平升高,受累垂体组织内可见“泡沫”样细胞,局部可见少量B淋巴细胞浸润。本文报告1例表现为垂体腺瘤卒中的黄色瘤性垂体炎患者,总结其诊断与治疗经过并复习相关文献,以期提高对此类疾病的诊断与鉴别诊断水平。

病历资料

患者 男性,32岁。因头痛伴恶心、呕吐3天,于2018年7月25日入院。患者入院前3天“受凉”后出现头痛,呈双侧颞部阵发性胀痛,发作时伴心慌出汗、恶心呕吐(非喷射状),呕吐物为胃内容物,持续约10分钟,每日发作6~7次,自行服用“藿香正气水”疼痛症状无缓解,并呈进行性加重,常夜间痛醒,且发作频率显著增加,由每日发作6~7次增至每30分钟发作1次,病程中无言语不清、意识障碍、视物旋转、吞咽困难、饮水呛咳、肢体麻木无力等,大小便正常。发病后3天至我院就诊,以“头痛原因待查”入院。患者既往身体健康,无溃疡性结肠炎、桥本甲状腺炎、类风湿性关节炎和干燥综合征等病史;个人史及家族史无特殊。

诊断与治疗经过 体格检查:体温36 ℃,心率为77次/min,呼吸为20次/min,血压134/81 mm Hg(1 mm Hg = 0.133 kPa);双侧瞳孔等大、等圆,直径约2.50 cm,对光反射灵敏,无视野缺损和视力障碍;四肢肌力、肌张力正常,共济运动和深浅感觉无异常,生理反射正常,双侧病理征未引出,无颈强直,脑膜刺激征阴性。实验室检查:血常规中性粒细胞计数9.78×10^9/L[$(1.80\sim6.30)\times10^9$/L]、中性粒细胞比例89%(40%~75%),血清钾3.30 mmol/L(3.50~5.50 mmol/L)、血清钠136 mmol/L(135~145 mmol/L),腺垂体功能[促甲状腺激素(TSH)、促肾上腺皮质激素(ACTH)、生长激素、卵泡刺激素(FSH)、黄体生成素(LH)、催乳素]和皮质醇均于正常值范围。影像学检查:头部CT显示鞍区呈软组织密度影,较饱满(图1a);MRI显示蝶鞍扩大,鞍内可见一类圆形肿物影,大小约为2.40 cm×1.40 cm×1.00 cm,T_1WI呈较均匀的稍高信号,其内可见条片状高信号,T_2WI和FLAIR成像呈等或低混杂信号,且边界清晰(图1b~1d)。临床诊断:垂体腺瘤卒中。于2018年7月27日行内镜下经鼻蝶入路垂体腺瘤切除术,术中可见肿瘤组织呈灰红色,大小约2 cm×1 cm×1 cm,质地柔软,血供丰富,瘤内有陈旧性出血和凝血块,手术全切除肿瘤。手术标本行HE染色和免疫组化染色。(1)大体标本观察:送检标本为灰褐色组织块,大小约1.20 cm×1.00 cm×1.00 cm,质地柔软,可见出血。(2)HE染色:送检组织大部分为凝血块,低倍镜(×100)下局部可见大量组织细胞呈片状密集浸润(图2a);高倍镜(×400)下可见组织细胞体积增大,胞质内充满细小脂滴,呈淡染泡沫状,即黄色瘤样组织细胞,胞核呈圆形、卵圆形或肾形(图2b),间质血管丰富、伴出血,管腔中含较多嗜中性粒细胞。(3)免疫组化染色:采用EnVision二步法,检测用抗体为CD68、波形蛋白(Vim)、S-100蛋白(S-100)、CD1α和Ki-67抗原,均购自北京中杉金桥生物技术有限公司。结果显示,黄色瘤样组织细胞胞质CD68和Vim呈强阳性(图3a,3b),但不表达S-100和CD1α(图3c,3d),Ki-67抗原标记指数为10%~20%(图3e)。组织病理诊断:鞍区黄色瘤性垂体炎。患者共住院10天,出院时症状缓解;术后随访5年,无复发,垂体功能恢复正常。

