个案报道

脊柱幼年性黄色肉芽肿 1 例报道

Juvenile xanthogranuloma of spine: a case report

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黄色肉芽肿是一种良性非朗格汉斯细胞组织细胞增生性病变,因好发于婴幼儿,也被称为幼年性黄色肉芽肿(juvenile xanthogranuloma,JXG)[1],偶可发生于成年人。皮肤为常见发病部位,表现为无痛性单发或多发皮肤隆起,影像学易误诊为神经鞘瘤等。Touton 细胞是 JXG 典型细胞,但当 Touton 细胞稀少时,肉芽肿形态缺乏特异性,易误诊为结核等。JXG 可发生于眼虹膜、宫颈、肺、肝脏及脾脏,发生在脊柱罕见,目前仅有十余例脊柱 JXG 英文文献报道[2-20]。我院收治 1 例脊柱 JXG 的患者,报道如下。

患者男性,7 岁,腰背部疼痛半年,曾在当地医院行理疗、止痛等治疗,症状改善不明显,于 2014 年 6 月 22 日收入我院骨科治疗。查体:患者神志清楚,身体前倾受限,双侧骶棘肌痉挛,左侧股四头肌肌力 4+级,四肢肌张力增高,双侧膝腱反射及跟腱反射亢进,双侧 Babinski 征(+)。当日辅助检查:胸腰椎 X 线平片未见明显病变(图 1a);CT 检查(图 1b)显示左侧 T12 椎板及 L1 椎弓、椎板骨质破坏、椎体破坏,可见团块状肿物影,大小约 5.1×4.3×3.1cm,密度不均匀,CT 值约 41HU,部分边缘硬化,病变向椎管内、外突出,相应水平硬膜囊及脊髓明显受压向对侧移位;MRI 显示左侧 T12~L1 椎板、椎体病变呈等 T1 等 T2 信号,部分区域信号略不均匀,可见斑点状短 T1 信号影,增强扫描 T12~L1 椎板、椎体病灶略不均匀强化,其内可见斑片状未强化信号(图 1c~f)。初步诊断为 T12~L1 占位性病变。

患者于 2014 年 6 月 30 日行胸腰椎病损切除减压植骨融合内固定术。全麻生效后,患者俯卧位,胸腹部悬空,取胸腰部后正中切口,沿棘突两侧分离肌肉,充分显露 T11~L3 棘突、椎板和横突。术中见直径大小约为 5cm 肿物,与肌肉分界不清,沿分界模糊处外缘分离肿物,可见 T12 及 L1 部分椎板消失、L1 左侧椎弓根及关节突消失。肿物累及部分椎板组织,钝性分离肿物,有部分黄白质脆物质流出,可见硬膜囊受压变窄。充分清除黄白物质及肿物,留做病理检查,并于双侧 T11、T12、L2、L3 及 L1 右侧椎弓根置入椎弓根螺钉固定。

病理学检查显示纤维间质内大量泡沫样细胞及 Touton 样多核巨细胞,散在淋巴细胞,偶见嗜酸性粒细胞,出血明显,胆固醇结晶形成(图 2a~c)。免疫组化染色 CD68 阳性(图 2d),CD1a 和 S-100 阴性。结合组织学形态和免疫组化结果诊断为黄色肉芽肿。术后恢复良好,随访 5 年无复发(图 3)。

讨论 现有文献报道脊柱 JXG 病例共 19 例,其中男性 9 例,女性 10 例,性别无明显差异;发病年龄为 6 个月~47 岁;脊柱 JXG 的发病部位自上颈椎至骶尾部均有报道,均为溶骨性病变,累及脊髓时可出现神经压迫症状,根据累及神经节段不同,可出现斜颈,吞咽困难,脊髓空洞症,颈部、胸背部及腰部疼痛,四肢麻痹等症状(表 1)[2-20]。从现有文献报道来看,腰背部疼痛(4 例)、四肢麻痹(7 例)是脊柱 JXG 最常出现的临床症状。本例患者发病部位为 T12~L1 椎板、椎体,且表现出腰背部疼痛、肌肉痉挛等症状,符合文献报道的脊柱 JXG 常见症状。

