Eur Spine J
DOI 10.1007/s00586-017-5030-x

CASE REPORT

A case report of atypical long segmental thoracic hypertrophic pachymeningitis with ossification of ligamentum flavum and literature review

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Received: 18 December 2016 / Accepted: 2 March 2017

Abstract
Background Thoracic spinal stenosis caused by ossification of ligamentum flavum (OLF) is frequently seen, but long segmental thoracic spinal cord compressed by consequent thickened ligament posteriorly was rarely reported.
Object To report a case of thoracic spinal cord compression caused by atypical long segmental thoracic hypertrophic pachymeningitis (HP) with OLF.
Methods A 55-year-old woman presenting with weakness and numbness in lower extremities was admitted to our department. Combined with physical examination and MRI results, diagnosis of HP with OLF was considered. Due to progressive neurological symptoms, thoracic decompression with internal fixation was performed.
Results The patient felt a reduced numbness and improvement in motor functions 5 days after surgery. Pathological examination suggested the diagnosis of HP with OLF.
Conclusions HP is a rare condition characterized as thickening and enhancement of the dura mater on contrast-enhanced MRI and chronic inflammatory hyperplasia changes on biopsy. A case of atypical HP complicated with OLF is described. Chondrocytes infiltration in histological examination indicates the potential of ossification in HP.

Keywords Myelopathy · Thoracic spine · Hypertrophic pachymeningitis · Ossification of ligamentum flavum

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Introduction

Long segmental thoracic spinal cord compressed by consequent thickened ligament posteriorly is rare. Hypertrophic Pachymeningitis (HP) can lead to this performance which is identified by thickening and enhancement of the dura mater on contrast enhanced MRI or chronic inflammatory changes on biopsy test. Here a case of chronic myelopathic symptoms in a 55-year-old woman whose thoracic spinal cord was compressed by long consequent ligament and fibrous tissue is presented. MRI and histological examination prompted a possible diagnosis of atypical thoracic hypertrophic pachymeningitis.

Case report

A 55-year-old woman had suffered weakness and numbness in left lower extremity for 1 year, then she got the same symptoms in her right lower extremity half a year ago. She felt hard to walk unaided when admitted. The patient got no history of back trauma. A physical examination revealed 4/5 muscle strength in lower limbs. Decreased pin-prick and touch sensation below bilateral knees was detected. Knee tendon reflex was normal. Patellar and ankle clonus were negative. Babinski sign was not presented. A computed tomographic (CT) scan showed a striped lesion located posteriorly within the spinal canal from T3 to L1 levels, with non-enhancement on contrast images by iodinated agents. Multiple ossification of ligamentum flavum (OLF) was also observed (Fig. 1). Magnetic resonance imaging (MRI) with gadopente tate dimeglumine (Gd-DTPA) of the spine presented an epidural lesion located between T3 and L1 compressing the spinal cord posteriorly, with low signal intensity on T1 and

Published online: 01 April 2017

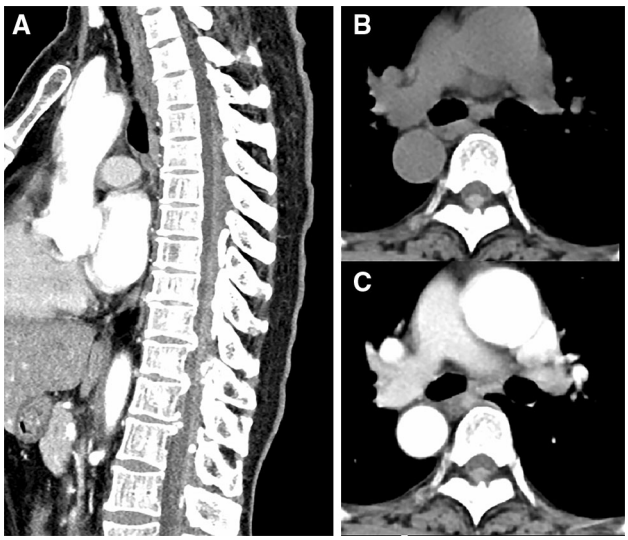

Fig. 1 Computed tomographic scan images. Sagittal **a** image showed a striped lesion located posteriorly within the spinal canal from T3 to L1 levels, with higher density than spinal cord. Multiple OLF was also observed. Axial pre- (**b**) and post-iodinated agents (**c**) images of the thoracic spine showed a non-enhancement lesion between spinal cord and ossified ligamentum flavum

