·标准与指南·

# 颅咽管瘤分型

斯良楠 陈金桃 林志雄

【摘要】 颅咽管瘤与周围神经血管粘连紧密，手术难度较大，围手术期并发症较多，患者多预后不良。基于肿瘤组织学或解剖学分型用于指导手术原则及手术入路，以及药物治疗或联合治疗方案研究较多，但尚未形成共识。本文综述颅咽管瘤的组织学、解剖学和分子分型，为今后实现颅咽管瘤的融合分型指导精准治疗提供新的思路。

【关键词】 颅咽管瘤； 解剖学； 外科手术； 综述

## The research of craniopharyngioma classification

SI Liang-nan, CHEN Jin-tao, LIN Zhi-xiong

*Department of Neurosurgery, Beijing Sanbo Brain Hospital, Capital Medical University, Beijing 100093, China*

*Corresponding author: LIN Zhi-xiong (Email: lzx1967@sina.com)*

【Abstract】 The tumor tissue of craniopharyngioma is closely adherent to peripheral neurovascular tissue, so the operation to remove lesion is more difficult, the perioperative complications are very serious, and the prognosis of patients is poor. There are many studies on the use of tumor histology or anatomical classification to guide surgical principles and surgical approaches, as well as drug therapy or combination therapy, but no consensus has been reached. This paper reviews the histological, anatomical and molecular typing of craniopharyngioma, providing new ideas for the future realization of the fusion typing of craniopharyngioma to guide the precise treatment.

【Key words】 Craniopharyngioma; Anatomy; Surgical procedures, operative; Review

This study was supported by Capital Health Research and Development Special Fund (No. 2022-2-8013).

**Conflicts of interest:** none declared

颅咽管瘤（CP）是一种临床较为罕见的颅内肿瘤，好发于儿童，发病率为（0.5～2）/100万人年[1]。尽管其在组织学上属于良性上皮肿瘤（WHO Ⅰ级），但由于病变与周围神经血管粘连紧密，故手术难度大、围手术期并发症多，患儿大多预后不良。正如神经外科先驱Harvey Cushing教授所言：颅咽管瘤是神经外科医师所面对的最棘手的问题[2]。由于颅咽管瘤的发生部位特殊，尤其在肿瘤生长过程中可与下丘脑发生粘连[3]，故针对其施行的外科治疗主要基于组织学或解剖学分型制定手术方案、选择手术入路，以及药物化疗或多种方案联合治疗，遗憾的是，至今尚无相关研究对这些分型进行归纳总结。基于此，本文拟对颅咽管瘤的组织学分型、解剖学分型和分子分型进行系统介绍，以期实现肿瘤的融合分型，指导精准治疗。

### 一、颅咽管瘤的组织学分型

既往颅咽管瘤在组织学上可分为两种亚型，即牙釉质细胞瘤型颅咽管瘤（ACP）和乳头状型颅咽管瘤（PCP）[4]。前者可发生于任何年龄，峰值年龄5～15和45～60岁[5]；肿瘤多呈囊实性，囊液如“机油”样，囊壁或实性部分存在钙化，CT图像极易辨认[5]；绝大多数患者病变与周围组织粘连紧密，或侵犯相邻组织，术中不易分离[6]。PCP大多于成年期发病（40～55岁），病变以实性为主，具有低侵袭性，若发生囊性变，囊液多呈清亮、透明[5]；病变与周围组织边界相对清晰，术中易于剥离[6]。

关于不同亚型颅咽管瘤的致病原因，有学者认为，ACP是由于*CTNNB1*基因（编码β-连环蛋白）外

doi：10.3969/j.issn.1672-6731.2023.10.008

基金项目：首都卫生发展科研专项基金资助项目（项目编号：首发2022-2-8013）

作者单位：100093 北京，首都医科大学附属三博脑科医院神经外科

通讯作者：林志雄，Email：lzx1967@sina.com

显子3体细胞基因变异阻断β-连环蛋白磷酸化和Wnt/β-连环蛋白信号转导通路的激活，进而诱发病变[7-8]。然而，与该基因相关的多项研究并未发现ACP存在*CTNNB1*基因变异，而且不同研究报告的*CTNNB1*基因变异发生率亦存在显著差异（16%～100%）[9-13]，究其原因，检测技术导致的敏感性差异是*CTNNB1*基因变异出现差异的主要原因[13]。目前，关于散发性ACP的病因学研究除*CTNNB1*基因变异外，尚未发现与其发病相关的其他体细胞基因变异[14]，对于一些家族性ACP患者（非散发性）而言，*APC*基因的体细胞或胚系突变可以被检测到，提示家族性ACP可能存在非*CTNNB1*基因依赖性途径[15]。与ACP相比，有关PCP的病因学研究则证实其主要是由*BRAF* V600E体细胞基因变异导致丝裂原激活蛋白激酶（MAPK）信号转导通路被激活而致病[7]，此特点也是PCP与ACP等疾病进行鉴别诊断的重要生物学标志物。近年来，陆续可见儿童PCP的报道[15-17]，2022年，林志雄教授研究团队首次在病例总结的基础上提出儿童PCP影像学特征以及诊断与鉴别诊断标准，其研究成果对临床制定手术方案具有重要辅助价值[18]。鉴于ACP和PCP在基因组学、组织学、影像学和发病年龄等方面存在差异，《2021年世界卫生组织中枢神经系统肿瘤分类（第五版）》将二者判定为不同独立类型的颅咽管瘤，而非颅咽管瘤的两种亚型[19]，既往将二者归于颅咽管瘤的两种亚型是否基于二者存在某些共性，目前尚无文献阐明。

## 二、基于颅咽管瘤与下丘脑关系的解剖学分型与手术原则

关于颅咽管瘤的手术原则主要有两种：激进性治疗（全切除肿瘤）和保守治疗（次全切除或者部分切除后辅助放疗消除残留病变）[20]。采用保守治疗的患者，肿瘤复发或发生恶性变后再次治疗极为困难[21]。由于颅咽管瘤在组织学和细胞学上属于良性肿瘤（WHO Ⅰ级肿瘤），通过手术彻底切除肿瘤有治愈的可能，但大多数儿童颅咽管瘤累及下丘脑或发生紧密粘连，故手术过程中极易损伤下丘脑，使手术风险显著增加。下丘脑受累程度与颅咽管瘤患儿的预后密切相关，肿瘤与下丘脑的粘连程度决定手术治疗方案。因此，术前准确评估肿瘤与下丘脑的粘连程度或下丘脑受累程度是非常必要的。目前用于评估颅咽管瘤与下丘脑粘连程度或下丘脑受累程度的分级体系主要有以下3种。（1）Puget分级体系[22]：根据下丘脑受累程度分为鞍内、灰结节和第三脑室底共3级，该分级体系简单、实用，但准确性欠佳。（2）Hori T分级体系[23]：根据MRI冠状位和矢状位肿瘤直径、结构，以及与前床突、室间孔和乳头体的位置关系分为5级，但迄今尚未见该分级体系在颅咽管瘤大样本临床研究中的应用，其准确性尚有待验证。（3）Prieto分级体系[24]：依据影像学显示的肿瘤所贴附组织或结构的解剖位置、肿瘤贴附形态、肿瘤与周围组织结构的粘连程度等独立因素分别分型，然后综合3项分型最终形成肿瘤对下丘脑的粘连程度分级，并以此制定手术方案；Prieto分级体系具有较好的客观性和准确性[3,24]，本节将重点介绍Prieto分级体系。在Prieto分级体系中，肿瘤所贴附解剖结构的位置可以分为6型，即蝶鞍垂体腺型、垂体柄-漏斗外侧型、第三脑室底型、第三脑室底和第三脑室壁型、第三脑室内型和全面贴附型（图1）[3,24]；其贴附形态亦分为6型，分别为带蒂型、无柄型、帽状型、环状型、碗状型和环包型（图2）[3,24]；粘连程度分为4型，即疏松型、紧密型、融合型和替换型（图3）[3,24]。根据上述分型，再进一步将肿瘤对下丘脑的粘连程度或者下丘脑受累程度共分为5级：Ⅰ级（轻度），蝶鞍垂体腺型或垂体柄-漏斗外侧型、无柄型、疏松型或紧密型；Ⅱ级（中度），第三脑室内型、带蒂型或无柄型、疏松型或紧密型；Ⅲ级（重度），垂体柄-漏斗外侧型、无柄型或帽状型、疏松型或紧密型；Ⅳ级（极重度），第三脑室底和第三脑室壁型、碗状型或环状型或环包型，紧密型或融合型或替换型；Ⅴ级（危重），全面贴附型、环状型、替换型。其中，Ⅰ～Ⅲ级属于低风险，为激进性手术治疗适应证，而Ⅳ～Ⅴ级属于高风险，以保守治疗为宜[3]。