脊柱 JXG 影像学缺乏特异性,易误诊为脊膜瘤或神经鞘瘤等[4]。文献报道的 19 例脊柱 JXG 病例中,MRI 呈现等 T1 等 T2 信号病例 4 例(4/12,33%),等 T1 高 T2 信号病例 3 例(3/12,25%),等 T1 低 T2 信号病例 2 例(2/12,17%),低 T1 高 T2 信号病例 2 例(2/12,17%),低 T1 低 T2 信号 1 例(1/12,8%)[2-20]。上述数据显示等 T1 等 T2 信号病例相对多见。本例患者 MRI 呈现等 T1 等 T2 信号,与文献报道中最常见的 MRI 表现一致。

病理学检查的主要鉴别诊断疾病包括朗格汉斯细胞组织细胞增生症(Langerhans cell histiocytosis,LCH)、Rosai-dorfman 病和黄色瘤。鉴别诊断要点:(1)LCH。脊柱 JXG 的早期病变与 LCH 极为相似。LCH 也为溶骨性病变,

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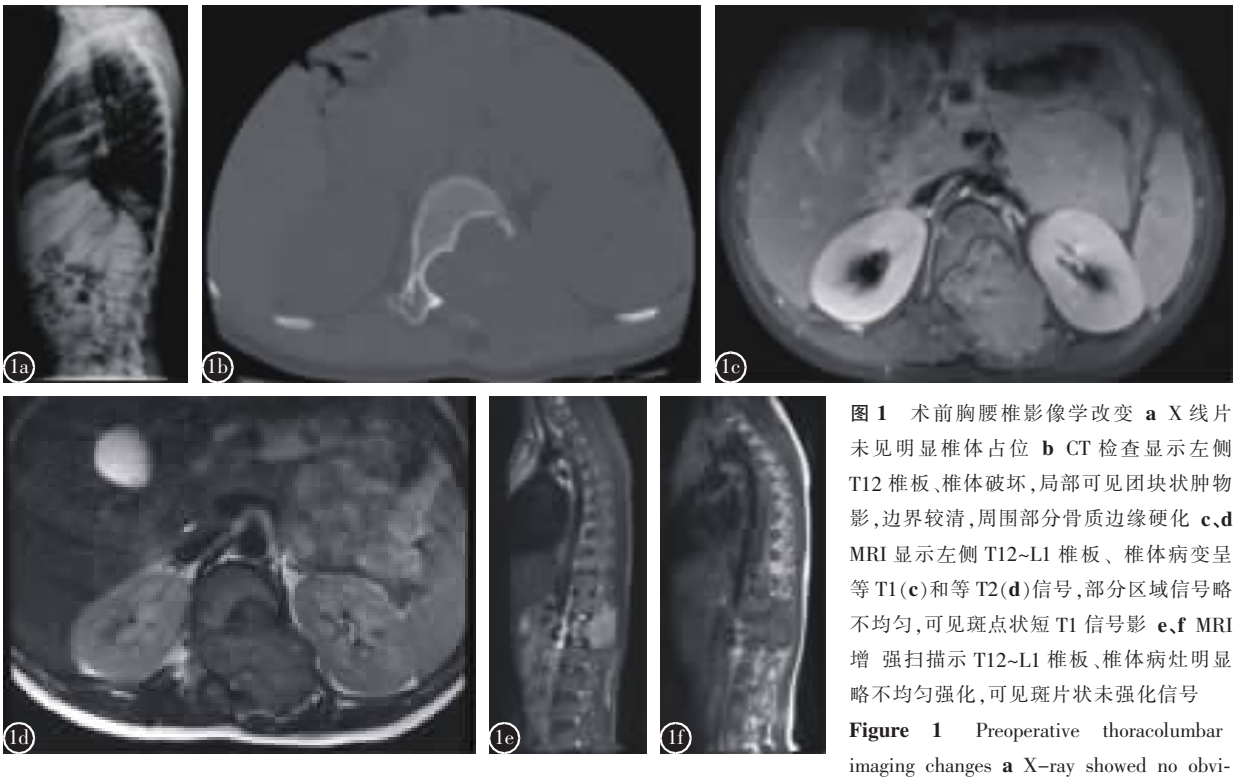