讨 论

鞍区解剖结构复杂且包括不同组织成分和细胞类型,至少有25种疾病表现为鞍区占位效应,其中8%为非肿瘤性病变[2-3]。黄色瘤性垂体炎是临床罕见的原发性垂体炎[1],发病机制尚未阐明,可能与自身免疫机制有关,诸如溃疡性结肠炎、桥本甲状腺炎、类风湿性关节炎和干燥综合征等[4-6]。原发性垂体炎各亚型中以淋巴细胞性垂体炎最常见,主要发生于女性,特别是妊娠期女性,少数可并发其他自身免疫性疾病,临床表现为头痛(48%)和视野缺损(40%),约70%患者伴腺垂体功能障碍[7];其次为肉芽肿性垂体炎,亦好发于女性,可出现头痛、视觉减退等症状[8],组织学形态为上皮样肉芽肿性炎症,部分区域可见淋巴细胞、浆细胞浸润并破坏垂体腺泡,与淋巴细胞性垂体炎相似;坏死性垂体炎以垂体组织坏死为主,组织学形态可见致密淋巴细胞、浆细胞和嗜酸性粒细胞浸润伴纤维化;IgG4相关垂体炎则通常见于IgG4相关疾病,主要发生于男性和老年人群,平均发病年龄64.2岁[9],临床表现为腺垂体和(或)神经垂体功能障碍。黄色瘤性垂体炎由Folkerth等于1998年首次报道[2],与其他亚型垂体炎相比,女性少见,平均发病年龄39.3岁[10-11];临床特征与其他鞍区病变相似,可出现头痛、高催乳素血症、性欲减退、尿崩症等[12],亦可表现为局部出血、坏死和炎症,但具体发病机制尚不清楚[13-14];

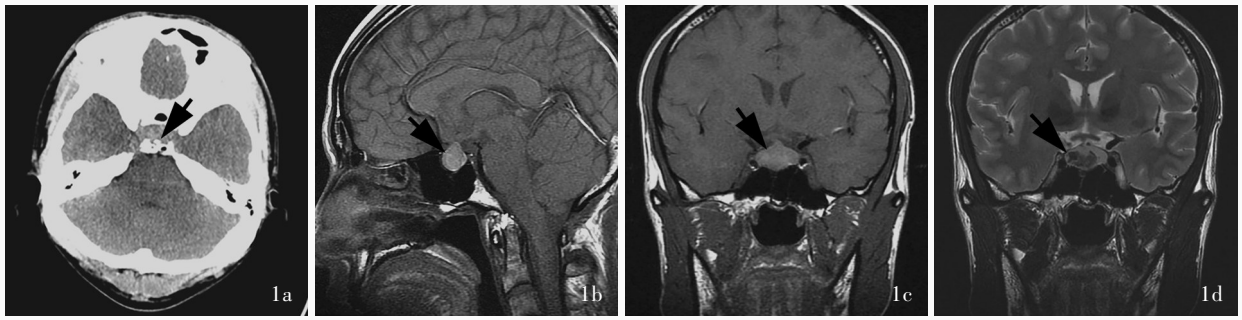

图1　术前头部影像学所见　1a　横断面CT显示垂体饱满，密度增高（箭头所示）　1b　矢状位T_1WI显示垂体饱满，呈不均匀稍高信号影（箭头所示）　1c　冠状位T_1WI显示垂体占位性病变，呈稍高信号，大小约2.40 cm×1.40 cm×1.00 cm（箭头所示）　1d　冠状位T_2WI显示垂体占位性病变，呈等或低混杂信号（箭头所示）

Figure 1　Preoperative head imaging findings　Axial CT showed a plump pituitary with increased intensity (arrow indicates, Panel 1a). Sagittal T_1WI showed a plump pituitary with slightly hyperintensity (arrow indicates, Panel 1b). Coronal T_1WI showed an occupying lesion with a slightly hyperintensity of 2.40 cm × 1.40 cm × 1.00 cm in pituitary (arrow indicates, Panel 1c). Coronal T_2WI showed an occupying lesion with isointensity and hypointensity in pituitary (arrow indicates, Panel 1d).