## 三、基于颅咽管瘤与周围神经血管关系的解剖学分型与手术入路

当手术原则确定之后，选择正确并适宜的手术入路即成为手术成功的关键。1907年，Victor Horsley教授通过经颅入路成功完成全球首例颅咽管瘤切除术[18]；同年，Anton von Eiselsberg教授实施第1例经蝶入路手术[3]，自此经颅入路和经蝶入路即成为颅咽管瘤切除术的两种基本入路。1912年，Harvey Cushing教授完成其首例经蝶入路颅咽管瘤切除术，由于死亡率过高，故更推荐经颅入路[3]。因此，20世纪早中期经颅入路被绝大多数神经外科医师视为颅咽管瘤切除术的首选入路，而且随着临床

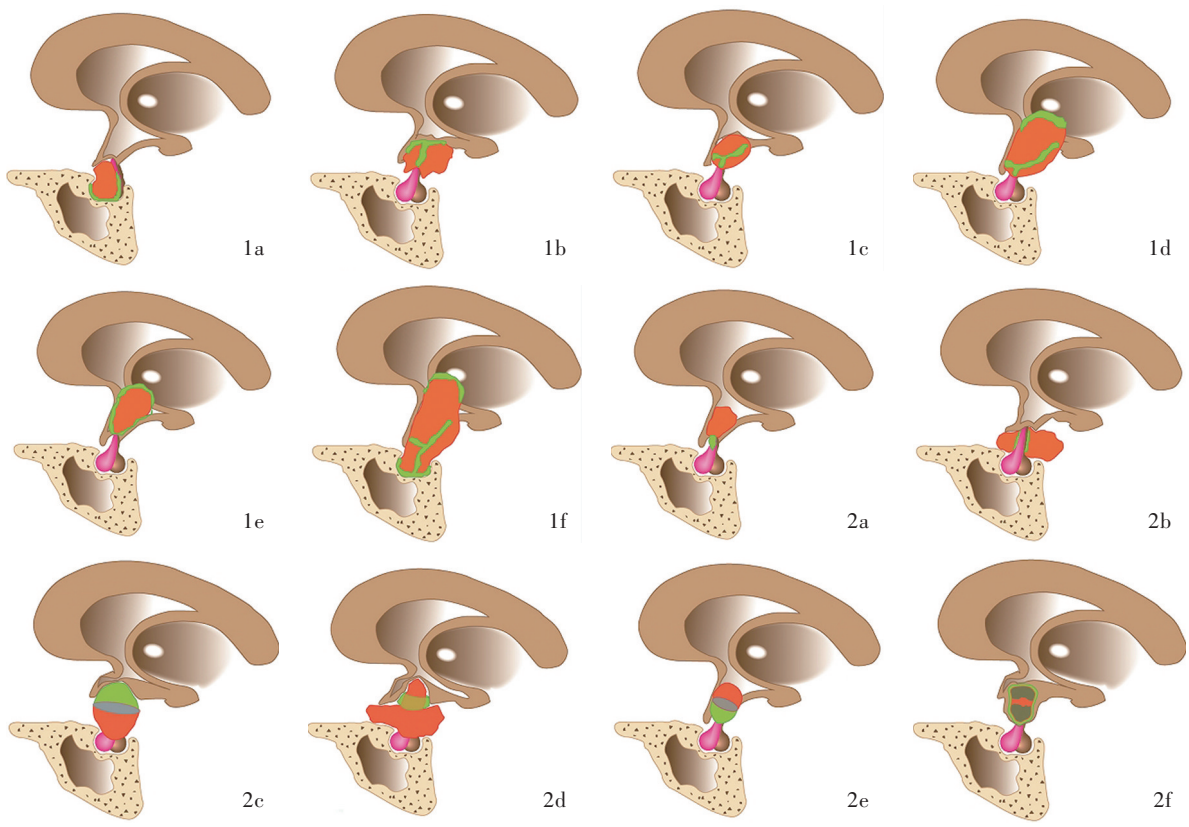


**图1** 颅咽管瘤解剖学分型示意图(根据肿瘤与周围组织结构贴附位置共分为6型[24];橙色区域代表肿瘤组织,绿色区域代表下丘脑及垂体柄,粉色区域为腺垂体) 1a 蝶鞍垂体腺型:贴附于鞍膈以下,包括垂体腺与垂体柄的连接处 1b 垂体柄-漏斗外侧型:贴附于垂体柄或漏斗-灰结节外侧面 1c 第三脑室底型:所粘连结构包括漏斗-灰结节全层 1d 第三脑室底和第三脑室壁型:粘连于第三脑室底神经层,以及一处或多处第三脑室前壁或部分侧壁 1e 第三脑室内型:仅粘连于第三脑室壁室管膜层 1f 全面贴附型:肿瘤贴附于以上所有结构 **图2** 颅咽管瘤形态学分型示意图(根据肿瘤组织贴附形态共分为6型[24];橙色区域代表肿瘤组织,绿色区域代表下丘脑及垂体柄,粉色区域为腺垂体) 2a 带蒂型:贴附点由一根狭窄的纤维血管干构成 2b 无柄型:肿瘤贴附面如一个宽大的补丁,附着于周围组织结构 2c 帽状型:肿瘤贴附面宽广,上部(上1/3~1/2部)向上推挤第三脑室底壁,后者如同"戴帽子" 2d 环状型:周围组织结构与肿瘤接触面如带子般环绕肿瘤中心表面 2e 碗状型:肿瘤贴附面宽广,下部(下1/3~1/2部)向下挤压接触面组织结构,如"碗"状 2f 环包型:周围组织结构与肿瘤接触面(通常是一种很薄的神经胶质层)如"包装纸"样包裹肿瘤表面大部分

**Figure 1** CP classification according to anatomical structures attached to the tumor[24]. The orange area represents the tumor tissue, the green area represents the hypothalamus and the pituitary stalk, and the pink area is the adenohypophysis Sella-gland: tumor attachment occurs within the sella turcica, below the diaphragma sellae, including the junction of the sella-pituitary gland (PG) with the pituitary stalk (PS, Panel 1a). PS-infundibulum (outer aspect): attachment to the solid portion of the PS and the outer aspect of the infundibulum-tuber cinereum (Panel 1b). Third ventricle floor (TVF): attachment to the entire thickness of the infundibulum-tuber cineveum (Panel 1c). TVF and walls: attachment to the TVF and third ventricle walls (Panel 1d). Third ventricle lining: attachment to the ependymal lining of the third ventricle (Panel 1e). Global: attachment to all above structures (Panel 1f). **Figure 2** Morphological patterns of CP adherence[24]. The orange area represents the tumor tissue, the green area represents the hypothalamus and the pituitary stalk, and the pink area is the adenohypophysis Pedicle pattern: the attachment consists of a narrow fibrovascular stem (Panel 2a). Sessile pattern: a wide patch of the tumor surface is attached to the anatomical structure (Panel 2b). Cap-like pattern: wide attachment between the upper third to upper half portion of a tumor pushing the TVF upward, which looks like wearing a hat (Panel 2c). Ring-like pattern: the attachment encircles the center of the tumor surface as a band (Panel 2d). Bowl-like pattern: wide attachment between the lower third to half portion of a tumor pushing the contiguous structures downward, like bowl (Panel 2e). Circumferential pattern: the attachment involves most of the tumor surface, usually as a very thin layer of nervous-gliotic tissue, like wrapping paper (Panel 2f).