图 1 术前胸腰椎影像学改变 **a** X 线片未见明显椎体占位 **b** CT 检查显示左侧 T12 椎板、椎体破坏，局部可见团块状肿物影，边界较清，周围部分骨质边缘硬化 **c**、**d** MRI 显示左侧 T12~L1 椎板、椎体病变呈等 T1(**c**)和等 T2(**d**)信号，部分区域信号略不均匀，可见斑点状短 T1 信号影 **e**、**f** MRI 增强扫描示 T12~L1 椎板、椎体病灶明显略不均匀强化，可见斑片状未强化信号

Figure 1 Preoperative thoracolumbar imaging changes **a** X-ray showed no obvious occupation of vertebral body **b** CT examination showed destruction of the left thoracic 12 vertebral lamina, local mass, clear boundary and sclerosing of the surrounding bone **c, d** MRI showed lesion with iso-T1 (c) iso-T2 (d) signals, and the signal intensity in some areas was slightly uneven, with speckled short T1 signal **e, f** Enhanced scan of the lesion showed significant slightly heterogeneous enhancement, and patchy unenhanced signal

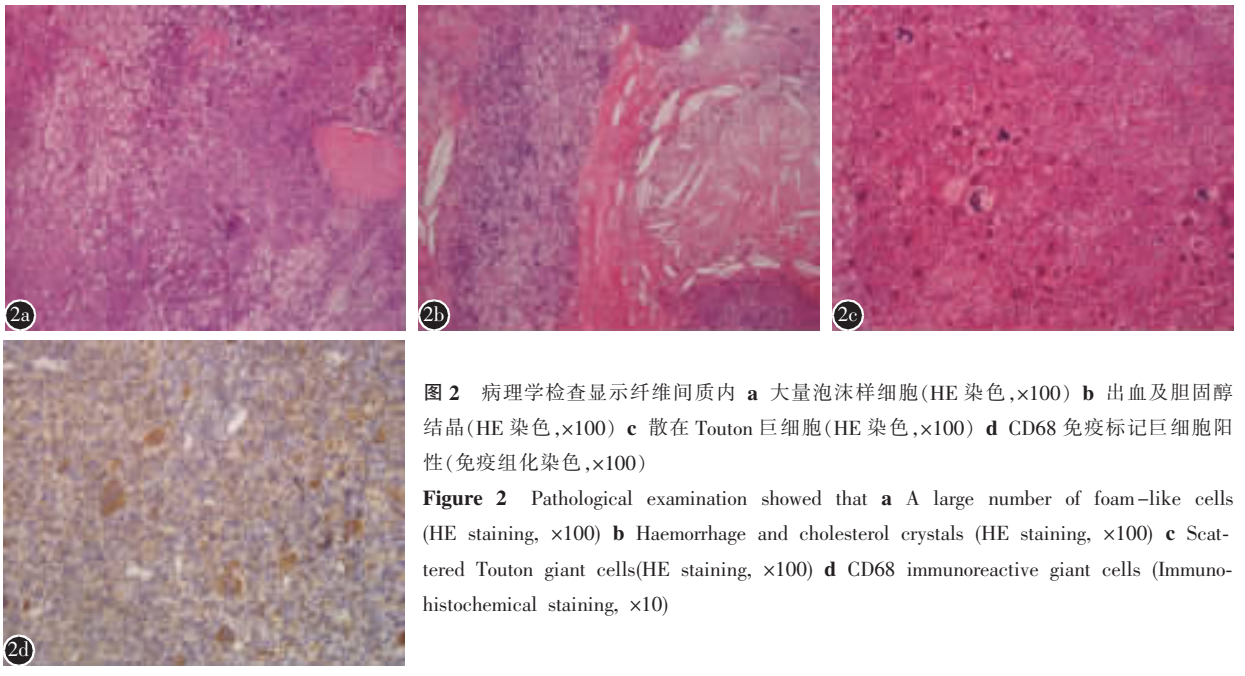

图 2 病理学检查显示纤维间质内 **a** 大量泡沫样细胞(HE 染色，×100) **b** 出血及胆固醇结晶(HE 染色，×100) **c** 散在 Touton 巨细胞(HE 染色，×100) **d** CD68 免疫标记巨细胞阳性(免疫组化染色，×100)

Figure 2 Pathological examination showed that **a** A large number of foam-like cells (HE staining, ×100) **b** Haemorrhage and cholesterol crystals (HE staining, ×100) **c** Scattered Touton giant cells(HE staining, ×100) **d** CD68 immunoreactive giant cells (Immunohistochemical staining, ×10)

