

颅内植物性异物肉芽肿:一例报告并文献复习

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【摘要】 **目的** 颅内植物性异物肉芽肿临床十分罕见,对其临床表现和组织病理学特征进行探讨,避免误诊。**方法与结果** 报告 1 例颅内植物性异物肉芽肿患者的临床表现、组织病理学特征和免疫表型,并复习相关文献。男性患者,23 岁。主要表现为发作性四肢强直性抽搐,病程 7 年。头部 MRI 检查显示,左侧侧脑室前角前下方额叶皮质内长约 1.60 cm 的小结节状混杂信号影,邻近额叶组织有胶质化表现。术中可见左侧额底病灶与硬脑膜粘连,大小约为 3 cm × 2 cm,呈灰褐色,质地较韧,边界不清,部分钙化,血供丰富。光学显微镜观察显示,肉芽肿伴纤维组织增生、透明变性、钙化及淋巴细胞、浆细胞浸润,未见肿瘤细胞及寄生虫病变;病变组织表达波形蛋白和 CD68,不表达胶质纤维酸性蛋白、S-100 蛋白和上皮膜抗原。**结论** 颅内植物性异物肉芽肿根据其部位不同临床表现多样,根据异物种类及存留时间的长短,其影像学也存在多样性,但是可以通过组织病理学和免疫组织化学检测明确诊断,与肿瘤、寄生虫病变相鉴别,并初步明确其植被类型。

【关键词】 肉芽肿; 异物; 植物; 脑损伤; 免疫组织化学; 病理学

Craniocerebral vegetal foreign body granuloma: a case report and review of literature

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【Abstract】 Objective Craniocerebral vegetal foreign body granuloma is rare lesion which is very difficult to diagnose clinically, and is easy to be misdiagnosed. This article aims to reveal the clinical manifestations and histopathological features of it. **Methods** A case of cerebral vegetal foreign body granuloma was reported focusing on the following aspects: clinical manifestations, histopathological features and immunophenotype and the relevant literature was reviewed. **Results** A 23-year-old male patient presented with paroxysmal stiffness accompanied by convulsion of extremities and no response for calling for 7 years. Cranial MRI scan demonstrated a small nodular mixed signal shadow about 1.60 cm in length located in the frontal cortex under the anterior horn of the left compartment with gliosis near frontal lobe. A resection was performed, and a lesion (about 3 cm × 2 cm) was found in the bottom of the left frontal lobe. The lesion was greyish brown, tenacious, irregular bordered, partly calcified and with rich blood supply. There was no tumor or parasite but proliferation of fibrous tissue, hyaline degeneration, calcification, infiltration of lymphocytes and plasma cells in the granuloma lesion under microscope. The immunohistochemical staining showed the lesion was positive for vimentin (Vim) and CD68, while negative for glial fibrillary acidic protein (GFAP), S-100 protein (S-100) and epithelial membrane antigen (EMA). **Conclusion** Clinical manifestations of craniocerebral vegetal foreign body granuloma are various according to the occurrence in different parts. Besides, its imaging features are various depending on the kind of foreign body and the persistent duration. However, histopathological observation and immunohistochemical staining facilitate its diagnosis and identification from tumor and parasitic disease. Furthermore, the type of plant can also be distinguished roughly.

【Key words】 Granuloma, foreign - body; Plants; Brain injuries; Immunohistochemistry; Pathology

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颅内植物性异物肉芽肿临床较为罕见,我们报告 1 例外伤性颅内植物性异物肉芽肿病例,对其临床表现、影像学和组织形态学特点进行分析,并探讨该病的诊断与鉴别诊断。