经验的积累和手术技术的进步与发展,在此基础上又逐渐演化、分解出目前临床常用的4种经颅入路,包括前正中入路(经额下入路和经前纵裂入路)、前外侧入路(经翼点入路和经眶颧入路)、脑室内入路(经胼胝体穹隆间入路和经皮质脑室内入路)以及后外侧入路(经岩骨入路)[25]。尽管如此,仍有部分耳鼻咽喉科医师"钟情"于经蝶入路,而且随着显微外科和神经内镜技术的进步与发展,神经内镜辅助下经蝶入路行颅咽管瘤切除术也已成为许多神经外科医师的首选。颅咽管瘤手术治疗的宗旨是:最小程度损伤下丘脑、最大程度切除肿瘤,术者需根据肿瘤与周围神经血管的解剖关系、结合个人经验

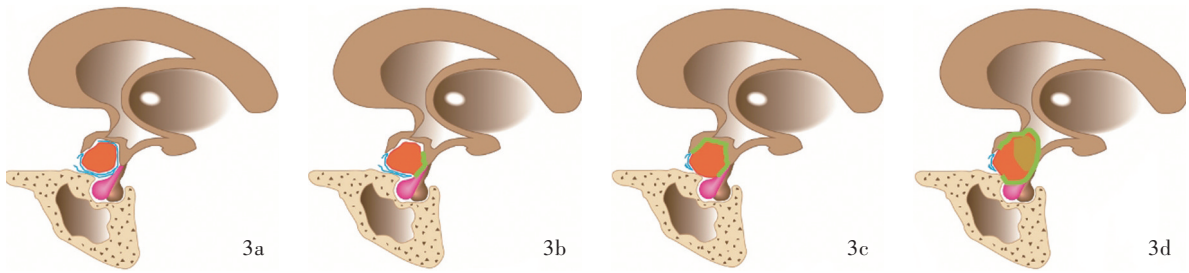


**图3**　颅咽管瘤粘连程度分型示意图(根据肿瘤与周围组织结构粘连程度共分为4型[24];橙色区域代表肿瘤组织,绿色区域代表下丘脑及垂体柄,粉色区域为腺垂体)　3a　疏松型:贴附疏松,术中通过轻柔牵拉或钝性分离即可剥离肿瘤与周围组织,同时完整保留正常组织结构　3b　紧密型:肿瘤与周围组织贴附紧密,需锐性分离方可剥离肿瘤与周围组织并保留正常组织结构　3c　融合型:肿瘤囊壁与周围组织结构沿贴附面相互融合,术中难以分离,即使谨慎锐性分离仍可造成正常组织结构损伤　3d　替换型:由于肿瘤细胞的侵袭,贴附于肿瘤的组织结构已丧失其完整性,无法辨认

**Figure 3**　Adhesion strength of CP[24]. The orange area represents the tumor tissue, the green area represents the hypothalamus and the pituitary stalk, and the pink area is the adenohypophysis　Loose adherence: the adherence is loose. The tumor can be easily separated from the attached structure by gentle tugging or by blunt dissection, preserving the integrity of the anatomical structure (Panel 3a). Tight adherence: the tumor adheres closely to the involved structure. Separation of the tumor requires the use of sharp dissection to preserve the integrity of the anatomical structure involved (Panel 3b). Fusion adherence: the CP capsule and the adjacent anatomical structure are fused together along the plane of attachment. No safe cleavage plane for tumor dissection can be identified, and even careful sharp dissection may cause damage to the normal tissue (Panel 3c). Replacement adherence: the anatomical structure adhered to the tumor has lost its integrity and is no longer recognizable, because it has been replaced or invaded by the CP (Panel 3d).

正确选择手术入路。近40余年来,研究者制定一系列关于颅咽管瘤与周围神经血管组织关系的解剖学分型[3,26-39],便于精准评估颅咽管瘤的解剖位置、确定手术入路。此部分内容重点阐述神经内镜技术广泛应用前后临床分析较多的颅咽管瘤分型及手术入路选择。

1.神经内镜广泛应用之前的手术入路选择和颅咽管瘤分型　在神经内镜广泛应用于颅咽管瘤手术之前,临床上主要根据Samii和Tatagiba[26]以及Morisako等[28]的颅咽管瘤解剖学分型选择手术入路。(1)Samii分型(1997年版):根据肿瘤纵向侵犯程度共分为鞍内型(Ⅰ型)、鞍上池型(Ⅱ型)、第三脑室下部型(Ⅲ型)、第三脑室上部型(Ⅳ型)和侧脑室透明隔型(Ⅴ型)共5种类型。2009年,Komotar等[25]在Samii和Tatagiba[26]颅咽管瘤解剖学分型基础上提出不同的手术入路适应证,其中经蝶入路主要适用于Samii分级Ⅰ~Ⅱ型(鞍内型和鞍上池型),避免或减少视路损伤是该入路的优点,但术后发生脑脊液漏的风险较高且不适宜蝶窦未气化的患儿;前正中入路(额下入路)以Samii分级Ⅲ~Ⅳ型(第三脑室内)为最佳适应证,可顺利通过终板到达第三脑室,但存在额窦开放的风险,对于存在视交叉前置的患儿手术难度较大;前外侧入路主要适用于肿瘤位于鞍内、鞍上、视交叉前或视交叉后的患儿,适应证较为广泛,即使存在视交叉前置者也可直接到达鞍上池,但该入路对肿瘤位于对侧视神经-颈内动脉三角、对侧颈内动脉后区域、同侧第三脑室后部区域者手术视野较差,然而,经眶颧入路(即扩大的前外侧入路)可通过移除部分眶上缘、颧弓,使经翼点入路手术的显露范围扩大,便于到达后床突、基底动脉尖端、鞍上区域,可提高上述区域肿瘤切除术的可操作性[27];后外侧入路(经岩骨入路)主要适用于较大的视交叉后病变,手术视野良好,与经额下入路相比,对前穿支动脉损伤较小;经脑室内入路(经胼胝体穹隆间入路)适用于脑室内病变,其优点是室间孔扩张,但可发生牵拉损伤;经侧脑室皮质造瘘入路以合并侧脑室扩大的第三脑室内病变为适应证,较经胼胝体穹隆间入路牵拉损伤小,但易造成皮质破坏并增加术后癫痫的发生风险[25]。(2)Morisako分型(2016年版)[28]:根据肿瘤所在位置共分为4种类型,分别为鞍内型、视交叉前型、视交叉后型和第三脑室内型(图4),据此分型,该作者提出不同的手术入路适应证。鞍内型病变以经蝶入路为宜;视交叉前型病变存在两种情况,病变向外侧延伸不明显者采用经蝶入路,病变明显向外侧延伸者以前外侧入路(尤其是经眶颧入路)为首选;视交叉后型病变也存在两种情况,若病变无明显钙化或最大直径<30毫米,经前外侧入路(尤其是经眶颧入路)较具优势,若病变呈明显钙化或最大直径>30毫米,以经后外侧入路(经岩骨入路)为宜;