也可发生在脊柱，常无症状，也可发生骨痛、骨折和软组织累及等压迫症状，但 Langerhans 细胞核型不规则、有核沟、胞质丰富，表达 CD1a、S-100 和胰岛蛋白(langerin)，病变中常见嗜酸性粒细胞，电镜下可见 Birbeck 颗粒。而 JXG 表达 CD68 和溶菌酶(lysozyme)等[15]，不表达 S-100 蛋白和 CD1a。(2)Rosai-dorfman 病。该病变内见浆细胞、淋巴细胞及大量组织细胞，组织细胞胞质丰富、淡染，胞质内可见淋巴细胞和浆细胞聚集，称为“穿入”运动。组织细胞表达 S-100，不表达 CD1a 和 langerin。(3)黄色瘤。和 JXG 相似，黄色瘤可见胆固醇结晶，但黄色瘤常伴有高胆固醇血症[21]。

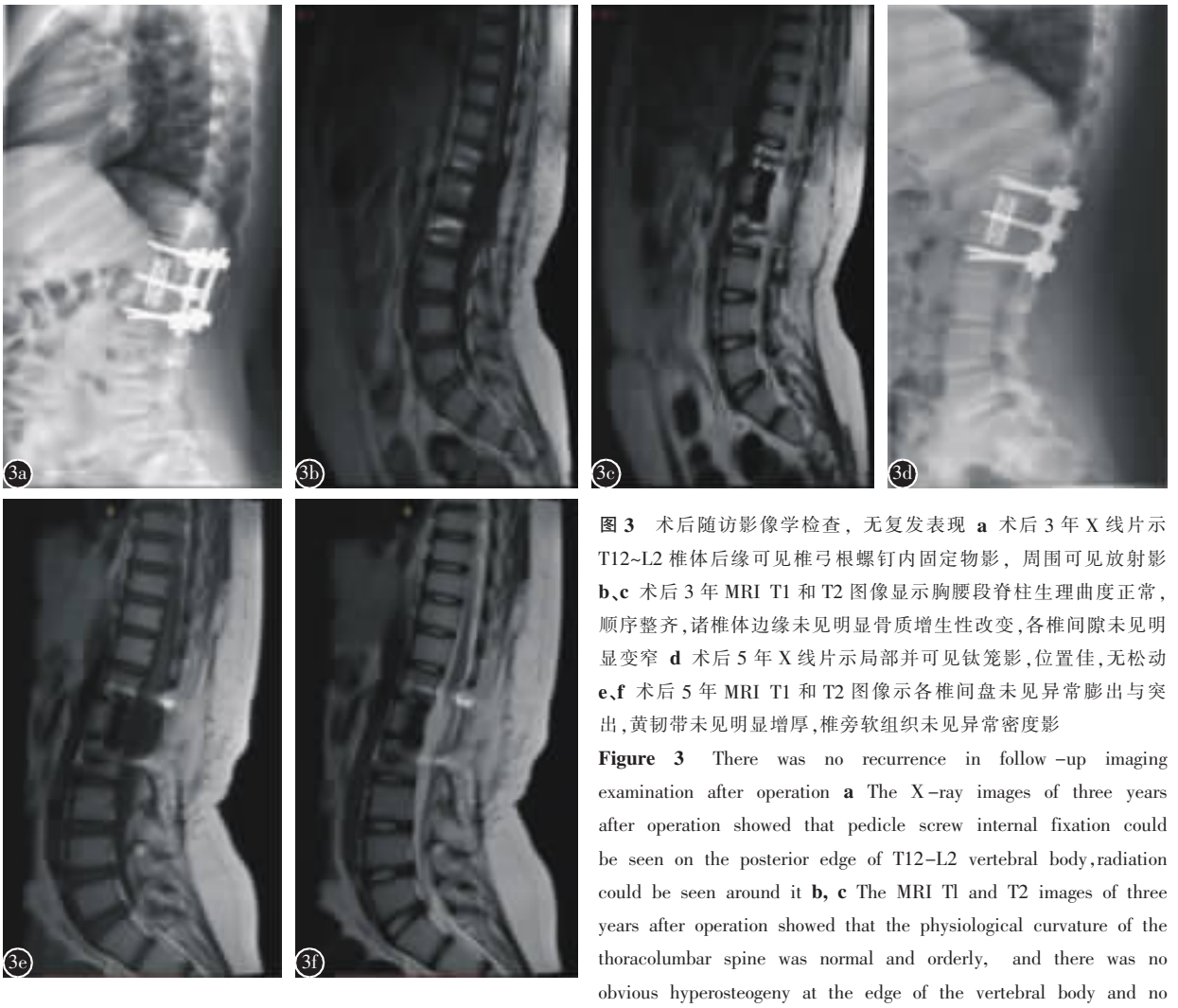

图 3 术后随访影像学检查，无复发表现 **a** 术后 3 年 X 线片示 T12~L2 椎体后缘可见椎弓根螺钉内固定物影，周围可见放射影 **b、c** 术后 3 年 MRI T1 和 T2 图像显示胸腰段脊柱生理曲度正常，顺序整齐，诸椎体边缘未见明显骨质增生性改变，各椎间隙未见明显变窄 **d** 术后 5 年 X 线片示局部并可见钛笼影，位置佳，无松动 **e、f** 术后 5 年 MRI T1 和 T2 图像示各椎间盘未见异常膨出与突出，黄韧带未见明显增厚，椎旁软组织未见异常密度影

Figure 3 There was no recurrence in follow-up imaging examination after operation **a** The X-ray images of three years after operation showed that pedicle screw internal fixation could be seen on the posterior edge of T12-L2 vertebral body, radiation could be seen around it **b, c** The MRI Tl and T2 images of three years after operation showed that the physiological curvature of the thoracolumbar spine was normal and orderly, and there was no obvious hyperosteogeny at the edge of the vertebral body and no obvious narrowing of the intervertebral space **d** The