病历摘要

患者 男性,23 岁。主因发作性四肢强直性抽搐、呼之不应 7 年,于 2012 年 6 月 12 日入四川大学华西医院。患者于 7 年前无明显诱因午睡时突然出现四肢强直性抽搐、呼之不应、双眼上翻、面色发绀、牙关紧闭、口吐白沫,发作时间约持续 1 min,醒后不能回忆发作过程,自述头痛、乏力。当地医院头部 CT 检查显示左侧额叶海绵状血管瘤。遂入我院接受伽玛刀治疗,同时给予卡马西平(得理多)0.20 g(2 次/d),治疗 2 年症状明显改善,未再发作。5 年前(2007 年)再度出现强直性抽搐发作,之后 2009 和 2011 年分别发作 1 次,发作时间无昼夜之分,白天发作时伴倒地,其余症状同前;发作前无先兆、无失神发作。入院前 1 个月(2012 年 5 月 20 日)发作 1 次,至我院就诊,予以左乙拉西坦(开普兰)0.50 g(2 次/d)、胞磷胆碱钠(欣可来)0.20 g(3 次/d)口服,治疗期间又发作 4 次(6 月 3 日和 9 日分别发作 2 次),间隔时间约 5 h,发作间期意识清楚。左乙拉西坦治疗 1 个月后,由于仍频繁发作自行停药,改为口服卡马西平 0.20 g(2 次/d)。家属诉其发病后言语速度缓慢,为求进一步诊断与治疗再次入我院。患者自发病以来,精神、食欲、睡眠尚可,大小便正常,体质量无明显变化。

既往史、个人史及家族史 出生时经产钳助产。8 岁时(具体时间不详)因爬树坠落致头部外伤,于当地诊所行简单清创缝合术(由于术后病理检查发现组织学改变,补充询问病史而知)。无结核病史,无不良嗜好,余无特殊。父母无类似疾病病史。

体格检查 患者体温 36.3 ℃,脉搏 80 次/min,呼吸 20 次/min,血压 114/76 mm Hg(1 mm Hg = 0.133 kPa)。神志清楚,皮肤、巩膜无黄染,全身浅

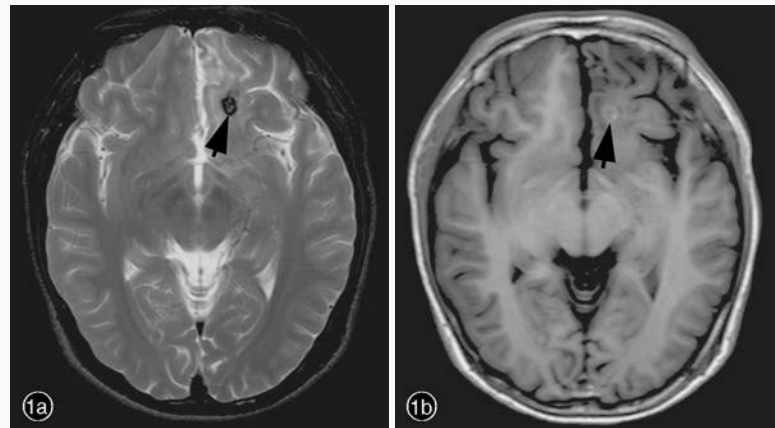


图 1 头部 MRI 检查所见 1a 横断面抑脂 T₂WI 显示,左侧额叶底部近中线皮质下结节样混杂信号影(箭头所示),周围可见轻度水肿 1b 横断面 T₁WI 显示,病灶中心呈略低信号,周围呈环形略高信号(箭头所示)

Figure 1 Cranial MRI findings. Axial T₂WI demonstrated a small nodular mixed signal shadow located in the frontal cortex under the anterior horn of the left compartment with gliosis near frontal lobe (arrow indicates, Panel 1a). Axial T₁WI revealed slightly hypointense in the central of the lesion, while slightly circular hyperintense in the peripheral area (arrow indicates, Panel 1b).

表淋巴结未触及,颈静脉正常。心界正常,心律齐,各瓣膜区未闻及杂音,胸廓无异常;双肺叩诊呈清音,呼吸音清,未闻及干湿啰音及胸膜摩擦音。腹部外形正常,全腹柔软,无压痛及反跳痛,腹部未触及包块,肝脾肋下未触及,肾脏未触及。双下肢无水肿。神经科专科检查:神志清楚,高级神经功能正常。双侧瞳孔等大、等圆,对光反射灵敏,其余脑神经无异常。四肢肌力 5 级、肌张力正常,腱反射对称引出,肢体感觉无明显减退,病理征阴性,脑膜刺激征阴性。共济运动无异常。

辅助检查 入院后完善各项实验室检查,血液一般检查与物理性质,以及肝、肾功能试验均于正常水平。血清钙 2.08 mmol/L(2.10 ~ 2.70 mmol/L),血清无机磷 1.50 mmol/L(0.81 ~ 1.45 mmol/L)。头部 MRI 检查显示,左侧侧脑室前角前下方额叶皮质内长约 1.60 cm 的小结节状混杂信号,考虑多系海绵状血管瘤,邻近额叶组织可见胶质化表现(图 1)。