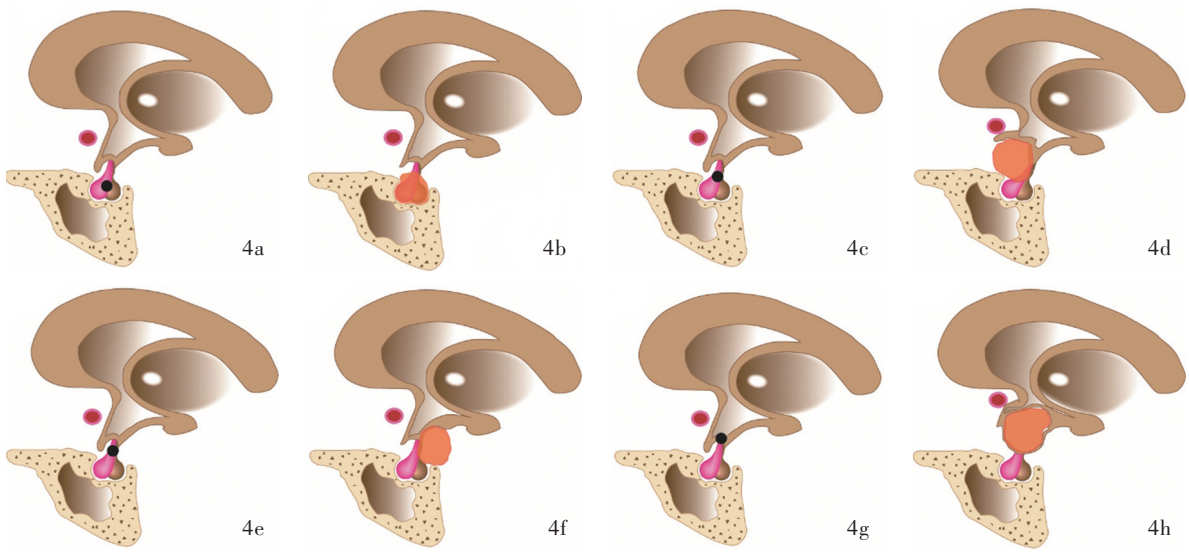


**图4** Morisako(2016年版)颅咽管瘤解剖学分型示意图(根据肿瘤所在位置共分为4型[28];橙色区域代表肿瘤组织,粉色区域代表腺垂体,黑点代表肿瘤起始点,红点代表前交通动脉) 4a,4b 鞍内型:肿瘤起源于垂体柄鞍内部分 4c,4d 视交叉前型:肿瘤起源于鞍上垂体柄前部,视交叉和前交通动脉均上抬 4e,4f 视交叉后型:肿瘤起源于鞍上垂体柄后部并主要向后生长,视交叉和前交通动脉位于正常解剖位置 4g,4h 第三脑室内型:肿瘤起源于第三脑室底

**Figure 4** Morisako 2016 anatomical classification of CP [28]. The orange areas represent the tumor tissue, the pink areas represent the adenohypophysis, the black dots indicate the tumor origin, the red dots indicate the anterior communicating artery Intrasellar type: the tumor originates from the intrasellar part of the pituitary stalk (Panel 4a, 4b). Prechiasmatic type: the tumor originates from the anterior part of the pituitary stalk and grows upward. Both of the optic chiasm and the anterior communicating artery are elevated upward in this lesion type (Panel 4c, 4d). Retrochiasmatic type: the tumor originates from the posterior part of the pituitary stalk and grows up toward the posterior fossa. Both of the optic chiasm and the anterior communicating artery remain in their normal positions (Panel 4e, 4f). Intra-third ventricle type: the tumor originates from the floor of the third ventricle (Panel 4g, 4h).

第三脑室内型病变选择前中入路(经额下入路和经前纵裂入路)最佳。

2.根据颅咽管瘤解剖学分型于神经内镜辅助下的经蝶入路 (1)Tang分型(2018年版)[29]:首先根据肿瘤与垂体柄关系分为中央型和偏侧型;然后再根据肿瘤在下丘脑-垂体柄轴上的起源点分为下丘脑垂体柄型、鞍上垂体柄型和鞍内垂体柄型3种亚型(图5,6)。内镜辅助下经蝶入路手术主要是利用视交叉-垂体柄间隙,手术过程采取双人四手操作,沿肿瘤生长轴直视肿瘤腹侧探查肿瘤起源,并于直视下剥离肿瘤与周围粘连的组织结构。一般情况下,对肿瘤起源部位呈"指套"样浸润的组织结构需采取锐性分离,而非肿瘤起源部位,肿瘤组织与周围组织结构多呈推挤、压迫关系,无浸润或粘连者,宜采取钝性分离,分离过程中应尽量保持解剖结构于原位,避免对下丘脑等重要结构过度牵拉,以4毫米口径的吸引器吸力较为安全[29]。(2)Lei分型(2021年版)[30]:分为鞍内型、鞍内-鞍上型、鞍上型、第三脑室型共4种类型,其中鞍内型、鞍内-鞍上型及鞍上型首选内镜辅助下经蝶入路,相比显微镜手术,内镜视角可以减少手术损伤并避免肿瘤残留。但是第三脑室型不宜采用内镜辅助下经蝶入路[30],应选择经颅入路手术为宜。(3)QST分型[31]:QST分型是漆松涛教授2011年提出的颅咽管瘤分型(图7),其对源于鞍膈下区域并紧密贴附于残留垂体腺的肿瘤称作Q型;起源于垂体柄中下段,并且主要向鞍上池内延伸的肿瘤称作S型;起源于漏斗灰结节部并与下丘脑紧密贴附者称作T型。此外,漆松涛教授研究团队还详细对比分析内镜下经蝶入路和显微镜下经颅入路的优劣[32]:认为Q型肿瘤采用经蝶入路可以提供更为直观、清晰的视角,并且在手术初期即可于鞍内分离出肿瘤起源点,更易完整切除肿瘤并保留残留垂体组织;反之,经颅入路处理鞍内病变易出现手术视野盲点,因此经颅入路切除Q型颅咽管瘤,术后发生垂体功能低下的风险远高于经蝶入路。S型肿瘤经蝶入路和经颅入路均可到达病灶起源点,两种入路的病变全切率、复发率及术后并发垂体功能低下的概率相当;但内镜下经蝶入路可以提供更加清晰的手术视野,术中可以更好地保护视神经和穿支动脉,与显微镜下经颅入路相

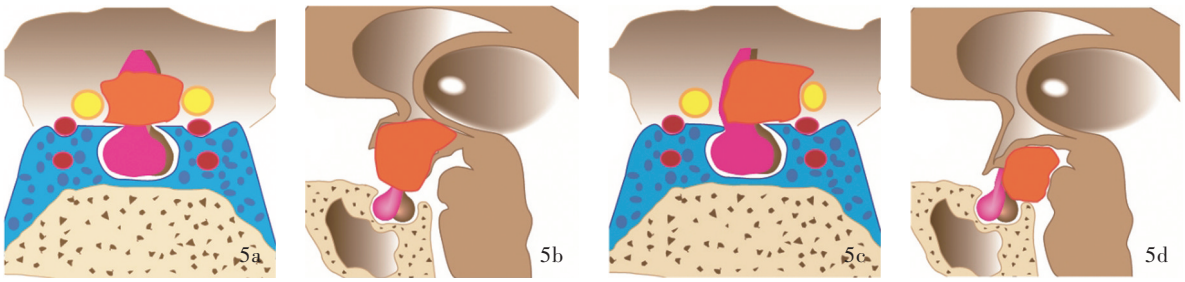


**图5**　神经内镜辅助手术的颅咽管瘤Tang分型(2018年版)示意图(根据肿瘤与垂体柄关系分型[29];橙色区域代表肿瘤组织,黄点代表视神经,粉色区域代表腺垂体,红点代表颈内动脉,蓝色区域代表海绵窦)　5a,5b　中央型:肿瘤于下丘脑-垂体柄轴内居中生长,无法观察到明确的起源点　5c,5d　偏侧型:肿瘤沿下丘脑-垂体柄轴偏外侧生长,垂体被推向肿瘤一侧(前、后、左、右均可),于下丘脑-垂体柄轴可见明确的肿瘤起源点

**Figure 5**　The novel endoscopic classification of CP (Tang 2018)[29]. The orange areas represent tumor tissue, the yellow dots indicate the optic nerve, the pink areas represent adenohypophysis, the red dots indicate the internal carotid artery, the blue areas represent the cavernous sinus　Central type CP grows within and along the hypothalamic-pituitary stalk axis and no pedicle or definite origin site can be identified (Panel 5a, 5b). Peripheral type CP arises from the hypothalamic-pituitary stalk axis but expands and grows laterally in an exophytic pattern, the pituitary is usually displaced to circumferential surface of the tumor (Panel 5c, 5d).