X-ray images of five years after operation showed that titanium cage could be seen locally, the position was good, there was no loosening **e, f** The MRI Tl and T2 images of five years after operation showed that here was no abnormal bulge and herniation of intervertebral disc, no obvious thickening of ligamentum flavum and no abnormal density of paraspinal soft tissue

此外，有研究[15]显示发生在皮肤之外的 JXG 病例 Touton 细胞明显减少，因此非典型部位出现非特异性肉芽肿改变，容易误诊为结核等。本病例病理学检查显示 S-100 和 CD1a 均阴性，结合实验室检查该患者没有高胆固醇血症，可排除上述疾病可能。

JXG 是一种良性增生性病变，为自限性疾病[15]，多数在 3~6 年内会自然消退或逐渐稳定，以保守治疗为主，严重椎体破坏影响功能者需进行手术治疗。现有脊柱 JXG 病例报道中手术方法包括椎板切除(11 例)、椎体切除(2 例)、椎体切除后自体骨移植(2 例)、化疗配合椎体椎板切除(2 例)、椎板形成术(1 例)，放疗配合椎板切除(1 例)(表 1)[2-20]。JXG 可多器官累及，造成凝血功能障碍，呈现恶性肿瘤征象，从而危及患者生命，需采用放疗和化疗，常用化疗药物包括糖皮质激素、长春新碱、甲氨蝶呤、依托泊苷等[22-25]，但因病例数有限，对全身性 JXG 病变的治疗方案仍处于摸索阶段，还需要更多证据支持。

随着病例报道不断增加，JXG 的分子遗传学改变也逐渐被发现。神经纤维瘤蛋白 1(NF1)和 NF2 是丝裂原活化蛋白激酶(MAPK)通路中的蛋白质，在调节细胞周期、细胞生长和分化以及细胞衰老中具有关键作用[26]。有文献报道，携带 NF1 或 NF2 种系突变的青少年黄色肉芽肿患者患幼年型粒-单核细胞白血病的风险增加，也有报道 LCH 和 Erdheim-Chester 病可以与 JXG 伴发，与 BRAF 基因突变有关[27-30]。

综上所述，脊柱 JXG 是一种良性非朗格汉斯细胞组织细胞增生性病变，常造成椎体和椎板破坏，压迫硬膜囊出现脊髓损伤症状。病理检查是诊断 JXG 的金标准，青少年患者出现椎体破坏性病变，推荐行 MRI 检查以提高 JXG 的检出率。完整手术切除病损复发率低。目前报道的脊柱 JXG 病例有限，其治疗方案优化有待更多证据支持。