诊断与治疗经过 根据入院前后各项检查结果,临床诊断考虑为左侧额叶占位性病变,继发性癫痫。于 2012 年 7 月 9 日于全身麻醉下行左侧额叶占位性病变切除术、左侧额叶癫痫灶切除术。术中可见左侧额底病灶与硬脑膜粘连,大小约为 3 cm × 2 cm,呈灰褐色、质地较韧,边界不清,部分钙化,血供丰富。手术完整切除病灶,并行组织病理学检查。(1)大体标本观察:灰白色破碎组织块,大小约

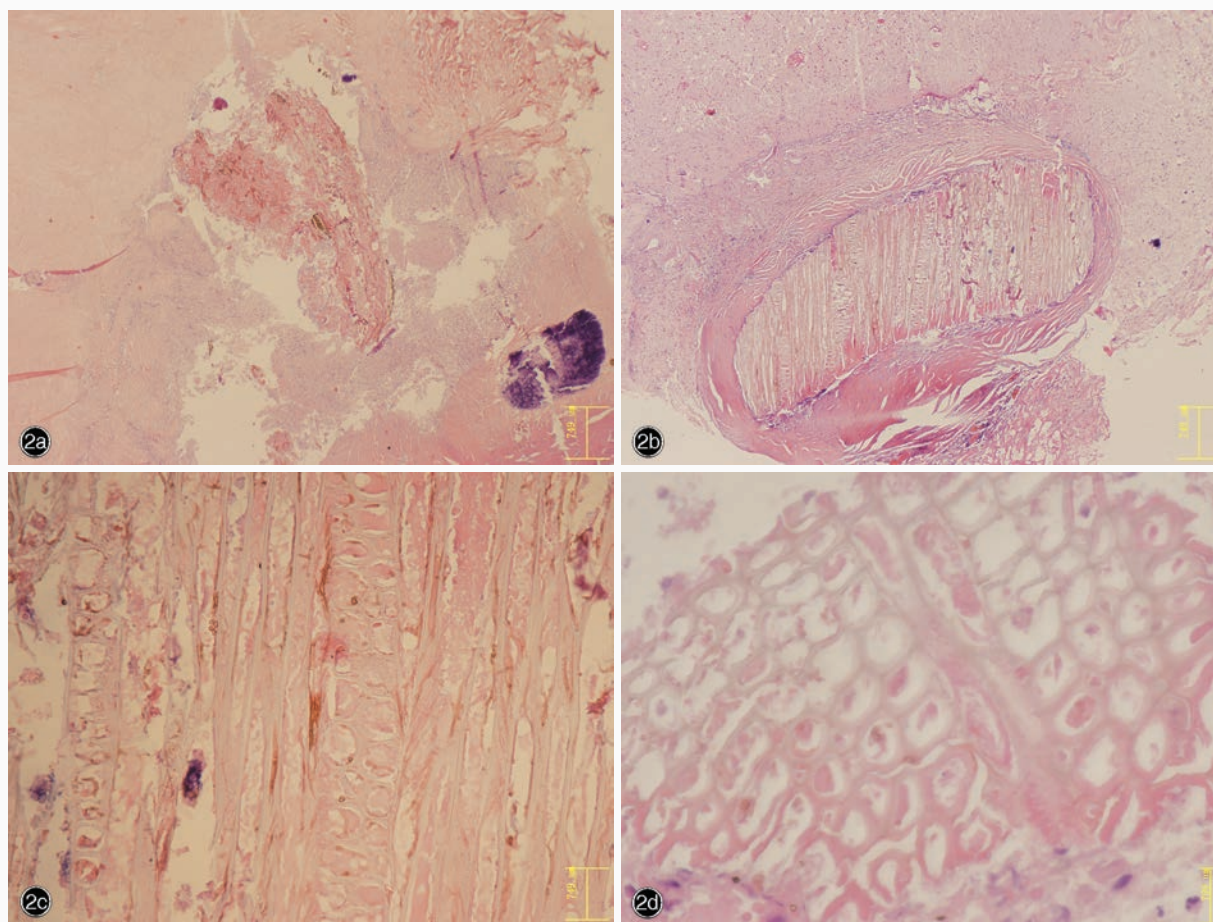


图 2 光学显微镜观察所见 HE 染色 2a 植物性异物肉芽肿伴纤维组织增生、透明变性、钙化及淋巴细胞、浆细胞浸润 $\times 10$ 2b 植物性异物肉芽肿伴纤维组织增生、透明变性和淋巴细胞、浆细胞浸润 $\times 15$ 2c 植物性异物组织为筛板和筛孔组成的网状结构,其间填充少许蛋白黏液样物质 $\times 100$ 2d 植物性异物组织为筛板和筛孔组成的网状结构,其间填充少许蛋白黏液样物质 $\times 200$