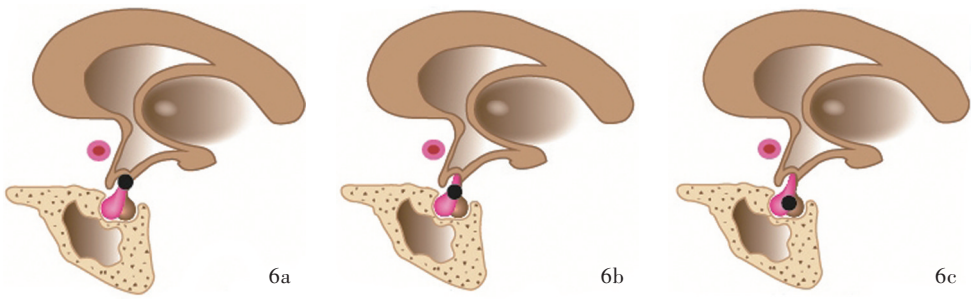


**图6**　神经内镜辅助手术的颅咽管瘤Tang分型(2018年版)示意图(根据肿瘤在下丘脑-垂体柄轴上的起源点分为3型[29];红点代表前交通动脉,黑点代表肿瘤起源点,粉色区域代表腺垂体)　6a　下丘脑垂体柄型:肿瘤起源于漏斗-灰结节,可向上扩展生长侵入第三脑室和(或)向下扩展进入鞍上池　6b　鞍上垂体柄型:肿瘤起源于垂体柄鞍上池部分,以鞍上池下段更为常见,于鞍上池第三脑室外生长　6c　鞍内垂体柄型:肿瘤起源于垂体柄鞍内部分,可向上生长或向蝶窦、海绵窦方向生长

**Figure 6**　The novel endoscopic classification in different origin sites of 3 subtypes of peripheral CP (Tang 2018) along the hypothalamic-pituitary stalk axis[29]. The red dots indicate the anterior communicating artery, the black spots indicate the tumor origin, the pink areas represent adenohypophysis　Hypothalamic stalk CP originates from the infundibulum-tuber cinereum, which usually extends up to the third ventricle and/or down to the suprasellar (Panel 6a). Suprasellar stalk CP derives from pituitary stalk suprasellar segment, usually low portion of the suprasellar, and commonly locates extraventriclely (Panel 6b). Intrasellar stalk CP originates from the part of pituitary stalk under diaphragma, which may grow upward, or toward the sphenoid sinus and cavernous sinus (Panel 6c).

比,内镜下经蝶入路可以更好地改善视神经功能、降低视神经损伤风险。T型肿瘤于内镜下经蝶入路虽然可降低视交叉后手术操作时视神经损伤的风险,但因缺少第三脑室底的保护措施,可使下丘脑损伤风险增加,故对于此类型的颅咽管瘤患者更提倡显微镜下经颅入路手术。有研究显示,内镜下经蝶入路切除颅咽管瘤不仅能够较好地保留视神经功能,且术后较少发生尿崩症、下丘脑肥胖等并发症,但术后脑脊液漏的发生风险较高[33],随着颅底重建技术的不断进步,尤其是带蒂鼻中隔黏膜瓣的广泛应用使脑脊液漏的发生风险大大降低[30]。尽管在内镜技术的辅助下经蝶入路已经适用于绝大多数类型的颅咽管瘤,但对于合并远外侧延伸型和第三脑室内型的患儿仍非适应证,对于前者,由于经蝶入路存在手术盲点,选择显微镜下经颅入路更为适宜[30],而后者,需符合以下5项影像学标准者方可行经蝶入路的激进性治疗:垂体柄完好且大小正常,从垂体腺延伸出;蝶鞍内无肿瘤;视交叉池显影良好;乳头体角<60°;冠状位扫描下丘脑位于肿瘤1/3以下[40]。

## 四、基于颅咽管瘤的分子分型与精准治疗

目前颅咽管瘤的分子分型研究尚处于初级阶段,鉴于PCP与周围组织边界清晰、易于分离且主要发生于成人,此节仅对好发于儿童的ACP的分子分型研究进展进行概述。

截止目前,针对*CTNNB1*基因变异的ACP分子

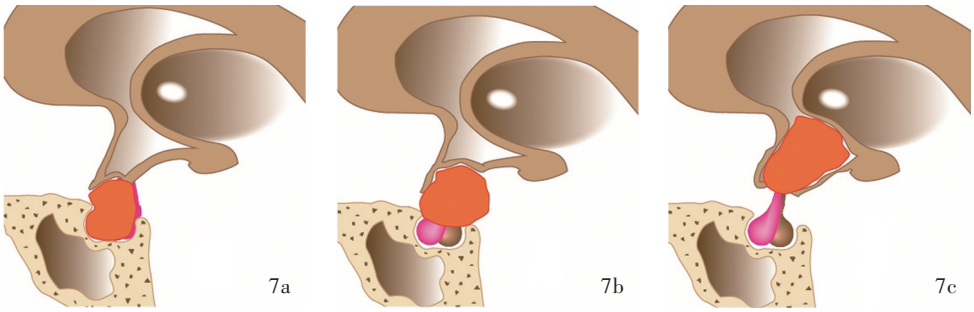


**图7** 颅咽管瘤QST分型[31](橙色区域代表肿瘤组织,粉色区域代表腺垂体) 7a Q型:肿瘤起源于鞍膈下区域 7b S型:肿瘤起源于鞍上垂体柄区域 7c T型:肿瘤起源于漏斗-灰结节

**Figure 7** The CP of QST classification[31]. The orange areas represent the tumor tissue, and the pink areas indicate the adenohypophysis Type Q of CP originates below the diaphragmatic area (Panel 7a). Type S of CP originates from the pituitary talk area (Panel 7b). Type T of CP originates from the infundibulum-tuber cinereum (Panel 7c).

靶向治疗的尝试无一获得成功。尽管*CTNNB1*基因变异被视为ACP的始动因素,但有研究表明仍存在野生型病变,不过尚无足够的临床数据支持[40-41]。有学者尝试将ACP分为野生型和突变型,其中针对RNA序列的研究提示,ACP野生型与突变型之间存在明显的异质性,但转录组和DNA甲基化分析则显示二者之间无明显差异[42]。鉴于基因分子分型的失败,有学者则开始探索通过其他靶点的治疗以控制肿瘤细胞进展。晚近研究发现,颅咽管瘤囊壁细胞表达细胞程序性死亡蛋白配体1(PDL1),细胞程序性死亡蛋白1(PD1)则在β-连环蛋白核内聚集的螺纹样细胞内表达,提示PD1/PDL1免疫检查点靶向治疗颅咽管瘤具有潜在临床价值[43],但是具体何种类型患儿可以从治疗中获益,尚待进一步确定。Yuan等[44]经检索公共数据库GSE60815和GSE94349(http://www.ncbi.nlm.gov/geo)共获得39例ACP患儿的RNA数据,并通过筛查和分析将其中725种与APC相关的免疫学基因分为两种类型,即免疫抵抗型和免疫基因型,其结果显示,这两种免疫学基因类型对免疫检测点阻断(ICB)治疗的反应效果有所不同。目前认为,Yuan等[44]的分类仅是一种基于生物信息学的分类,既未与影像学或组织学等临床数据进行对比分析,亦未在临床实践中加以验证,而且该分型并未阐明这两种分型与ACP基因驱动路径之间的关系[45-47]。因此许多学者悲观地认为,无法基于RNA组学对ACP进行分型[48],但最近发表的一项研究提出一种新的分型,即基于蛋白质组学和磷酸蛋白组学理论将肿瘤细胞分为免疫耐受型和免疫原型[49],根据这一新的分型方法,免疫原型肿瘤细胞MAPK/细胞外信号调节激酶(MEK)路径的蛋白质谱改变类似既往发现的*BRAF* V600E基因变异表达,提示MEK路径抑制剂对ACP治疗可能有效[42,50]。

