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成人颅内生殖细胞瘤1例报告伴文献复习

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摘 要

目的：探讨颅内生殖细胞肿瘤(Intracranial Germ Cell Tumors, iGCTs)的临床特点、诊断及治疗策略。方法：回顾性分析1例37岁男性松果体生殖细胞瘤(germinoma)患者的临床资料，并结合文献复习总结其诊疗经验。结果：患者因复视伴头晕入院，术后病理确诊生殖细胞瘤，术后接受全脑全脊髓照射治疗(Craniospinal Irradiation, CSI)，肿瘤控制良好。结论：成人颅内生殖细胞肿瘤较为罕见，生殖细胞瘤是其常见的病理类型，对放疗高度敏感，全脑全脊髓照射治疗可取得良好疗效。然而，成人患者最佳放疗范围和剂量尚缺乏统一标准，仍需进一步研究与长期随访。

关键词

颅内生殖细胞肿瘤，生殖细胞瘤，松果体区肿瘤，全脑全脊髓照射，全脑室照射，新辅助化疗

Intracranial Germ Cell Tumors in Adults: A Case Report and Literature Review

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Abstract

Objective: To investigate the clinical features, diagnosis and treatment strategies of Intracranial Germ Cell Tumors (iGCTs). Methods: We retrospectively analyzed the clinical data of a 37-year-old male patient with a pineal region germinoma and summarized the experience of diagnosis and treatment by reviewing the literature. Results: The patient was admitted to the hospital due to diplopia and dizzi-

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ness. Postoperative pathology confirmed germinoma. Following craniospinal irradiation, the tumor was well controlled. Conclusions: Adult intracranial germinoma is rare, and germinoma is a common pathological type, highly sensitive to radiotherapy. Craniospinal irradiation achieves excellent local control. Nevertheless, the optimal radiation strategy in adults remains controversial, highlighting the need for individualized treatment and long-term surveillance.

Keywords

Intracranial Germ Cell Tumors, Germinoma, Pineal Region Tumors, Craniospinal Irradiation, Whole Ventricular Irradiation, Neoadjuvant Chemotherapy

1. 引言

颅内生殖细胞肿瘤是一种罕见的恶性肿瘤，发病率约为 0.08 例/10 万[1]。发病有显著的年龄、性别差异，好发于儿童和青少年，青春期前后是发病的高峰期，男性发病率显著高于女性[1] [2]。生殖细胞瘤是颅内生殖细胞肿瘤最常见病理类型，通常累及大脑中线区域，包括鞍区，松果体区以及基底节区，松果体区是最常见的受累部位[3]。我们治疗 1 例罕见的成人松果体区生殖细胞瘤患者，结合文献回顾，评估现有治疗方案的合理性。

2. 病例资料

患者男性，37 岁，因“复视伴头晕 1 年”2024 年 11 月入院。患者 1 年前无明显诱因下出现复视，伴间断性头晕，症状持续未缓解。2024 年 11 月 11 日来绍兴市人民医院眼科就诊，头颅 MRI 检查显示松果体区占位，伴有脑积水和侧脑室旁间质性脑水肿。神经外科会诊后收入住院。患者既往体健，无头部外伤史，无肿瘤家族史。入院查体：血压：152/91 mmHg，神志清，精神偏软，双侧瞳孔约 3 mm，对光反射存在，眼球无明显运动障碍，颈软，呼吸平稳，四肢肌力 5 级，巴氏征阴性。血常规、生化、乙肝三系、传染病检查未见明显异常，皮质醇：早晨 8 时 552 nmol/L，下午 4 时 312 nmol/L，凌晨 12 时 44.7 nmol/L；促肾上腺皮质激素：早晨 8 时 73 pg/mL，下午 4 时 31.3 pg/mL，凌晨 12 时 11.2 pg/mL；泌乳素：414.42；孕酮：0.797，AFP 阴性，血清 β-HCG < 1.20 mIU/mL，血清生长激素 < 0.05 ug/L。头颅增强 MRI 显示松果体区 17 × 11 × 13 mm 占位，明显均匀强化，双侧脑室及第 3 脑室扩张(图 1)。CTA 提示颅内大动脉未见异常。入院诊断：颅内占位性病变；梗阻性脑积水。2024 年 11 月 23 日行松果体肿物切除术，术后病理：生殖细胞瘤，大小 1.5 × 1.0 × 0.8 cm。免疫组化(图 2)：CD117 (+)，D2-40 (+)，SALL4 (+)，PLAP (+)，CD99 (−)，CKpan (−)，EMA (−)，GFAP (−)，Ki67 (+, 60%)，S100 (−)，CgA (−)，SYN (−)，Vim (+)，SSTR2 (−)，IDH-1 (−)，LCA (CD45) (−)，PR (−)，HCG (−)，AFP (局部+)，PAS 染色(+)。复查增强 MRI 显示松果体区占位术后(图 3)。根据 SIOPE 制定的“全脑全脊髓高精度放疗勾画共识指南”[4]，2024 年 12 月 11 日行全脑全脊髓放疗，6MV-X 线，VMAT 放疗技术，PGTV 瘤床 3610 cGy/19F/DT；PTV 全脑 3040 cGy/16F/DT，PTV 全脊髓 2400 cGy/16F/DT。放疗过程顺利，患者放疗后复视、头痛头胀好转。2025 年 2 月 19 日患者复诊，一般状况良好，头颅 CT 提示松果体区占位术后，未见肿瘤复发或转移。

