Histopathological and Cytogenetic Analysis of Epidural Adipose Tissue in Symptomatic Lumbar Epidural Lipomatosis

Taketoshi Yasuda (yasuda@med.u-toyama.ac.jp)
University of Toyama
Kayo Suzuki
University of Toyama
Shoji Seki
University of Toyama
Kenta Watanabe
University of Toyama
Hiroto Makino
University of Toyama
Masahiko Kanamori
University of Toyama
Yoshiharu Kawaguchi
University of Toyama

Research Article

Keywords: lumbar epidural lipomatosis, lipoma, histopathological findings, cytogenetic analysis, laminectomy, adipose tissue

Posted Date: November 22nd, 2021

DOI: https://doi.org/10.21203/rs.3.rs-1049484/v1

Abstract

Lumbar epidural lipomatosis (LEL) is characterized by the abnormal accumulation of unencapsulated adipose tissue in the spinal epidural space. Symptomatic LEL occurs in middle aged and elderly patients, and it is most often seen in males. The purpose of this study was to elucidate the histopathological and cytogenetic characteristics of the epidural lipomatosis in patients with symptomatic LEL. Six patients undergoing decompressive spinal surgery (mean age, 69.4 years) were enrolled between 2013 and 2017. Three cases were steroid-induced and 3 cases were diagnosed as idiopathic LEL. We compared the differences in histological morphology between the subcutaneous fat tissue and epidural fat tissue in each patient. We also analyzed the karyotype of resected epidural lipomatous tissue using the G-band method. The epidural adipocytes were histologically more irregular and smaller compared with the subcutaneous adipocytes in all cases. The mean size of subcutaneous adipocytes and epidural adipocytes was 5,485.6 ± 2,584.1 μm^2 and 2,705.4 ± 1,069.1 μm^2, respectively. In cytogenetic analysis of the epidural adipocytes, loss of the Y chromosome (LOY) was found in all 6 cases. The mechanisms related to the development of LEL are not well understood. In this study, the size of the lipid component of epidural adipocytes was significantly smaller than that of subcutaneous adipocytes in LEL. Cytogenetically, LOY was frequently recognized. Although this may be an effect rather than a cause, LOY may be related to morphologic changes in and proliferation of adipocytes in LEL. LOY might partially contribute to the pathological mechanism or expression of LEL.

Background

Spinal epidural lipomatosis (SEL) is a relatively rare condition first described by Lee et al. in 1975 [1]. SEL is characterized by the accumulation of unencapsulated adipose tissue in the spinal epidural space, which leads to a variety of neurological symptoms [2]. The administration of exogenous steroids to treat a number of different disorders can result in secondary SEL [2, 3], as can endocrinopathies such as Cushing's syndrome [4] or hypothyroidism [5]. In addition, idiopathic SEL can occur without any history of endocrine disorders or steroid use [6, 7]. SEL predominantly affects men, and over 75% of all reported cases are associated with obesity [8–10]. However, no criteria for the clinical symptoms or imaging characteristics of SEL have been established.

Among patients with SEL, 39–42% have also been found to have lumbar epidural lipomatosis (LEL) [11–13]. A diagnosis of SEL is primarily based on the findings of magnetic resonance imaging (MRI), which is widely considered to be the most sensitive modality used to assess adipose tissue [14, 15]. Excessive deposition of epidural fat (EF) demonstrating a hyperintense and intermediate signal intensity on T1- and T2-weighted imaging, respectively, is found in the spinal epidural space in most cases of SEL [14], while a characteristic "Y-sign" or square/stellate dural sac is frequently seen on axial MRI in cases of LEL [16].

Lipoma is a benign tumor composed of mature adipocytes [17]. It can occur in any part of the body, but intraspinal extradural lipomas are rare [18–20]. True adult spinal lipomas not associated with spinal dysraphism account for 0.4–0.8% of all intraspinal tumors [18]. Like LEL, spinal lipoma is also diagnosed

on MRI. An intraspinal mass showing signal hyperintensity on T1-weighted imaging and intermediate signal intensity on T2-weighted imaging is commonly found [19, 20]. Given the rarity and lack of other remarkable MRI findings of spinal lipoma, this lesion can easily be overlooked or misdiagnosed [19].

In both spinal lipoma and LEL, histopathological findings show mature adipocytes that vary only slightly in size and shape and have small, eccentric nuclei. It is difficult to distinguish between spinal lipoma and LEL by histopathological findings alone. Therefore, additional diagnostic tools are necessary to distinguish between true spinal lipoma and LEL. Cytogenetically, lipomas frequently show karyotypic abnormalities such as rearrangement of 12q13-15 and deletions of 13q [17]. On the other hand, no reports have been published on cytogenetic analysis in LEL. We therefore hypothesized that morphological and cytogenetical abnormalities may exist in LEL. Given this background, this study aimed to elucidate the histopathological characteristics and conduct a cytogenetic analysis of LEL tissue in patients undergoing decompressive surgery.

Methods

Six patients underwent decompressive surgery for LEL in our institutions between 2013 and 2017. The clinical and imaging findings of all cases were reported previously [21], and the demographic data are shown in Table 1. All patients were Japanese men with a mean age of 71.3 years (range 64–79 years) at the time of surgery. Three of the patients had a history of steroid administration, and the other three had no history of steroid administration or endocrinopathies. All patients presented with neurological deficits in the lower extremities with intermittent claudication as seen in cauda equina syndrome (CES) and/or radiculopathy. Neural symptoms were classified into three types according to a previous report [22]: radicular type, presenting as unilateral radicular pain; cauda equina type, showing symptoms with less dermatome-specific neurogenic claudication; and mixed type, showing characteristics of both radicular and cauda equine types. The symptoms were those of CES in four patients, mixed CES and radiculopathy in one, and radiculopathy in one.