最近林志雄教授研究团队对143例颅咽管瘤患者共151份标本进行全外显子组测序(WES),并对其中84例行RNA测序、95例行DNA甲基化分析(全球最大宗资料)[13],结果显示,ACP在RNA层面存在完全不同的分子分型,并与甲基化分型相一致,即ACP存在3种不同分子亚型,分别为WNT型、ImA型和ImB型。其中,WNT型可通过Wnt/β-连环蛋白通路被过度激活;而ImA型和ImB型则免疫浸润程度更高,但ImA型呈现明显的神经胶质增生反应。通过免疫组化和蛋白质谱分析已证实这3种亚型的分子特征;CT和MRI观察,WNT型以实性成分为主,而ImA型和ImB型则以囊性成分为主;预后统计,WNT型患者几乎无复发,生存期明显长于ImB型,多因素Cox回归分析提示,该分型是除肿瘤切除程度外最显著的预后预测因子;根据TIDE(tumor immune dysfunction and exclusion)模型预测,3种亚型中以ImA型从免疫抑制剂治疗中获益最大,而WNT型呈现免疫排斥状态;单样本基因富集分析(GSEA)显示,唯有ImA型和ImB型样本中富集干扰素-α响应通路,与临床试验结果的回顾分析一致:干扰素-α仅在以囊性成分为主的ACP中出现治疗反应。

虽然,目前尚无有关PCP的分子分型报道,但针对其的靶向治疗业已取得进展[51-52],故有学者认为已经进入肿瘤精准治疗的时代[53]。

综上所述,颅咽管瘤的组织学和解剖学分型对制定手术方案、选择手术入路是不可或缺的,未来

颅咽管瘤新分型应为融合组织学、解剖学、分子分型的精准化分型，唯有如此，方能对制定手术方案、选择手术入路以及各项辅助治疗（放疗、化疗或联合治疗）有益，从而实现颅咽管瘤的精准治疗。

**利益冲突** 无

## 参 考 文 献


[1] Zhu L, Zhang L, Hu W, Chen H, Li H, Wei S, Chen X, Ma X. A multi-task two-path deep learning system for predicting the invasiveness of craniopharyngioma [J]. Comput Methods Programs Biomed, 2022, 216:106651.

[2] Pascual JM, Prieto R. Harvey Cushing and pituitary Case Number 3 (Mary D.): the origin of this most baffling problem in neurosurgery[J]. Neurosurg Focus, 2016, 41:E6.

[3] Prieto R, Rosdolsky M, Hofecker V, Barrios L, Pascual JM. Craniopharyngioma treatment: an updated summary of important clinicopathological concepts[J]. Expert Rev Endocrinol Metab, 2020, 15:261-282.

[4] Yu SP, Ming HL, Ren BC, Lin Y, Zhang C, Li T, Yang XJ. Summary of each WHO Classification of Tumors of the Central Nervous System prior to the fifth edition[J]. Zhongguo Xian Dai Shen Jing Ji Bing Za Zhi, 2021, 21:725-745.[于圣平, 明浩朗, 任炳成, 林雨, 张辰, 李涛, 杨学军. 世界卫生组织中枢神经系统肿瘤分类第一版至第四版修订版提要[J]. 中国现代神经疾病杂志, 2021, 21:725-745.]

[5] Müller HL, Merchant TE, Warmuth-Metz M, Martinez-Barbera JP, Puget S. Craniopharyngioma [J]. Nat Rev Dis Primers, 2019, 5:75.

[6] Henderson F Jr, Schwartz TH. Update on management of craniopharyngiomas[J]. J Neurooncol, 2022, 156:97-108.

[7] Gaston-Massuet C, Andoniadou CL, Signore M, Jayakody SA, Charolidi N, Kyeyune R, Vernay B, Jacques TS, Taketo MM, Le Tissier P, Dattani MT, Martinez-Barbera JP. Increased Wingless (Wnt) signaling in pituitary progenitor/stem cells gives rise to pituitary tumors in mice and humans[J]. Proc Natl Acad Sci USA, 2011, 108:11482-11487.

[8] Brastianos PK, Taylor-Weiner A, Manley PE, Jones RT, Dias-Santagata D, Thorner AR, Lawrence MS, Rodriguez FJ, Bernardo LA, Schubert L, Sunkavalli A, Shillingford N, Calicchio ML, Lidov HG, Taha H, Martinez-Lage M, Santi M, Storm PB, Lee JY, Palmer JN, Adappa ND, Scott RM, Dunn IF, Laws ER Jr, Stewart C, Ligon KL, Hoang MP, Van Hummelen P, Hahn WC, Louis DN, Resnick AC, Kieran MW, Getz G, Santagata S. Exome sequencing identifies BRAF mutations in papillary craniopharyngiomas[J]. Nat Genet, 2014, 46:161-165.

[9] Goschzik T, Gessi M, Dreschmann V, Gebhardt U, Wang L, Yamaguchi S, Wheeler DA, Lauriola L, Lau CC, Müller HL, Pietsch T. Genomic alterations of adamantinomatous and papillary craniopharyngioma [J]. J Neuropathol Exp Neurol, 2017, 76:126-134.

[10] Yoshimoto K, Hatae R, Suzuki SO, Hata N, Kuga D, Akagi Y, Amemiya T, Sangatsuda Y, Mukae N, Mizoguchi M, Iwaki T, Iihara K. High-resolution melting and immunohistochemical analysis efficiently detects mutually exclusive genetic alterations of adamantinomatous and papillary craniopharyngiomas [J]. Neuropathology, 2018, 38:3-10.

[11] Jucá CEB, Colli LM, Martins CS, Campanini ML, Paixão B, Jucá RV, Saggioro FP, de Oliveira RS, Moreira AC, Machado HR, Neder L, Antonini SR, de Castro M. Impact of the canonical Wnt pathway activation on the pathogenesis and prognosis of adamantinomatous craniopharyngiomas [J]. Horm Metab Res, 2018, 50:575-581.

[12] Apps JR, Stache C, Gonzalez-Meljem JM, Gutteridge A, Chalker J, Jacques TS, Forshew T, Hölsken A, Martinez-Barbera JP. CTNNB1 mutations are clonal in adamantinomatous craniopharyngioma[J]. Neuropathol Appl Neurobiol, 2020, 46:510-514.

[13] Wang X, Zhao C, Lin J, Liu H, Zeng Q, Chen H, Wang Y, Xu D, Chen W, Xu M, Zhang E, Lin D, Lin Z. Multi-omics analysis of adamantinomatous craniopharyngiomas reveals distinct molecular subgroups with prognostic and treatment response significance[J]. Chin Med J (Engl), 2023.[Epub ahead of print]

[14] Borrill R, Cheesman E, Stivaros S, Kamaly-Asl ID, Gnanalingham K, Kilday JP. Papillary craniopharyngioma in a 4-year-old girl with BRAF V600E mutation: a case report and review of the literature[J]. Childs Nerv Syst, 2019, 35:169-173.

[15] Passos J, Quidet M, Brahimi A, Flament C, Gibier JB, Caron S, Maurage CA, Buisine MP, Perbet R. Familial adenomatous polyposis associated craniopharyngioma secondary to both germline and somatic mutations in the APC gene [J]. Acta Neuropathol, 2020, 140:967-969.

[16] Schlaffer SM, Buchfelder M, Stoehr R, Buslei R, Hölsken A. Rathke's cleft cyst as origin of a pediatric papillary craniopharyngioma[J]. Front Genet, 2018, 9:49.

[17] Takagi K, Kikuchi K, Hiwatashi A, Togao O, Sangatsuda Y, Kuga D, Mizoguchi M, Yamamoto H, Iwaki T, Ishigami K. Papillary craniopharyngioma coexisting with an intratumoral abscess in a pediatric patient: a case report and review of the literature[J]. Acta Radiol Open, 2021, 10:20584601211030661.

[18] Zhao C, Zhou Z, Zhang Y, Qi X, Wang X, Lin D, Liu H, Wang Y, Weng C, Chen J, Hu W, Liao L, Lin Z. Diagnosis and management of pediatric papillary craniopharyngiomas [J]. World Neurosurg, 2022, 165:e148-158.