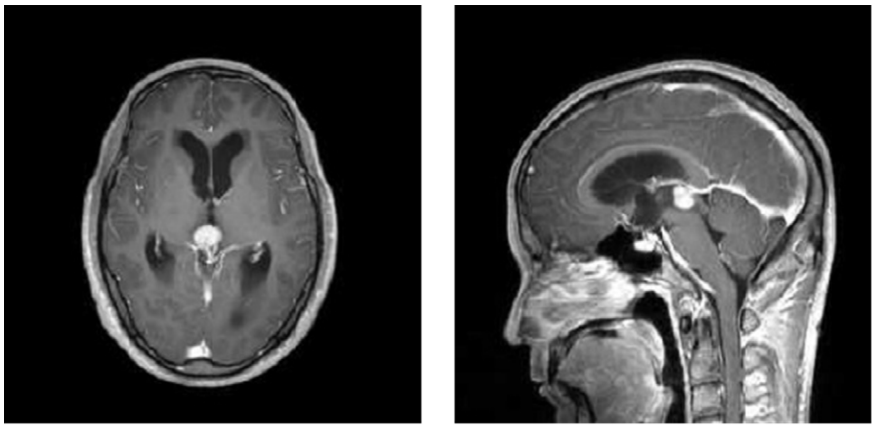

Figure 1. Contrast-enhanced T1WI showing a pineal region mass with homogeneous enhancement and dilatation of the lateral and third ventricles
图 1. T1WI 增强扫描示松果体区占位，明显均匀强化，双侧脑室及第 3 脑室扩张

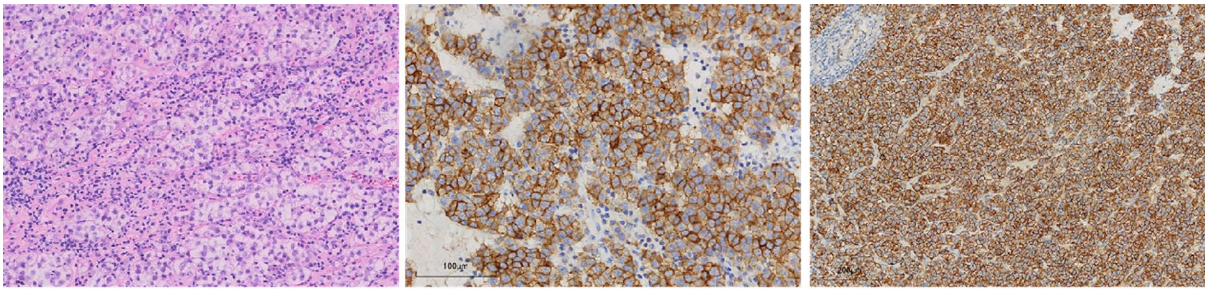

Figure 2. Microscopic view (original magnification × 100), (a) germinoma with hematoxylin-eosin stain; immunohistochemical staining (b) PLAP (+), (c) CD117 (+)
图 2. 显微镜观察(放大倍数 × 100)，(a) 生殖细胞瘤 H-E 染色；免疫组织化学染色(b) PLAP (+)，(c) CD117 (+)