Figure 2 Optical microscopy findings. HE staining There were proliferation of fibrous tissue, hyaline degeneration, calcification, infiltration of lymphocytes and plasma cells within vegetal foreign body granuloma. $\times 10$ (Panel 2a). There were proliferation of fibrous tissue, hyaline degeneration, infiltration of lymphocytes and plasma cells within vegetal foreign body granuloma. $\times 15$ (Panel 2b). The vegetal foreign body was composed of sieve plates and sieve pores filled with a little protein myxoid substance. $\times 100$ (Panel 2c). The vegetal foreign body was composed of sieve plates and sieve pores filled with a little protein myxoid substance. $\times 200$ (Panel 2d).

为 $3\text{ cm} \times 3\text{ cm} \times 1\text{ cm}$, 剖面呈灰白色、实性,质地中等、偏软,经体积分数为 4% 中性甲醛溶液固定,常规脱水、透明、石蜡包埋制备脑组织切片,分别行 HE 染色和免疫组织化学染色。(2) HE 染色:光学显微镜下观察,脑组织中可见筛孔状异物,周围肉芽肿形成伴纤维组织增生、透明变性、钙化和淋巴细胞、浆细胞浸润;未发现肿瘤细胞和寄生虫(图 2)。(3)免疫组织化学染色(EnVision 二步法和 Multimer 法):免疫组织化学检测所用 I 抗、II 抗、显色剂、染色系统参见表 1。结果显示,病灶细胞波形蛋白(Vim)表达阳性,胶质纤维酸性蛋白(GFAP)、S-100 蛋白(S-100)和上皮膜抗原(EMA)表达阴性;病灶周

围细胞 CD68 表达阳性(图 3)。结合临床病史和病理检查结果,诊断为颅内植物性异物肉芽肿,多系外伤所致。患者术后随访至今仍偶有癫痫发作。

讨 论

颅脑创伤十分常见,金属异物造成的脑损伤也早为人们所了解,而以植物作为颅内异物却十分罕见。由于患者早期多无临床症状,易被忽视,通过组织病理学检查可明确诊断,对临床治疗具有较好的指导作用。事实上,木质和金属等异物对脑组织的危害不尽相同,木质异物有其独特的表现。

对于木质等有机异物,在头部 X 线和常规 CT 检

表 1 免疫组织化学检测项目表

Table 1. Antibodies used for immunohistochemical examination

| Antibody I | Clone ID | Company | Restorative procedure | Dilution ratio | Antibody II and company | Dyeing system |
|------------|----------|----------------|-----------------------|----------------|-------------------------|---------------|
| Vim | V9 | Dako (Denmark) | Citric acid | 1 : 200 | Ventana (America) | EnVision |
| GFAP | 6F2 | Dako (Denmark) | Citric acid | 1 : 100 | Dako (Denmark) | Multimer |
| S-100 | 4C4.9 | Maixin (China) | Citric acid | 1 : 100 | Ventana (America) | EnVision |
| EMA | E29 | Dako (Denmark) | Citric acid | 1 : 150 | Dako (Denmark) | Multimer |
| CD68 | Pgm1 | Dako (Denmark) | Citric acid | 1 : 100 | Dako (Denmark) | EnVision |

Vim, vimentin, 波形蛋白; GFAP, glial fibrillary acidic protein, 胶质纤维酸性蛋白; S-100, S-100 蛋白; EMA, epithelial membrane antigen, 上皮膜抗原