表 1 脊柱 JXG 文献报道病例信息汇总

Table 1 Summary of case information reported in JXG literature

病例来源 Case source	性别 Gender	年龄 Age	发生部位(CT) Occurrence site	临床表现 Clinical manifestation	MRI信号 MRI signal	手术方法 Operation method	随访 Follow-up care
Rajasekhar et al, 2019[2]	男 Male	6岁 6 years	C1-C6 椎体 C1-C6 vertebral body	斜颈、吞咽困难、脊髓空洞症 Torticollis, dysphagia, syringomyelia	等 T1 高 T2 Equal T1 and high T2	椎体切除后自体骨移植 Autogenous bone transplantation after vertebrectomy	1年无复发 No recurrence for 1 year
Irmola et al, 2018[3]	女 Female	5岁 5 years	T11 椎体 T11 vertebral body	持续性腰痛和骨盆疼痛,进行性排尿困难 Persistent low back pain and pelvic pain, progressive dysuria	NA;低 T2 NA; low T2	皮下注射地诺单抗后,椎体切除 After subcutaneous injection of Dinozumab, the vertebrae were resected	3年无复发 No recurrence for 3 years
Shenoy et al, 2018[4]	女 Female	1岁 1 year	D6-8 IDEM	下肢轻瘫 Lower limb paresis	等 T1 低 T2 Equal T1 and low T2	椎板切除 Laminectomy	4年无复发 No recurrence for 4 years
Bhaisora et al, 2015[5]	男 Male	15岁 15 years	C5-C6 椎体 C5-C6 vertebral body	压缩性脊髓病,颈背部疼痛,进行性四肢麻痹等 Compression myelopathy, neck and back pain, progressive quadriplegia	等 T1 等 T2 Equal T1 and equal T2	椎体切除后自体骨移植 Autogenous bone transplantation after vertebrectomy	6个月无复发 No recurrence for 6 months
Purohit et al, 2014[6]	男 Male	18岁 18 years	T7-T10 水平硬膜外背侧 T7-T10 horizontal dorsal epidural	轻度四肢麻痹等 Mild limb paralysis	等 T1 等 T2 Equal T1 and equal T2	椎板切除 Laminectomy	3个月无复发 No recurrence for 3 months
Singhvi et al, 2014[7]	男 Male	9个月 9 months	C4-5 IDEM	双侧下肢无力 Bilateral lower limb weakness	NA	椎板切除 Laminectomy	1年无复发 No recurrence for 1 year
Konar et al, 2014[8]	男 Male	18岁 18 years	C2-C4 IDEM	进行性四肢麻痹和排尿困难 Progressive quadriplegia and dysuria	等 T1 低 T2 Equal T1 and low T2	椎板切除 Laminectomy	3个月无复发 No recurrence for 3 months
Wille et al, 2012[9]	NA	6个月 6 months	T3-T7	急性四肢麻痹 Acute limb paralysis	NA	椎板成形术 Laminoplasty	2年无复发 No recurrence for 2 years
Inoue et al, 2011[10]	男 Male	38岁 38 years	C7-T1 IDEM	T1 神经根病 T1 radiculopathy	等 T1 等 T2 Equal T1 and equal T2	椎板切除 Laminectomy	2年无复发 No recurrence for 2 years
Agabegi, 2011[11]	女 Female	47岁 47 years	L2 椎体 L2 vertebral body	背部疼痛,肠/膀胱受累 Back pain, intestinal/bladder involvement	NA	椎板部分切除及放疗 Partial laminectomy and radiotherapy	数月无复发 No recurrence for several months
Jain et al, 2011[12]	女 Female	22岁 22 years	T7 椎体 T7 vertebral body	背部疼痛 Back pain	低 T1 低 T2 Low T1, low T2	椎板切除 Laminectomy	无复发 * No recurrence
Castro-Gabo et al,2009[13]	男 Male	14岁 14 years	马尾 Ponytail	下肢麻痹 Lower limb paralysis	串珠样 Beaded sample	激素及长春新碱治疗联合椎板部分切除 Hormone and vincristine therapy combined with partial laminectomy	1年无复发 No recurrence for 1 year
Cao et al, 2008[14]	女 Female	18岁 18 years	C2 神经根 C2 nerve root	颈部疼痛 Neck pain	低 T1 高 T2 Low T1, high T2	椎板切除 Laminectomy	无复发 * No recurrence
Dehner LP, 2003[15]	女 Female	14岁 14 years	L3 椎体 L3 vertebral body	背部疼痛,椎体塌陷 Back pain, vertebral collapse	NA	NA	NA
Rampini et al, 2001[16]	女 Female	3岁 3 years	C5-C7 IDEM	痉挛性四肢瘫痪 Spastic quadriplegia	等 T1 等 T2 Equal T1 and equal T 2	椎板切除 Laminectomy	4个月无复发 No recurrence for 4 months
Oyama et al, 1997[17]	女 Female	18岁 18 years	C1 IDEM	左侧偏瘫,左侧感觉减退 Left hemiplegia, left hypoesthesia	NA	枕下颅骨及 C1 半椎板切除 Resection of suboccipital skull and C1 semi-lamina	无复发 * No recurrence
Kim et al, 1996[18]	男 Male	16个月 16 months	T1-2 IDEM	痉挛性麻痹 Spastic paralysis	等 T1 高 T2 Equal T1 and high T2	椎板切除 Laminectomy	3个月无复发 No recurrence for 3 months
Kitchen et al, 1995[19]	女 Female	15岁 15 years	S1 神经根 S1 nerve root	下腰痛/坐骨神经痛 Low back pain/sciatica	等 T1 高 T2 Equal T1, high T2	椎板切除 Laminectomy	无复发 * No recurrence
Shimosawa et al,1993[20]	女 Female	13个月 13 months	T6-T9	痉挛性麻痹 Spastic paralysis	低 T1 高 T2 Low T1 and high T2	椎板切除 Laminectomy	6个月无复发 No recurrence for 6 months