T2 weighted images and non-enhancement on T1 weighted-enhanced images (Fig. 2). Due to progressive neurological symptoms, the patient underwent a T3-L1 laminectomy, and a consequent white-colored fibrous tissue was stripped. Pia mater was visible (Fig. 3). Histological examination was performed afterwards. Pathological change presented as ligament and fibrous tissue with no inflammatory cells infiltrated. No obvious differences were observed in spinal cord side or lamina side of the specimen. In histological examination of pathological dura mater adhering to ossified ligamentum flavum, chondrocytes were found infiltrated (Fig. 4). Five days post of surgery, the patient felt a reduced numbness and improvement in motor function.

Discussion

Myelopathy caused by OLF has been reported frequently, but long segmental thoracic spinal cord compressed by consequent thickened ligament posteriorly is rare. The ligamentum flavum connects adjoining two laminas and discontinues in lamina part, of which both side flaps separated at the midline. While in this case, a consequent lesion was observed compressing the spinal cord posteriorly at the midline. In the operation the thickened dura mater was demonstrated, and the gross specimen presented as a long consequent fibrous tissue. So diagnosis of HP was given priority to be considered.

HP is an inflammatory process of the dura mater which is characterized as thickening and enhancement of the durra mater on contrast-enhanced MRI and chronic inflammatory hyperplasia changes seen on biopsy. According to etiology, HP is classified as idiopathic and secondary type. Autoimmune disorders was identified as secondary causes of HP in previous reports, such as Rheumatoid arthritis [1], Multifocal fibro sclerosis [2], Wegener's granulomatosis [3], Neuro-Behçet's disease [4], sarcoidosis [5], ANCA related diseases [6–8], IgG4 related diseases [9–12, 23] and antiphospholipid syndrome [13]. Some infectious diseases caused by bacteria [14, 37], fungi [15] and Spirochete [16, 17] has been reported associated with HP as well. Idiopathic hypertrophic pachymeningitis (IHP) should be an exclusive diagnosis. In this case diagnostic evidences and potential causal relationships were attempted to be found but failed. The serum CRP, ESR,

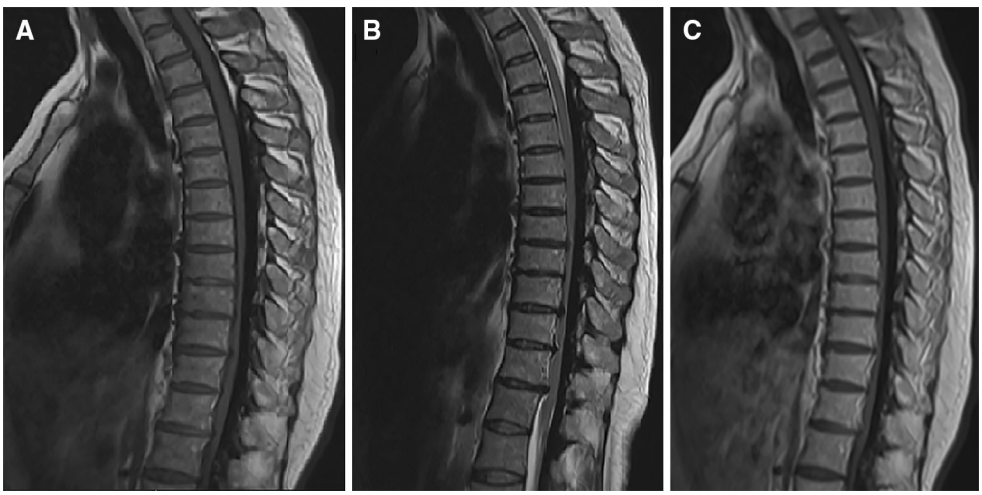

Fig. 2 Magnetic resonance images. Sagittal images showed low signal intensity on T1 (**a**) and T2 (**b**) weighted images and non-enhancement on T1 weighted-enhanced images (**c**)