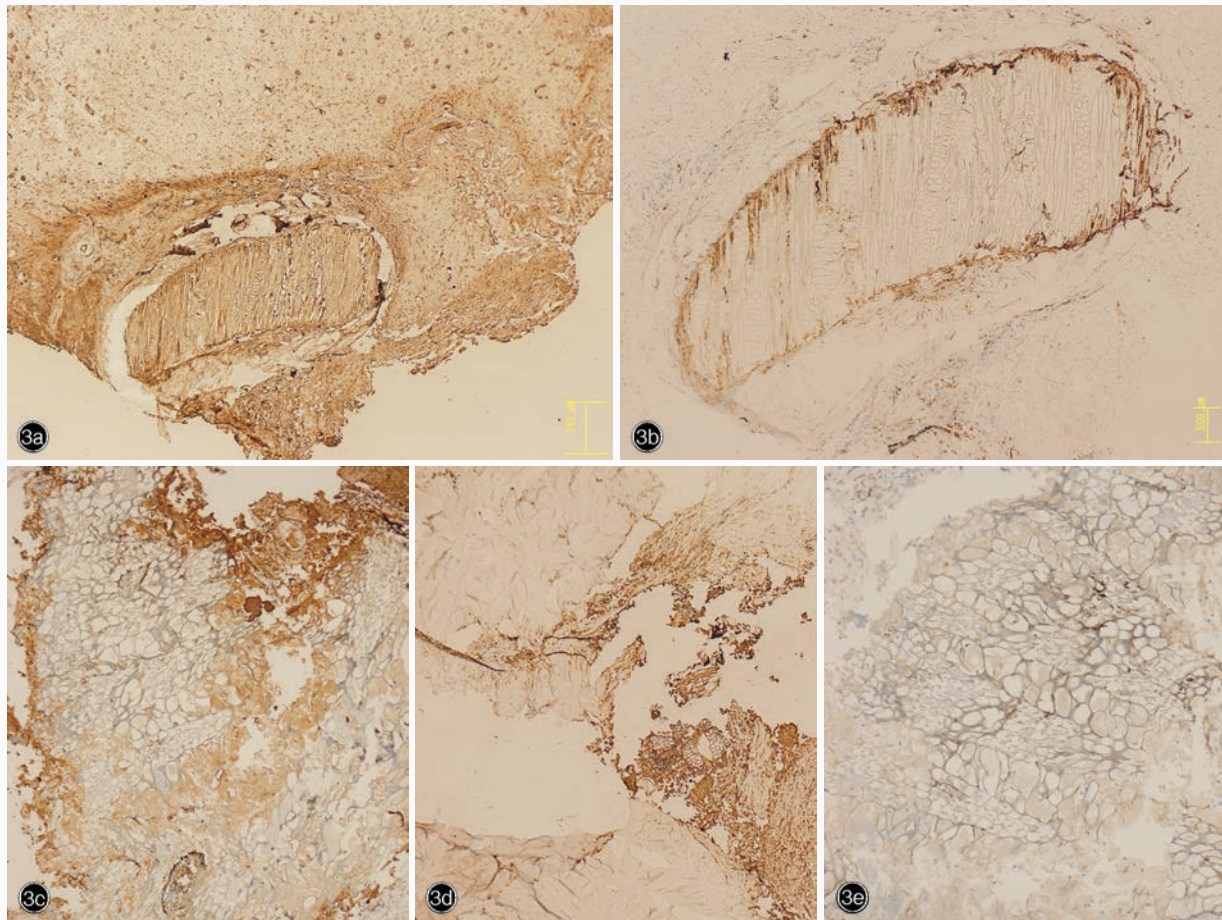


图 3 光学显微镜观察所见 3a 植物性异物肉芽肿组织波形蛋白表达阳性 免疫组织化学染色(EnVision 二步法) × 10 3b 植物性异物肉芽肿周围组织 CD68 表达阳性 免疫组织化学染色(EnVision 二步法) × 20 3c 植物性异物肉芽肿组织胶质纤维酸性蛋白表达阳性 免疫组织化学染色(Multimer 法) × 30 3d 植物性异物肉芽肿组织 S-100 蛋白表达阳性 免疫组织化学染色(EnVision 二步法) × 20 3e 植物性异物肉芽肿组织上皮膜抗原表达阳性 免疫组织化学染色(Multimer 法) × 40

Figure 3 Optical microscopy findings. Vim was positive within vegetal foreign body granuloma. Immunohistochemical staining (EnVision) × 10 (Panel 3a). CD68 was positive surrounding vegetal foreign body granuloma. Immunohistochemical staining (EnVision) × 20 (Panel 3b). GFAP was negative within the vegetal foreign body granuloma. Immunohistochemical staining (Multimer) × 30 (Panel 3c). S - 100 was negative within the vegetal foreign body granuloma. Immunohistochemical staining (EnVision) × 20 (Panel 3d). EMA was negative within vegetal foreign body granuloma. Immunohistochemical staining (Multimer) × 40 (Panel 3e).