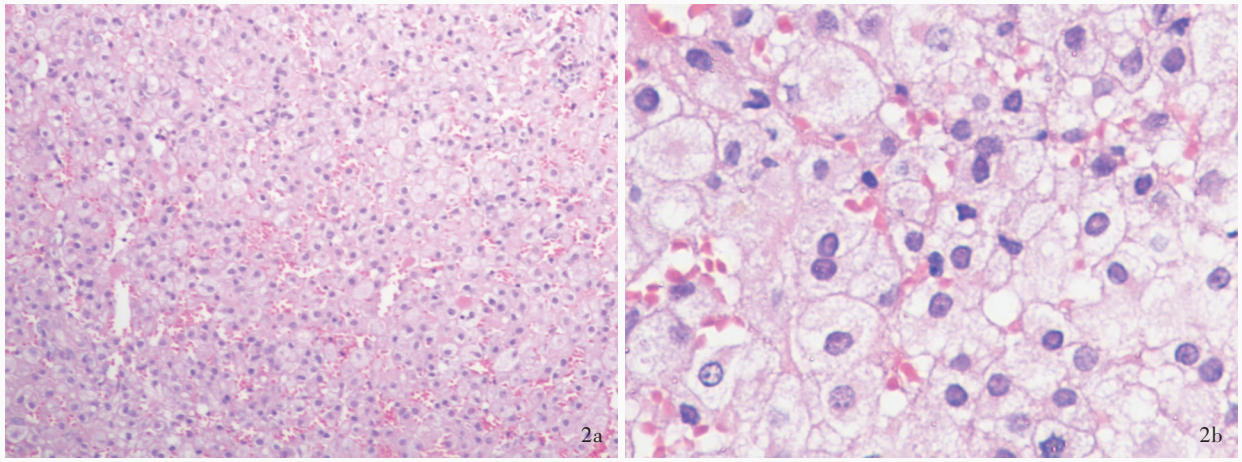

图2　光学显微镜观察所见　HE染色　2a　黄色瘤样组织细胞呈弥漫性片状浸润　×100　2b　黄色瘤样组织细胞胞质呈淡染泡沫状　×400

Figure 2　Light microscopy findings　HE staining　The xanthomatoid tissue cells showed diffuse lameller infiltration in the tissue (Panel 2a).　×100　The cytoplasm of xanthomatoid tissue cells was foamy (Panel 2b).　×400

MRI特征为腺垂体及垂体窝呈囊性增大，偶伴垂体柄增粗，海绵窦受累者于冠状位扫描呈现典型的“三角形”鞍区占位效应[15-16]；组织学形态特征为黄色瘤样组织细胞呈密集片状浸润，胞质富含脂质，呈泡沫状，间质血管丰富，管腔富含中性粒细胞，可能与血常规中性粒细胞计数增加有关，可无淋巴细胞浸润；免疫组化特征为黄色瘤样组织细胞胞质强阳性表达CD68和Vim，不表达S-100和CD1α[15]；超微结构观察，黄色瘤样组织细胞胞质富含脂滴和膜结合液泡[17-18]。本文患者仅有头痛、呕吐症状，无尿崩症、视野缺损和视力障碍；实验室检查仅血清钾和血清钠降低，垂体激素和皮质醇水平正常；组织学形态为充满脂质的组织细胞（即黄色瘤样组织细胞）浸润腺垂体，胞体增大，胞质内充满细小脂滴，呈淡染泡沫状，胞核呈圆形、卵圆形或肾形；免疫组化染色CD68和Vim呈强阳性，S-100和CD1α呈阴性。此外，含铁血黄素亦可作为黄色瘤性垂体炎的诊断依据，但本文患者垂体组织中未见含铁血黄素沉积，而是表现为新鲜出血。

绝大多数黄色瘤性垂体炎的影像学表现提示鞍区囊性病变，病变周围呈强化征象，故垂体炎的影像学鉴别诊断仍是难题[19]，因此，病理学检查十分必要[20]。神经内镜活检是诊断与鉴别诊断的“金标准”[21]，特别是通过临床表现、实验室和影像学检查难以鉴别诊断的疾病。临床应注意与朗格汉斯细胞组织细胞增生症（LCH）相鉴别，后者常累及垂体，病变多位于垂体柄，影像学检查显示垂体柄增粗、弯曲，组织学形态除大量多核巨细胞浸润外，还