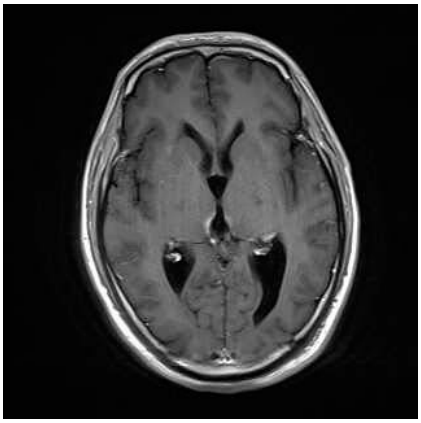

Figure 3. Contrast-enhanced T1WI showing the pineal region after surgery
图 3. T1WI 增强扫描示松果体区占位术后

3. 讨论

作为一种罕见的恶性肿瘤，颅内生殖细胞瘤的病因尚不明确，可能与胚胎期原始生殖细胞异常迁移有关[5]-[7]，因肿瘤的起源、亚型及临床表现的异质性，诊断和治疗具有挑战性。

生殖细胞瘤是颅内生殖细胞肿瘤最常见病理类型，生殖细胞瘤的临床症状与肿瘤的大小和位置密切相关，松果体区是颅内生殖细胞肿瘤最好发部位，松果体区的肿瘤可导致大脑导水管受压，早期出现头痛、恶心呕吐和视觉障碍等颅内压升高表现[8]。肿瘤压迫中脑四叠体可引起帕里诺综合征，表现上视麻痹、光近反射分离和集合－退缩性眼球震颤三联征，还伴有嗜睡、共济失调、癫痫发作和行为改变等表现[8]-[10]。而鞍上生殖细胞瘤通常表现为内分泌功能障碍，如尿崩症、生长迟缓和性早熟或延迟等[10]。

颅内生殖细胞瘤早期表现多为非特异性症状，常被延误诊断，其诊断需结合临床症状、影像表现和肿瘤标志物，脑脊液细胞学和组织病理活检是诊断的金标准。

颅内生殖细胞瘤在 MRI 通常表现为边界清晰的圆形或类圆形实性肿块，较大的病灶可伴有囊变、坏死灶及邻近脑实质浸润，T1 像呈低－等信号，T2 像呈等－高信号，增强后呈现均匀或不均匀强化，部分病例可见瘤周水肿。松果体生殖细胞常见钙化和小囊肿[11]-[14]。血清及脑脊液中甲胎蛋白(alpha-Fetoproteins, AFP)与 β-人绒毛膜促性腺激素(β-human chorionic gonadotropin, β-HCG)的水平可以作为初步分型的重要依据[15]。酪氨酸蛋白激酶 KIT (CD117/c-KIT)、转录因子 OCT4 (octamer-binding transcription factor 4)、胎盘碱性磷酸酶(Placental alkaline phosphatase, PLAP)这几项免疫组化标志物在细胞中的特异性表达也有助于生殖细胞瘤的诊断[16]-[18]。

本例患者生殖细胞瘤位于松果体区，表现典型的梗阻性脑积水包括视物重影，头晕头痛等症状，由于为非特异性症状，并未重视，发病 1 年后才来院就诊。CT 和 MRI 影像提示颅内存在与症状相关的占位性病变和梗阻性脑积水，血清学检查提示 β-HCG 水平较低，AFP 水平正常。考虑患者入院时颅内压明显升高，腰椎穿刺存在诱发脑疝的风险，且患者拒绝接受该操作，因此未进行脑脊液细胞学检测。通过手术治疗改善了梗阻性脑积水症状，术后病理报告观察到肿瘤细胞高度表达 CD117/c-KIT 和 PLAP，证实了生殖细胞瘤的诊断。

生殖细胞瘤对放疗高度敏感，放疗是其重要治疗手段。全脑全脊髓照射(Craniospinal Irradiation, CSI)一直是颅内生殖细胞瘤治疗的金标准，传统放疗方案是全脑全脊髓照射 36 Gy，原发灶追加剂量至 50~54 Gy，每次分割剂量 1.8 Gy，临床研究显示该方案的 10 年总生存率超过 90% [19]。然而，CSI 照射体积大，迟发性毒性反应，如神经认知功能损伤、内分泌功能障碍等严重影响了患者的生存质量[20]-[22]。