[19] 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.]

[20] Mortini P, Gagliardi F, Boari N, Losa M. Surgical strategies and modern therapeutic options in the treatment of craniopharyngiomas[J]. Crit Rev Oncol Hematol, 2013, 88:514-529.

[21] Qi S. Understanding treatment options in craniopharyngioma better[J]. Nat Rev Dis Primers, 2020, 6:28.

[22] Puget S, Garnett M, Wray A, Grill J, Habrand JL, Bodaert N, Zerah M, Bezerra M, Renier D, Pierre-Kahn A, Sainte-Rose C. Pediatric craniopharyngiomas: classification and treatment according to the degree of hypothalamic involvement [J]. J Neurosurg, 2007, 106(1 Suppl):3-12.

[23] Hori T. What is the role of radiosurgery in the management of sellar tumors[J]? Acta Neurochir Suppl, 2013, 116:45-48.

[24] Prieto R, Pascual JM, Rosdolsky M, Castro-Dufourny I, Carrasco R, Strauss S, Barrios L. Craniopharyngioma adherence: a comprehensive topographical categorization and outcome-related risk stratification model based on the methodical examination of 500 tumors[J]. Neurosurg Focus, 2016, 41:E13.

[25] Komotar RJ, Roguski M, Bruce JN. Surgical management of craniopharyngiomas[J]. J Neurooncol, 2009, 92:283-296.

[26] Samii M, Tatagiba M. Surgical management of craniopharyngiomas: a review [J]. Neurol Med Chir (Tokyo), 1997, 37:141-149.

[27] Gonzalez LF, Crawford NR, Horgan MA, Deshmukh P, Zabramski JM, Spetzler RF. Working area and angle of attack in three cranial base approaches: pterional, orbitozygomatic, and maxillary extension of the orbitozygomatic approach [J]. Neurosurgery, 2002, 50:550-555.

[28] Morisako H, Goto T, Goto H, Bohoun CA, Tamrakar S, Ohata K. Aggressive surgery based on an anatomical subclassification of craniopharyngiomas[J]. Neurosurg Focus, 2016, 41:E10.

[29] Tang B, Xie SH, Xiao LM, Huang GL, Wang ZG, Yang L, Yang XY, Xu S, Chen YY, Ji YQ, Zeng EM, Hong T. A novel endoscopic classification for craniopharyngioma based on its origin[J]. Sci Rep, 2018, 8:10215.

[30] Lei C, Chuzhong L, Chunhui L, Peng Z, Jiwei B, Xinsheng W, Yazhuo Z, Songbai G. Approach selection and outcomes of craniopharyngioma resection: a single - institute study [J]. Neurosurg Rev, 2021, 44:1737-1746.

[31] Fan J, Liu Y, Pan J, Peng Y, Peng J, Bao Y, Nie J, Wang C, Qiu B, Qi S. Endoscopic endonasal versus transcranial surgery for primary resection of craniopharyngiomas based on a new QST classification system: a comparative series of 315 patients [J]. J Neurosurg, 2021.[Epub ahead of print]

[32] Qi S, Lu Y, Pan J, Zhang X, Long H, Fan J. Anatomic relations of the arachnoidea around the pituitary stalk: relevance for surgical removal of craniopharyngiomas [J]. Acta Neurochir (Wien), 2011, 153:785-796.

[33] Marx S, Tsavdaridou I, Paul S, Steveling A, Schirmer C, Eördögh M, Nowak S, Matthes M, El Refaee E, Fleck SK, Baldauf J, Lerch MM, Stahl A, Hosemann W, Schroeder HWS. Quality of life and olfactory function after suprasellar craniopharyngioma surgery: a single - center experience comparing transcranial and endoscopic endonasal approaches [J]. Neurosurg Rev, 2021, 44:1569-1582.

[34] Cao L, Wu W, Kang J, Cai K, Li C, Liu C, Zhu H, Gen S, Zhang Y, Gui S. Feasibility of endoscopic endonasal resection of intrinsic third ventricular craniopharyngioma in adults [J]. Neurosurg Rev, 2022, 45:1-13.

[35] Tang B, Xie S, Huang G, Wang Z, Yang L, Yang X, Xu S, Zeng E, Hong T. Clinical features and operative technique of transinfundibular craniopharyngioma [J]. J Neurosurg, 2019. [Epub ahead of print]

[36] Hu W, Qiu B, Mei F, Mao J, Zhou L, Liu F, Fan J, Liu Y, Wen G, Qi S, Bao Y, Pan J. Clinical impact of craniopharyngioma classification based on location origin: a multicenter retrospective study[J]. Ann Transl Med, 2021, 9:1164.

[37] Jeswani S, Nuño M, Wu A, Bonert V, Carmichael JD, Black KL, Chu R, King W, Mamelak AN. Comparative analysis of outcomes following craniotomy and expanded endoscopic endonasal transsphenoidal resection of craniopharyngioma and related tumors: a single-institution study[J]. J Neurosurg, 2016, 124:627-638.

[38] Prieto R, Pascual JM, Castro-Dufourny I, Carrasco R, Barrios L. Craniopharyngioma: surgical outcome as related to the degree of hypothalamic involvement[J]. World Neurosurg, 2017, 104:1006-1010.

[39] Almeida JP, Workewych A, Takami H, Velasquez C, Oswari S, Asha M, Bernardo A, Gentili F. Surgical anatomy applied to the resection of craniopharyngiomas: anatomic compartments and surgical classifications [J]. World Neurosurg, 2020, 142: 611-625.

[40] Omay SB, Chen YN, Almeida JP, Ruiz-Treviño AS, Boockvar JA, Stieg PE, Greenfield JP, Souweidane MM, Kacker A, Pisapia DJ, Anand VK, Schwartz TH. Do craniopharyngioma molecular signatures correlate with clinical characteristics[J]? J Neurosurg, 2018, 128:1473-1478.

[41] Hara T, Akutsu H, Takano S, Kino H, Ishikawa E, Tanaka S, Miyamoto H, Sakamoto N, Hattori K, Sakata-Yanagimoto M, Chiba S, Hiyama T, Masumoto T, Matsumura A. Clinical and biological significance of adamantinomatous craniopharyngioma with CTNNB1 mutation[J]. J Neurosurg, 2018, 131:217-226.

[42] Apps JR, Carreno G, Gonzalez-Meljem JM, Haston S, Guiho R, Cooper JE, Manshaei S, Jani N, Hölsken A, Pettorini B, Beynon RJ, Simpson DM, Fraser HC, Hong Y, Hallang S, Stone TJ, Virasami A, Donson AM, Jones D, Aquilina K, Spoudeas H, Joshi AR, Grundy R, Storer LCD, Korbonits M, Hilton DA, Tossell K, Thavaraj S, Ungless MA, Gil J, Buslei R, Hankinson T, Hargrave D, Goding C, Andoniadou CL, Brogan P, Jacques TS, Williams HJ, Martinez-Barbera JP. Tumour compartment transcriptomics demonstrates the activation of inflammatory and odontogenic programmes in human adamantinomatous craniopharyngioma and identifies the MAPK/ERK pathway as a novel therapeutic target[J]. Acta Neuropathol, 2018, 135:757-777.

[43] Coy S, Rashid R, Lin JR, Du Z, Donson AM, Hankinson TC, Foreman NK, Manley PE, Kieran MW, Reardon DA, Sorger PK, Santagata S. Multiplexed immunofluorescence reveals potential PD-1/PD-L1 pathway vulnerabilities in craniopharyngioma[J]. Neuro Oncol, 2018, 20:1101-1112.

[44] Yuan F, Cai X, Zhu J, Yuan L, Wang Y, Tang C, Cong Z, Ma C. A novel immune classification for predicting immunotherapy responsiveness in patients with adamantinomatous craniopharyngioma[J]. Front Neurol, 2021, 12:704130.