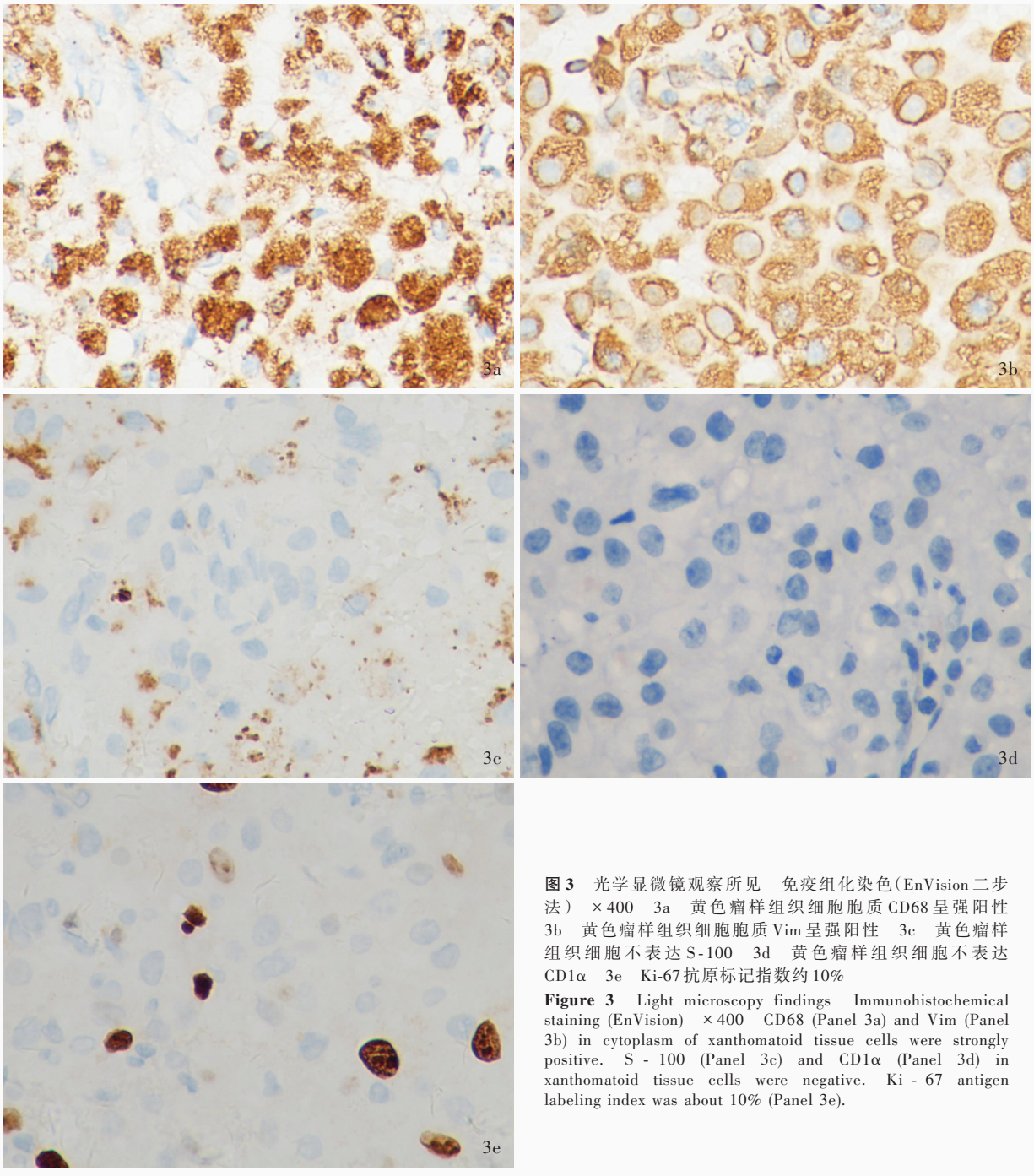

图3　光学显微镜观察所见　免疫组化染色(EnVision二步法)　×400　3a　黄色瘤样组织细胞胞质CD68呈强阳性　3b　黄色瘤样组织细胞胞质Vim呈强阳性　3c　黄色瘤样组织细胞不表达S-100　3d　黄色瘤样组织细胞不表达CD1α　3e　Ki-67抗原标记指数约10%

Figure 3　Light microscopy findings　Immunohistochemical staining (EnVision)　×400　CD68 (Panel 3a) and Vim (Panel 3b) in cytoplasm of xanthomatoid tissue cells were strongly positive.　S - 100 (Panel 3c) and CD1α (Panel 3d) in xanthomatoid tissue cells were negative.　Ki - 67 antigen labeling index was about 10% (Panel 3e).