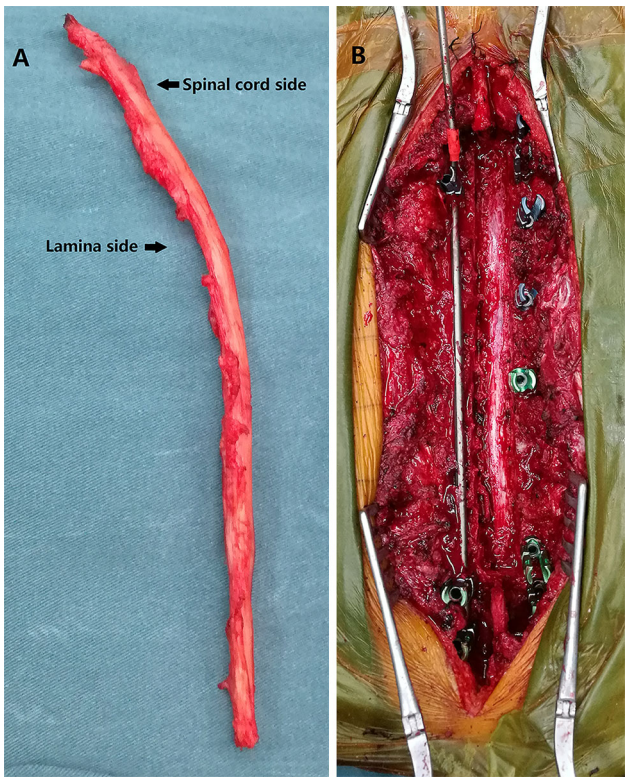

Fig. 3 **a** Part of pathological dura mater specimen. Lamina side was adherent to posterial tissue. Spinal cord side was smooth and easily stripped from pia mater. **b** Pia mater was visible after partial dura mater resection

ANCA, IgG levels were within the normal ranges. ANA and RF were negative.

Epidemiology of HP was rarely reported. In a nationwide survey of 159 cases in Japan [18], a prevalence of 0.949/100,000 population was clarified. The mean age at onset was 58.3 ± 15.8 years. ANCA-related HP was found in 54 cases (34.0%).

MRI findings of HP can present as peripheral enhancement pattern. This pattern represents more active inflammation in peripheral zone than in central zone of fibrosis [7, 19, 20]. Homogeneous enhancement pattern has been reported frequently in IHP [21–23]. A case of IHP with non-enhancement in MRI was also reported [24]. Similarly, in this case, contrast MRI presented low signal intensity on T1 and T2 weighted images and non-enhancement on T1 weighted-enhanced images. This kind of enhancement pattern is considered to be associated with the lack of inflammatory reaction in pathological dura matter tissue [20, 24, 25]. Moreover, in some previously reported cases of HP, hyperostosis [26, 27] or destruction [24, 28] of adjacent bone tissue was observed.

Histological examination is the key to the diagnosis of HP. Typical pathological manifestations of HP are characterized as dense fibrous tissue with a moderate infiltrate of inflammatory cells. While in our case, no obvious infiltration of inflammatory cells was observed among hyperplasic fibroblasts in histological examination, neither in spinal cord side nor in lamina side of the specimen. This pattern of performance might due to lack of inflammatory process and poor response to immunosuppressive therapy [7, 25]. Obvious OLF was also observed in this case. In previous case reports, thickening or ossification of dura mater were confined to the part of the tissue which attached to ossificated ligamentum flavum [32, 33]. In the case presented, thickened dura mater from T3 to T6 without ossificated ligamentum flavum compressing posteriorly was also observed. So the thickening of dura mater and ossification of ligamentum flavum should be two independent processes in this case. Histological examination of dura mater adherent to ossified ligamentum flavum was carried on and chondrocytes were found infiltrated. Such kind of performance is similar to which of ligamentum flavum in the process of ossification [29]. This change might be caused by mechanical stimulation from ossified ligamentum flavum. The role of mechanical compress in the process of ligamentum flavum hyperplasia and ossification has been reported [29–31]. Similarly, a possible mechanism and pathological outcome of HP with