注:NA,信息不详;* 随访时间不详;IDEM,硬膜外髓内
Note: NA, not applicable; * indicates that the specific follow-up time is unknown; IDEM, intradural extramedullary

参考文献

1. Höck M, Zelger B, Schweigmann G, et al. The various clinical spectra of juvenile xanthogranuloma: imaging for two case reports and review of the literature [J]. BMC Pediatr, 2019, 19(1): 128.
2. Rajasekhar R, Karthigeyan M, Salunke P, et al. A novel fixation technique using anterior C1 screw in a pediatric solitary cervical spinal juvenile xanthogranuloma[J]. Eur Spine J, 2019, 28(Suppl 2): 56-60.
3. Irmola T, Laitinen MK, Parkkinen J, et al. Solitary juvenile xanthogranuloma in the spine pretreated with neoadjuvant denosumab therapy followed by surgical resection in a 5-year-old child: case report and literature review[J]. Eur Spine J, 2018, 27(3): 555-560.
4. Shenoy A, Singhal SS, Shinde S. Solitary intraspinal juvenile xanthogranuloma in an infant[J]. Asian J Neurosurg, 2018, 13 (1): 172-175.
5. Bhaisora KS, Jaiswal AK, Mehrotra A, et al. Solitary juvenile xanthogranuloma of the cervical spine in a child: a case report and review of literature[J]. Asian J Neurosurg, 2015, 10 (1): 57.
6. Purohit D, Chanduka AK, Sharma V, et al. Juvenile xanthogranuloma of adult spine: a rare case and review of literature[J]. Asian J Neurosurg, 2014, 9(4): 239.
7. Singhvi S, Bhargava S. Isolated juvenile xanthogranuloma in thoracic spine: intraoperative cytological diagnosis of a rare presentation [J]. J Interdiscipl Histopathol, 2014, 2(3): 158-162.
8. Konar S, Pandey P, Yasha TC. Solitary juvenile xanthogranuloma in cervical spine: case report and review of the literature[J]. Turk Neurosurg, 2014, 24(1): 102-107.
9. Wille DA, Bozinov O, Scheer I, et al. Isolated intraspinal juvenile xanthogranuloma in an infant presenting as acute paraplegia[J]. Neuropediatrics, 2013, 44(3): 171-173.
10. Inoue H, Seichi A, Yamamuro K, et al. Dumbbell-type juvenile xanthogranuloma in the cervical spine of an adult [J]. Eur Spine J, 2011, 20(2): 343-347.
11. Agabegi SS, Iorio TE, Wilson JD, et al. Juvenile xanthogranuloma in an adult lumbar spine: a case report [J]. Spine, 2011, 36(1): 69-73.
12. Jain A, Mathur K, Khatri S, et al. Rare presentation of juvenile xanthogranuloma in the thoracic spine of an adult patient: case report and literature review[J]. Acta Neurochirurgica, 2011, 153(9): 1813-1818.
13. Castro-Gago M, Gómez-Lado C, Alvez F, et al. Juvenile xanthogranuloma of the cauda equine [J]. Pediatr Neurol, 2009, 40(2): 123-125.
14. Cao D, Ma J, Yang X, et al. Solitary juvenile xanthogranuloma in the upper cervical spine: case report and review of the literatures[J]. Eur Spine J, 2008, 17(Suppl 2): 318-323.