查时可无异常所见,漏诊率极高。据 Paiva 等^[1]报告,大多数患者都是由于继发感染、癫痫发作等并发症于伤后数年方才就医。因此,对于野外发生的

外伤应详细询问病史,并认真检查有无伤口,尤其是 X 线或常规 CT 检查对植物性异物难以识别的情况下,应行 MRI 检查^[2]。早期植物性异物 T₁WI 和

T₂WI 均呈低信号, T₂WI 低信号特征可与周围组织相鉴别, 有助于提示植物性异物的存在^[3]。颅内植物性异物损伤绝大多数发生在青少年, 年龄 2~35 岁, 以 20 岁以下人群好发, 发生率约 80%, 且以男性居多, 占 75%; 其中 80% 的患者致伤物为铅笔或木棍, 其余 20% 为树枝或弓箭等^[4]。伤后立即出现症状者占 29%, 1 周内出现症状者 31%, 其余 40% 的患者可于伤后 2 周方出现症状, 最长达 13 年之久^[4]。本文患者受伤至出现中枢神经系统症状的时间约为 8 年。

该例患者由于病程较长、病史不清、植物性异物退变, 并伴有机体继发性损害, 与一般的异物相鉴别有一定困难。其 MRI 表现为小结节状混杂信号影, 因此影像学检查考虑为海绵状血管瘤, 由此可见, 病理检查对于明确诊断不可或缺。

该例患者组织病理检查显示, 植物性异物肉芽肿伴纤维组织增生、透明变性、钙化, 以及淋巴细胞和浆细胞浸润; 从异物的网状排列结构及其间蛋白样物质填充的组织学形态, 可以基本确定为被子植物异物^[5-10], 结合补充询问病史, 系外伤后修复所致。创伤性颅内异物患者癫痫发作与脑内原发伤及异物是否存留等影响因素密切相关, 该例患者伤后较长时间方出现癫痫发作。Abbassioun 等^[11]对 13 例颅内异物患者之发病特点进行总结, 其中 5 例并发癫痫发作, 受伤至癫痫发作时间 7 天至 8 年。据 Caveness 等^[12]报告, 有 30%~50% 的脑损伤患者可出现癫痫发作, 其中 10% 发生于伤后 1 周内、80% 为伤后 2 年, 18% 可能至伤后 5 年方才出现癫痫发作症状与体征。

颅内植物性异物肉芽肿应注意与以下疾病相鉴别: (1) 寄生虫虫卵性异物肉芽肿。多有疫区感染史或中枢神经系统外寄生虫感染史, 血液和脑脊液嗜酸性粒细胞增多, 可呈急性脑膜脑炎或局限性癫痫发作或伴定位体征的颅内高压征, 亦可表现为智力减退或精神障碍。其组织学形态表现为在肉芽肿背景下可见寄生虫虫卵或虫体, 而本文病例的病灶组织在显微镜下可见异物由网状排列的导管样组织构成, 多个导管内充满了红染均质样物质, 其组织形态学与被子植物的导管结构极为相似。(2) 海绵状血管瘤。由呈囊性扩张相互连接的薄壁

血管构成, 常可见“假乳头”状结构, 可发生于身体的任何部位; 但是海绵状血管瘤多为先天性, 且以婴儿或幼儿好发, 少数亦可见于成人。影像学检查易将异物肉芽肿误诊为海绵状血管瘤, 但组织病理学形态上易于鉴别。

颅内植物性异物肉芽肿患者的治疗以手术切除病灶为主, 无论患者是否出现中枢神经系统症状, 均应施行神经外科手术切除病灶; 对于晚期才明确诊断为颅内硬植物(如木质、竹)异物肉芽肿的患者, 只要身体条件允许也不应放弃外科手术治疗的机会; 对于尚不能明确诊断颅内硬植物(如木质、竹)异物肉芽肿的患者, 只要高度怀疑颅内病变, 仍应积极争取手术探查, 表现有中枢神经系统症状者更应如此。

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