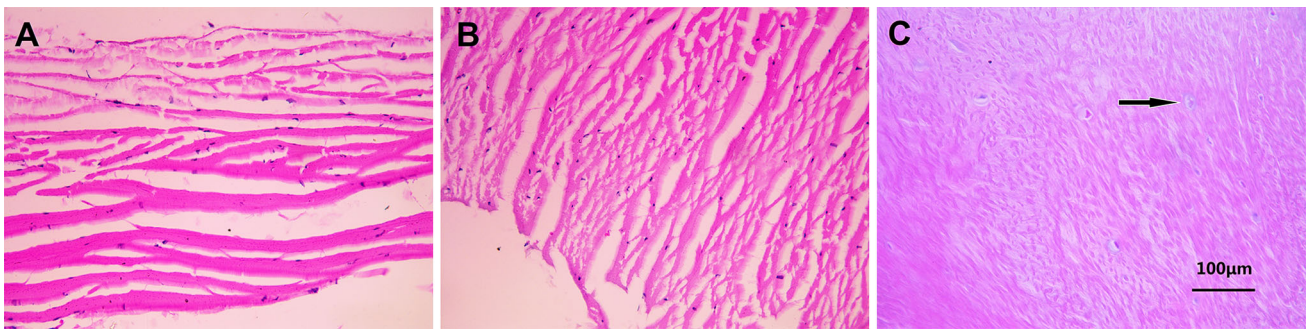

Fig. 4 Histological examination. Both of spinal cord side (**a**) and lamina side (**b**) of the pathological dura mater sample presented scattered fibroblasts. **c** Tissue section of pathological dura mater adhering to ossified ligamentum flavum revealed chondrocytes infiltration (hematoxylin-eosin stain, original magnification, ×400)

ossification of ligamentum flavum was proposed. When ossified ligamentum flavum compresses the dura mater, with activity of spine, relative friction between the dura mater and ossified ligamentum flavum will lead to adhesion. Osteogenic cytokines will transfer to dura mater via adherent tissue and finally lead to chondrocytes differentiation. Several previous studies reported dura mater ossification occurred in OLF patients with an incidence ranging from 15.3 to 40% [32–34]. No previous study had shown the potential of ossification in HP. In histological examination of this case, chondrocytes were found infiltrated in particular area.

Because of low morbidity and lack of long time follow-up studies, there is no optimal management plan for patients with HP currently. In some cases of HP associated with infections, antimicrobial therapy was proved to be effective [35]. Steroid [7, 20, 25], cyclophosphamide [36] and methotrexate [37] therapy had shown limited efficacy in some alternative clinical trials. For the patients with progressed neurologic defection, decompression surgery should be considered. In the present case the patient suffered progressed myelopathic symptoms, so laminectomy and pathological dura mater resection were performed.

Conclusion

HP is a rare condition which is characterized as thickening and enhancement of the durra mater on contrast-enhanced MRI and chronic inflammatory hyperplasia changes on biopsy. A case of atypical HP complicated with OLF is described. MRI showed non-enhancement on T1 weighted images. Histological examination showed no infiltration of inflammatory cells. Chondrocytes infiltration indicates the potential of ossification in HP.

Compliance with ethical standards

Conflict of interest None of the authors has any potential conflict of interest.