15. Dehner LP. Juvenile xanthogranulomas in the first two decades of life: a clinicopathologic study of 174 cases with cutaneous and extracutaneous manifestations [J]. Am J Surg Pathol, 2003, 27(5): 579-593.
16. Rampini PM, Alimehmeti RH, Egidi MG, et al. Isolated cervical juvenile xanthogranuloma in childhood [J]. Spine, 2001, 26(12): 1392-1395.
17. Oyama H, Ikeda K, Inoue S, et al. A case of intradural xanthogranuloma in the upper cervical spine[J]. No Shinkei Geka, 1997, 25(8): 745-748.
18. Kim DS, Kim TS, Choi JU. Intradural extramedullary xanthoma of the spine: a rare lesion arising from the dura mater of the spine: case report[J]. Neurosurgery, 1996, 39(1): 182-185.
19. Kitchen ND, Davies MS, Taylor W. Juvenile xanthogranuloma of nerve root origin[J]. Br J Neurosurg, 1995, 9(2): 233-237.
20. Shimosawa S, Tohyama K, Shibayama M, et al. Spinal xanthogranuloma in a child: case report[J]. Surg Neurol, 1993, 39(2): 138-142.
21. Fu Y, Huang QL. Xanthoma combined with gout infiltration of the achilles tendon: a case report [J]. Clin Med Insights Arthritis Musculoskelet Disord, 2019, 12: 1179544119865261.
22. Meyer M, Grimes A, Becker E, et al. Systemic juvenile xanthogranuloma: a case report and brief review[J]. Clin Exp Dermatol, 2018, 43(5): 642-644.
23. Stover DG, Alapati S, Regueira O, et al. Treatment of juvenile xanthogranuloma[J]. Pediatric blood cancer, 2008, 51(1): 130-133.
24. Fan R, Sun J. Neonatal systemic juvenile xanthogranuloma with an ominous presentation and successful treatment [J]. Clin Med Insights Oncol, 2011, 5: 157-161.
25. Ito J, Shima H, Inoue K, et al. Haploidentical stem cell transplantation with posttransplant cyclophosphamide for refractory systemic juvenile xanthogranuloma[J]. Pediatr Blood Cancer, 2019, 66(10): e27926.
26. Tidyman WE, Rauen KA. The RASopathies: developmental syndromes of Ras/MAPK pathway dysregulation[J]. Curr Opin Genet Dev, 2009, 19(3): 230-236.
27. Bains A, Parham DM. Langerhans cell histiocytosis preceding the development of juvenile xanthogranuloma: a case and review of recent developments[J]. Pediatr Dev Pathol, 2011, 14(6): 480-484.
28. Haroche J, Abla O. Uncommon histiocytic disorders: Rosai-Dorfman, juvenile xanthogranuloma, and Erdheim-Chester disease [J]. Hematology Am Soc Hematol Educ Program, 2015, 2015: 571-578.
29. Raygada M, Arthur DC, Wayne AS, et al. Juvenile xanthogranuloma in a child with previously unsuspected neurofibromatosis type 1 and juvenile myelomonocyticleukemia [J]. Pediatric Blood Cancer, 2010, 54(1): 173-175.
30. Paxton CN, O'Malley DP, Bellizzi AM, et al. Genetic evaluation of juvenile xanthogranuloma: genomic abnormalities are uncommon in solitary lesions, advanced cases may show more complexity[J]. Mod Pathol, 2017, 30(9): 1234-1240.

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