为了降低治疗相关的远期毒性风险，目前临床研究都重点围绕降低放疗剂量展开。20 世纪 90 年代，德国协作组(MAKEI 83/86 及 MAKEI 89)的前瞻性临床试验首次系统评估了减量 CSI 方案[19]。试验中，患者分别接受 36 Gy 全脑全脊髓照射联合 14 Gy 原发灶追加照射或 30 Gy 全脑全脊髓照射联合 15 Gy 原发灶追加照射，结果表明，降低 CSI 剂量似乎可以达到相同的治疗效果。Rogers 等[23]一项荟萃分析指出：与传统高剂量 CSI 相比，减量 CSI 并未显著增加孤立性脊髓复发的风险。Cho 等[24]一项回顾性研究认为减量 CSI 应作为颅内生殖细胞瘤的标准治疗，接受低剂量 CSI 的患者随访期间均未出现复发。欧洲多中心研究 SIOP CNS GCT 96 评估了局限性生殖细胞瘤患者接受 24 Gy 全脑全脊髓照射联合 16 Gy 原发灶追加照射的疗效，结果显示 5 年 PFS 达到 97%，验证了减量 CSI 方案的显著疗效[25]。上述研究充分证实了从传统 CSI 向减量 CSI 过渡的合理性。

近年来，也有研究探索化疗作为生殖细胞瘤患者放疗的替代方案的可能性，但多项研究显示单独化疗的疗效不及单独放疗或放疗联合化疗[26]-[28]。

为不降低生存减少放疗的副作用，新辅助化疗联合减量放疗可能是可行的治疗方案。一项前瞻性研究采用化疗联合 40 Gy 局部放疗替代预防性 CSI，结果表明化疗联合放疗与传统放疗方案生存率无明显差异，降低了远期毒性风险[29]。SIOP CNS GCT II 试验基于化疗反应，对卡铂和依托泊苷化疗后达到完全缓解(complete response, CR)的患者，改用 24 Gy 全脑室照射替代局部放疗，结果表明 24 Gy 全脑照射可以考虑作为 CR 患者的标准巩固治疗，4 年 EFS 达到了 97% [30]。ACNS 1123 试验进一步探索了基于

化疗反应的减量放疗方案：接受卡铂和依托泊苷化疗后完全缓解的患者给予 18 Gy 全脑室照射联合 12 Gy 原发灶追加照射，3 年 PFS 达到了 94.5% [31]。此外，Cheng 等[32]的回顾性研究则认为卡铂和依托泊苷诱导化疗后，仅接受 24 Gy 全脑照射不追加照射也可以获得良好的生存率。

目前，对于颅内生殖细胞瘤，临床上已有一些疗效显著的治疗方案，但最佳治疗仍然存在争议。现有临床研究都基于儿童病例开展，成人患者循证医学依据不足，治疗策略多依赖儿科方案外推。然而，直接套用儿童治疗模式可能忽视成人患者的特殊需求，例如生育力保留、职业功能影响及不同毒性耐受性[33]。在治疗方面，新辅助化疗联合减量全脑室照射的优越性已在儿童试验(如 ACNS1123)中得到证实，但在成人病例中的长期疗效和安全性尚未充分验证。CSI 仍被推荐作为成年患者的首选，尤其在脑脊液细胞学结果不明确，难以排除微小播散或脑室系统受累的情况下，CSI 能够更有效地降低肿瘤局部复发及脑脊液播散转移风险。因此，本例患者采用减量 CSI 方案。此外，由于成人患者常处于生育和工作关键阶段，治疗后还面临更突出的神经认知功能受损、社会心理负担及生存质量下降的风险。因此，临床上必须制定个体化的诊疗方案，在维持高治愈率与降低长期毒性之间取得平衡。未来，应建立基于成人患者的多中心前瞻性研究，进一步明确最佳治疗策略，以改善患者长期预后与生存质量。

4. 结论

本例成人颅内生殖细胞瘤采用了减量 CSI 联合原发灶追加照射的方案，取得良好疗效，病灶完全控制，随访至今未见肿瘤复发或转移，未见明显毒性反应。为明确颅内生殖细胞瘤的最佳治疗，仍需更多临床研究为治疗提供循证医学依据。

声　明

该病例报道已获得病人的知情同意。

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