References

1. Rosenfeld JV, Kaye AH, Davis S, Gonzales M (1987) Pachymeningitis cervicalis hypertrophica: case report. J Neurosurg 66:137–139. doi:10.3171/jns.1987.66.1.0137
2. Levine MR, Kaye L, Mair S, Bates J (1993) Multifocal fibrosclerosis: report of a case of bilateral idiopathic sclerosing pseudotumor and retroperitoneal fibrosis. Arch Ophthalmol 111:841–843. doi:10.1001/archopht.1993.01090060129037
3. Nishino H, Rubino FA, Parisi JE (1993) The spectrum of neurologic involvement in Wegener's granulomatosis. Neurology 43:1334–1337. doi:10.1212/WNL.43.7.1334
4. Yoon BN, Kim SJ, Lim MJ et al (2015) Neuro-Behçet's disease presenting as hypertrophic pachymeningitis. Exp Neurobiol 24:252–255. doi:10.5607/en.2015.24.3.252
5. Subrati N, Vaqas B, Peterson D et al (2015) Hypertrophic pachymeningitis with sarcoidosis: a rare cause of craniocervical compression. BMJ Case Rep. doi:10.1136/bcr-2014-208604
6. Nakajima H, Yamane K, Kimura F et al (2016) Optic perineuritis associated with antineutrophil cytoplasmic autoantibody-related hypertrophic pachymeningitis: a case report. Neurol Sci 37:1–3. doi:10.1007/s10072-015-2454-0
7. Xia L, Zhao J, Qian W et al (2015) ANCA-Associated systemic vasculitis presenting with hypertrophic spinal pachymeningitis: a report of 2 cases and review of literature. Medicine (Baltimore) 94:e2053. doi:10.1097/MD.0000000000002053
8. Durant C, Martin J, Godmer P et al (2011) Exceptional osseous and meningeal spinal localization of ANCA-associated granulomatous vasculitis with hypertrophic spinal pachymeningitis. J Neurol 258:1172–1173. doi:10.1007/s00415-010-5886-8
9. Kim SH, Kim JS (2015) Immunoglobulin G4-related hypertrophic pachymeningitis mimicking chiari malformation. J Clin Neurol 12:238–240. doi:10.3988/jcn.2016.12.2.238
10. Lu LX, Dellatorre E, Stone JH et al (2014) IgG4-related hypertrophic pachymeningitis: clinical features, diagnostic criteria, and treatment. JAMA Neurol 71:785–793. doi:10.1001/jamaneurol.2014.243
11. Kim EH, Kim SH, Cho JM et al (2011) Immunoglobulin G4-related hypertrophic pachymeningitis involving cerebral parenchyma. J Neurosurg 115:1242–1247. doi:10.3171/2011.7.JNS1166
12. Della-Torre E, Passerini G, Furlan R et al (2013) Cerebrospinal fluid analysis in immunoglobulin G4-related hypertrophic pachymeningitis. J Rheumatol 40:1927–1929. doi:10.3899/jrheum.130678
13. Tokushige SI, Matsumoto H, Takemura T et al (2012) Secondary hypertrophic pachymeningitis in antiphospholipid syndrome. J Neuroimmunol 250:115–117. doi:10.1016/j.jneuroim.2012.05.006
14. Shiraishi W, Hayashi S, Iwanaga Y et al (2015) A case of synovitis, acne, pustulosis, hyperostosis, and osteitis (SAPHO) syndrome presenting with hypertrophic pachymeningitis. J Neurol Sci 349:229–231. doi:10.1016/j.jns.2014.12.020
15. Schiess RJ, Coscia MF, Mcclellan GA (1984) Petriellidium boydii pachymeningitis treated with miconazole and ketoconazole. Neurosurgery 14:220–224. doi:10.1227/00006123-198402000-00019
16. Agdal N, Hagdrup HK, Wantzin GL (1980) Pachymeningitis cervicalis hypertrophica syphilitica. Acta Derm Venereol 60:184–186
17. Vale TC, Moraes TE, Lara A et al (2012) Hypertrophic cervical spinal cord pachymeningitis due to Treponema pallidum infection. Neurol Sci 33:359–362. doi:10.1007/s10072-011-0738-6
18. Yonekawa T, Murai H, Utsuki S et al (2014) A nationwide survey of hypertrophic pachymeningitis in Japan. J Neurol Neurosurg Psychiatry 85:732–739. doi:10.1136/jnnp-2013-306410
19. Pai S, Welsh CT, Patel S et al (2007) Idiopathic hypertrophic spinal pachymeningitis: report of two cases with typical MR imaging findings. AJNR Am J Neuroradiol 28:590–592
20. Cb VDP, Chakraborty S, Côté I et al (2015) Case 216: hypertrophic spinal pachymeningitis. Radiology 275:303–307. doi:10.1148/radiol.15122159
21. Kim JH, Park YM, Chin DK (2011) Idiopathic hypertrophic spinal pachymeningitis: report of two cases and review of the literature. J Korean Neurosurg Soc 50:392–395. doi:10.3340/jkns.2011.50.4.392
22. Park SH, Whang CJ, Sohn M et al (2001) Idiopathic hypertrophic spinal pachymeningitis: a case report. J Korean Med Sci 16:683–688. doi:10.3346/jkms.2001.16.5.683
23. Takeuchi S, Osada H, Seno S et al (2014) IgG4-related intracranial hypertrophic pachymeningitis: a case report and