可见胞质嗜酸性、胞核呈明显核沟("咖啡豆"样)的朗格汉斯细胞,并伴嗜酸性粒细胞浸润,免疫组化染色肿瘤性朗格汉斯细胞CD1α和Langerin抗体阳性有助于二者的鉴别诊断。

治疗方面,与淋巴细胞性垂体炎不同,黄色瘤性垂体炎对糖皮质激素治疗反应较差,一旦出现进行性视野缺损或垂体功能障碍,通常需手术切除病变[14],进而改善垂体功能[13],但有可能导致医原性损伤和垂体功能减退,需激素替代治疗。

综上所述,黄色瘤性垂体炎是极为罕见的垂体病变,临床和影像学表现无特异性,难以与其他亚型垂体炎相区分,临床诊断极具挑战性,组织病理学检查十分必要。黄色瘤性垂体炎伴出血时应注意与垂体腺瘤卒中相鉴别。

利益冲突 无

参 考 文 献

[1] Liu XH, Li MC, Chen G, Wang RZ. Diagnosis and treatment of pituitary incidentalomas[J]. Zhongguo Xian Dai Shen Jing Ji Bing Za Zhi, 2022, 22:910-913.[刘小海, 李茗初, 陈革, 王任直. 垂体偶发瘤诊断与治疗进展[J]. 中国现代神经疾病杂志, 2022, 22:910-913.]

[2] Saeger W. Space occupying processes of the sellar region with emphasis on tumor-like lesions[J]. Pathologe, 2003, 24:247-254.

[3] Gutenberg A, Hans V, Puchner MJ, Kreutzer J, Brück W, Caturegli P, Buchfelder M. Primary hypophysitis: clinical-pathological correlations[J]. Eur J Endocrinol, 2006, 155:101-107.

[4] Oishi M, Hayashi Y, Fukui I, Kita D, Miyamori T, Nakada M. Xanthomatous hypophysitis associated with autoimmune disease in an elderly patient: a rare case report[J]. Surg Neurol Int, 2016, 7:S449-S453.

[5] Yang XJ, Chen H, Li JB, Sun CY, Yin HF. Integrated and layered diagnoses in the 2021 WHO Classification of Tumors of the Central Nervous System (fifth edition)[J]. Zhongguo Xian Dai Shen Jing Ji Bing Za Zhi, 2021, 21:764-768.[杨学军, 陈宏, 李佳博, 孙翠云, 尹洪芳. 2021年世界卫生组织中枢神经系统肿瘤分类(第五版)整合及分层诊断解读[J]. 中国现代神经疾病杂志, 2021, 21:764-768.]

[6] Joung JY, Jeong H, Cho YY, Huh K, Suh YL, Kim KW, Bae JC. Steroid responsive xanthomatous hypophysitis associated with autoimmune thyroiditis: a case report[J]. Endocrinol Metab (Seoul), 2013, 28:65-69.

[7] Wang S, Wang L, Yao Y, Feng F, Yang H, Liang Z, Deng K, You H, Sun J, Xing B, Jin Z, Wang R, Pan H, Zhu H. Primary lymphocytic hypophysitis: clinical characteristics and treatment of 50 cases in a single centre in China over 18 years[J]. Clin Endocrinol (Oxf), 2017, 87:177-184.

[8] Hunn BH, Martin WG, Simpson S Jr, McLean CA. Idiopathic granulomatous hypophysitis: a systematic review of 82 cases in the literature[J]. Pituitary, 2014, 17:357-365.