[45] Goldman S, Pollack IF, Jakacki RI, Billups CA, Poussaint TY, Adesina AM, Panigrahy A, Parsons DW, Broniscer A, Robinson GW, Robison NJ, Partap S, Kilburn LB, Onar-Thomas A, Dunkel IJ, Fouladi M. Phase Ⅱ study of peginterferon alpha-2b for patients with unresectable or recurrent craniopharyngiomas: a Pediatric Brain Tumor Consortium report [J]. Neuro Oncol, 2020, 22:1696-1704.

[46] Kilday JP, Caldarelli M, Massimi L, Chen RH, Lee YY, Liang ML, Parkes J, Naiker T, van Veelen ML, Michiels E, Mallucci C, Pettorini B, Meijer L, Dorfer C, Czech T, Diezi M, Schouten-van Meeteren AYN, Holm S, Gustavsson B, Benesch M, Müller HL, Hoffmann A, Rutkowski S, Flitsch J, Escherich G, Grotzer M, Spoudeas HA, Azquikina K, Capra M, Jiménez-Guerra R, MacDonald P, Johnston DL, Dvir R, Constantini S, Kuo MF, Yang SH, Bartels U. Intracystic interferon-alpha in pediatric craniopharyngioma patients: an international multicenter assessment on behalf of SIOPE and ISPN [J]. Neuro Oncol, 2017, 19:1398-1407.

[47] Bartels U, Laperriere N, Bouffet E, Drake J. Intracystic therapies for cystic craniopharyngioma in childhood [J]. Front Endocrinol (Lausanne), 2012, 3:39.

[48] Prince E, Whelan R, Donson A, Staulcup S, Hengartner A, Vijmasi T, Agwu C, Lillehei KO, Foreman NK, Johnston JM, Massimi L, Anderson RCE, Souweidane MM, Naftel RP, Limbrick DD, Grant G, Niazi TN, Dudley R, Kilburn L, Jackson EM, Jallo GI, Ginn K, Smith A, Chern JJ, Lee A, Drapeau A, Krieger MD, Handler MH, Hankinson TC; Advancing Treatment for Pediatric Craniopharyngioma Consortium. Transcriptional analyses of adult and pediatric adamantinomatous craniopharyngioma reveals similar expression signatures regarding potential therapeutic targets [J]. Acta Neuropathol Commun, 2020, 8:68.

[49] Petralia F, Tignor N, Reva B, Koptyra M, Chowdhury S, Rykunov D, Krek A, Ma W, Zhu Y, Ji J, Calinawan A, Whiteaker JR, Colaprico A, Stathias V, Omelchenko T, Song X,

Raman P, Guo Y, Brown MA, Ivey RG, Szpyt J, Guha Thakurta S, Gritsenko MA, Weitz KK, Lopez G, Kalayci S, Gümüş ZH, Yoo S, da Veiga Leprevost F, Chang HY, Krug K, Katsnelson L, Wang Y, Kennedy JJ, Voytovich UJ, Zhao L, Gaonkar KS, Ennis BM, Zhang B, Baubet V, Tauhid L, Lilly JV, Mason JL, Farrow B, Young N, Leary S, Moon J, Petyuk VA, Nazarian J, Adappa ND, Palmer JN, Lober RM, Rivero-Hinojosa S, Wang LB, Wang JM, Broberg M, Chu RK, Moore RJ, Monroe ME, Zhao R, Smith RD, Zhu J, Robles AI, Mesri M, Boja E, Hiltke T, Rodriguez H, Zhang B, Schadt EE, Mani DR, Ding L, Iavarone A, Wiznerowicz M, Schürer S, Chen XS, Heath AP, Rokita JL, Nesvizhskii AI, Fenyö D, Rodland KD, Liu T, Gygi SP, Paulovich AG, Resnick AC, Storm PB, Rood BR, Wang P; Children's Brain Tumor Network, Clinical Proteomic Tumor Analysis Consortium. Integrated proteogenomic characterization across major histological types of pediatric brain cancer[J]. Cell, 2020, 183:1962-1985.e31.

[50] Patel K, Allen J, Zagzag D, Wisoff J, Radmanesh A, Gindin T, Nicolaides T. Radiologic response to MEK inhibition in a patient with a WNT-activated craniopharyngioma[J]. Pediatr Blood Cancer, 2021, 68:e28753.

[51] Fasano M, Della Corte CM, Caterino M, Pirozzi M, Rauso R, Troiani T, Martini G, Napolitano S, Morgillo F, Ciardiello F. Dramatic therapeutic response to dabrafenib plus trametinib in BRAF V600E mutated papillary craniopharyngiomas: a case report and literature review[J]. Front Med (Lausanne), 2022, 8:652005.

[52] Brastianos PK, Twohy E, Geyer S, Gerstner ER, Kaufmann TJ, Tabrizi S, Kabat B, Thierauf J, Ruff MW, Bota DA, Reardon DA, Cohen AL, De La Fuente MI, Lesser GJ, Campian J, Agarwalla PK, Kumthekar P, Mann B, Vora S, Knopp M, Iafrate AJ, Curry WT Jr, Cahill DP, Shih HA, Brown PD, Santagata S, Barker FG 2nd, Galanis E. BRAF-MEK inhibition in newly diagnosed papillary craniopharyngiomas[J]. N Engl J Med, 2023, 389:118-126.

[53] Blakeley JO, Shannon K. Precision oncology for papillary craniopharyngioma[J]. N Engl J Med, 2023, 389:179-181.

（收稿日期：2023-04-28）
（本文编辑：袁云）

·小词典·

## 中英文对照名词词汇（五）

细胞外囊泡 extracellular vesicles（EVs）
细胞外信号调节激酶 extracellular signal-regulated kinase（ERK）
下丘脑-垂体-肾上腺 hypothalamic-pituitary-adrenal（HPA）
纤维蛋白原 fibrinogen（FIB）
纤维母细胞生长因子 fibroblast growth factor（FGF）
线粒体外膜 outer mitochondrial membrane（OMM）
腺苷酸活化蛋白激酶 adenosine monophosphate-activated protein kinase（AMPK）
Ras相关GTP结合蛋白7 Ras-related GTP binding protein 7（Rab7）
ATG8相互作用基序 ATG8-interacting motifs（AIM）
LC3相互作用区域 LC3 interacting region（LIR）
90项症状清单 Symptom Checklist 90（SCL-90）
小干扰RNA small interfering RNA（siRNA）
小鼠胚胎纤维母细胞 mouse embryonic fibroblast（MEF）
信号转导与转录激活因子3 signal transducer and activator of transcription 3（STAT3）
选择性5-羟色胺再摄取抑制剂 selective serotonin reuptake inhibitor（SSRI）
血栓弹力图 thrombelastography（TEG）
牙釉质细胞瘤型颅咽管瘤 adamantinomatous craniopharyngioma（ACP）
UNC-51样激酶1 UNC-51-like kinase 1（ULK1）
Toll样受体4 Toll-like receptor 4（TLR4）
游离三碘甲状腺原氨酸 free tri-iodothyronine（$FT_3$）
PTEN诱导激酶1 PTEN induced putative kinase 1（PINK1）
运动诱发电位 motor-evoked potential（MEP）
脂多糖 lipopolysaccharide（LPS）
植物状态/无反应觉醒综合征 vegetative state/unresponsive awakening syndrome（VS/UWS）
肿瘤坏死因子-α tumor necrosis factor-α（TNF-α）
肿瘤坏死因子受体 tumor necrosis factor receptor（TNFR）
肿瘤坏死因子受体相关因子 tumor necrosis factor receptor-associated factor（TRAF）
肿瘤相关巨噬细胞 tumour-associated macrophages（TAMs）
重症监护病房 intensive care unit（ICU）
转化生长因子β活化激酶1 transforming growth factor-β activated kinase 1（TAK1）
自身免疫性脑炎 autoimmune encephalitis（AE）
自噬相关16样蛋白1 autophagy related protein 16 like protein 1（ATG16L1）
自噬相关蛋白13 autophagy-related protein 13（ATG13）
组蛋白去乙酰化酶6 histone deacetylase 6（HDAC6）
最大似然估计法 mum likelihod estimation（MLE）
做作性障碍 factitious disorder（FD）