review of the literature. J Korean Neurosurg Soc 55:300–302. doi:10.3340/jkns.2014.55.5.300
24. Jee TK, Lee SH, Kim ES et al (2014) Idiopathic hypertrophic spinal pachymeningitis with an osteolytic lesion. J Korean Neurosurg Soc 56:162–165. doi:10.3340/jkns.2014.56.2.162
25. Ezzeldin M, Shawagfeh A, Schnadig V et al (2014) Hypertrophic spinal pachymeningitis: idiopathic vs. IgG4-related. J Neurol Sci 347:398–400. doi:10.1016/j.jns.2014.10.012
26. Noda D, Tsugu H, Nishikawa W et al (2008) Case of idiopathic hypertrophic pachymeningitis presenting with hyperostosis. No shinkei geka 36:717–723
27. Lin CK, Lai DM (2013) IgG4-related intracranial hypertrophic pachymeningitis with skull hyperostosis: a case report. BMC Surg 13:1–5. doi:10.1186/1471-2482-13-37
28. Lee YS, Lee HW, Park KS et al (2014) Immunoglobulin g4-related hypertrophic pachymeningitis with skull involvement. Brain Tumor Res Treat 2:87–91. doi:10.14791/btrt.2014.2.2.87
29. Yayama T, Uchida K, Kobayashi S et al (2007) Thoracic ossification of the human ligamentum flavum: histopathological and immunohistochemical findings around the ossified lesion. J Neurosurg Spine 7:184–193. doi:10.3171/SPI-07/08/184
30. Li F, Chen Q, Xu K (2006) Surgical treatment of 40 patients with thoracic ossification of the ligamentum flavum. J Neurosurg Spine 4:191–197. doi:10.3171/spi.2006.4.3.191
31. Tsukamoto N, Maeda T, Miura H et al (2006) Repetitive tensile stress to rat caudal vertebrae inducing cartilage formation in the spinal ligaments: a possible role of mechanical stress in the development of ossification of the spinal ligaments. J Neurosurg Spine 5:234–242. doi:10.3171/spi.2006.5.3.234
32. Mizuno J, Nakagawa HN, Song J (2005) Dural ossification associated with cervical ossification of the posterior longitudinal ligament: frequency of dural ossification and comparison of neuroimaging modalities in ability to identify the disease. J Neurosurg Spine 2:425–430. doi:10.3171/spi.2005.2.4.0425
33. Muthukumar N (2009) Dural ossification in ossification of the ligamentum flavum: a preliminary report. Spine (Phila Pa 1976) 34:2654–2661. doi:10.1097/BRS.0b013e3181b541c9
34. Wang W, Kong L, Zhao H et al (2007) Thoracic ossification of ligamentum flavum caused by skeletal fluorosis. Eur Spine J 16:1119–1128. doi:10.1007/s00586-006-0242-5
35. Kanai M, Shimizu H (2009) A case of hypertrophic pachymeningitis treated successfully with antibiotics: the remarkable effect of minocycline hydrochloride in reducing the serum C-reactive protein value. No Shinkei Geka 37:673–679
36. Zhuoyou C, Chuanzhong Q, Xinsheng D (2011) Idiopathic hypertrophic pachymeningitis successfully treated with intravenous cyclophosphamide. Neurol India 59:915–916. doi:10.4103/0028-3886.91384
37. Ruiz-Sandoval JL, Bernard-Medina G, Ramos-Gómez EJ et al (2006) Idiopathic hypertrophic cranial pachymeningitis successfully treated with weekly subcutaneous methotrexate. Acta Neurochir (Wien) 148:1011–1014. doi:10.1007/s00701-006-0775-8