[9] Shikuma J, Kan K, Ito R, Hara K, Sakai H, Miwa T, Kanazawa A, Odawara M. Critical review of IgG4-related hypophysitis[J]. Pituitary, 2017, 20:282-291.

[10] Mathkour M, Zeoli T, Werner C, Scullen T, Garces J, Keen J, Ware M. Recurring primary xanthomatous hypophysitis behaving like pituitary adenoma: additional case and literature review[J]. World Neurosurg, 2020, 138:27-34.

[11] Niyazoglu M, Celik O, Bakkaloglu DV, Oz B, Tanriöver N, Gazioglu N, Kadioglu P. Xanthomatous hypophysitis[J]. J Clin Neurosci, 2012, 19:1742-1744.

[12] Guan H, Guo SQ, Jia TL. Clinical guidance and International Classification of Disease coding analysis in the 2017 WHO classification of pituitary neuroendocrine tumors[J]. Zhongguo Xian Dai Shen Jing Ji Bing Za Zhi, 2022, 22:54-59.[关宏, 郭淑芹, 贾同乐. 2017版WHO垂体神经内分泌肿瘤分类临床指导及国际疾病分类法编码分析[J]. 中国现代神经疾病杂志, 2022, 22:54-59.]

[13] Gopal-Kothandapani JS, Bagga V, Wharton SB, Connolly DJ, Sinha S, Dimitri PJ. Xanthogranulomatous hypophysitis: a rare and often mistaken pituitary lesion[J]. Endocrinol Diabetes Metab Case Rep, 2015, 2015:140089.

[14] Gubbi S, Hannah-Shmouni F, Verbalis JG, Koch CA. Hypophysitis: an update on the novel forms, diagnosis and management of disorders of pituitary inflammation[J]. Best Pract Res Clin Endocrinol Metab, 2019, 33:101371.

[15] Tang F, Liu H, Zhou S, Liu J, Xiao E, Tan C. MRI manifestation of xanthomatous hypophysitis: a case report and review of the literature[J]. Zhong Nan Da Xue Xue Bao Yi Xue Ban, 2015, 40:228-232.

[16] Tang F, Zhou SK, Liu J, Liu H. Imaging findings of xanthomatoid pituitaritis: one case report[J]. Zhonghua Fang She Xue Za Zhi, 2015, 49:626.[唐菲, 周顺科, 刘军, 刘辉. 黄色瘤样垂体炎影像表现一例[J]. 中华放射学杂志, 2015, 49:626.]

[17] Deodhare SS, Bilbao JM, Kovacs K, Horvath E, Nomikos P, Buchfelder M, Reschke K, Lehnert H. Xanthomatous hypophysitis: a novel entity of obscure etiology[J]. Endocr Patho, 1999, 10:237-241.

[18] Guan H, Li ZH, Sun JR, He JH, Zhang LN. The 2017 WHO classification and International Classification of Disease coding analysis of non-neuroendocrine tumors in the pituitary gland[J]. Zhongguo Xian Dai Shen Jing Ji Bing Za Zhi, 2022, 22:116-125.[关宏, 李志红, 孙吉瑞, 贺建辉, 张丽娜. 2017版WHO垂体非神经内分泌肿瘤分类临床指导及国际疾病分类法编码分析[J]. 中国现代神经疾病杂志, 2022, 22:116-125.]

[19] Caranci F, Leone G, Ponsiglione A, Muto M, Tortora F, Muto M, Cirillo S, Brunese L, Cerase A. Imaging findings in hypophysitis: a review[J]. Radiol Med, 2020, 125:319-328.

[20] Zhou X, Zhu H, Yao Y, Lian X, Feng F, Wang L, Liu S, Deng K, You H, Yang H, Lu L. Etiological spectrum and pattern of change in pituitary stalk thickening: experience in 321 patients[J]. J Clin Endocrinol Metab, 2019, 104:3419-3427.

[21] Wang Z, Zhu J, Yao Y, Zhu H, Deng K, Lu L, Zhang Y, Duan L, Wang L, Yang H, Xiao Y, Zhao D, You H, Feng F, Ma J, Wang X, Pan H. Clinical and pathological features of 124 patients with indistinguishable sellar lesions and central diabetes insipidus[J]. J Clin Neurosci, 2020, 80:215-222.

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