All patients subsequently underwent trumpet laminectomy [23] with epidural lipomatosis resection. The indication for surgery was the presence of neurogenic symptoms that failed to respond to conservative treatment for more than 3 months. We excluded patients who were treated with reduction surgery for spinal deformities, such as degenerative scoliosis with a Cobb angle more than 10 degrees, lumbar kyphosis with a Cobb angle more than 10 degrees, and spondylolisthesis with a Meyerding grade higher than 1.

We diagnosed LEL of grade II or more, as described by Borré et al. [14], at the axial plane parallel to the superior end plate of the S1 vertebral body on T1-weighted axial MRI. Briefly, grade II represents moderate overgrowth of EF, defined as having an EF/spinal anteroposterior diameter (SpiC) index of more than 50% at the spinal level responsible for symptoms. By contrast, patients with an EF/SpiC index less than 50% were excluded. MRI was assessed by two different spine surgeons (TY and KS). LEL involved one to five

lumbar intervertebral levels on MRI. The LEL grade was classified based on MRI results [14] and was grade II in one patient and grade III in five.

The present study was approved by the Ethics Committee at Toyama University Hospital. All patients provided written informed consent to participate in this analysis. All methods were performed in accordance with the relevant laboratory guidelines and regulations.

Histopathological Analysis

During the approach in surgery, a 5´5-mm sample of subcutaneous fat tissue was collected. Then, the epidural lipomatous tissue was collected after laminectomy. The tissue was fixed with 4% paraformaldehyde in phosphate-buffered saline and embedded in paraffin to obtain 4 mm-thick sections. Deparaffinized sections were stained with hematoxylin and eosin. The sections were examined under an upright microscope. To investigate the differences in histological morphology between the subcutaneous fat and epidural lipomatous tissue in the same patient, the size of the overall lipid component of the adipocytes was compared by two different individuals (TY and KS). The mean overall lipid component of 10 adipocytes per field as measured in three microscopic fields (´200 magnification) at random was determined. Measurements were analyzed using ImageJ processing software [24] and compared.

Cytogenetic Analysis

Chromosome analysis was performed on G-bands by trypsin using Giemsa (GTG)-banded cells (SRL, Inc., Tokyo, Japan) according to the manufacturer's procedures. A representative fresh tissue sample from the surgical resection was received for conventional cytogenetic analysis. Culturing, harvesting, and preparation of slides were performed as previously described [25]. Briefly, the tissues were disassociated mechanically and enzymatically and cultured in RPMI 1640 (Sigma-Aldrich Japan Co., Tokyo, Japan) supplemented with 20% fetal bovine serum (Life Technologies Japan, Ltd., Tokyo, Japan) for 3–8 days. Cultured cells received an overnight exposure to colcemid (0.02 mg/mL). Following hypotonic treatment (0.8% sodium citrate for 20 min), the cells were fixed three times with a solution of methanol:glacial acetic acid (3:1). Chromosome analysis was performed on GTG-banded metaphases of 20 cells, and the karyotypes were expressed according to the International System for Human Cytogenetic Nomenclature 2013 (ISCN, 2013) [26].

Statistical Analysis

Values were expressed as means ± standard deviation (SD). Significant differences between means were analyzed using Student's *t* test, and a P value of less than 0.05 was considered statistically significant.

Results

Histopathological Findings

Histopathological examination in LEL showed the presence of normal mature adipocytes in all cases. They did not display nuclear atypia, and there was no increased mitosis, hyperchromasia, or multinucleation of adipocytes in LEL tissue. Lipoblasts were not identified. In all cases, the size of the lipid component of epidural adipocytes was significantly smaller than that of subcutaneous adipocytes. The mean sizes of the lipid component of subcutaneous adipocytes and epidural adipocytes were 5485.6 ± 2584.1 and 2705.4 ± 1069.1 mm^2, respectively, demonstrating that the overall size of the lipid component of epidural adipocytes was significantly smaller than that of subcutaneous adipocytes. There was no significant difference between the size of the lipid component of adipocytes in idiopathic versus secondary LEL. The histopathological findings are summarized in Table 2.

Cytogenetic Findings

In all cases of both idiopathic and secondary LEL, loss of the Y chromosome was shown. The cytogenetic findings are summarized in Table 3.

Illustrative Case (Case 5)

A 77-year-old man was admitted to our hospital because of left leg pain and CES. He had a 3-year history of intermittent low back pain accompanied by asymmetric, slowly progressive bilateral leg pain, predominantly on the left. He had a body mass index of 26.2 kg/m^2. He had been receiving oral prednisolone 7.5 mg/day for polymyalgia rheumatica for 3 years.

Lumbar radiogram showed mild age-appropriate lumbar spondylosis. MRI sagittal section made clear LEL showing a high signal area on a T1- and T2-weighted imaging (Fig. 1). LEL compressed the dural sac all around, deforming the dural sac into square/stellate-like shape at the L3-5 level (Fig 2a). At the L5–S1 level, the dural sac showed a characteristic diamond-shaped deformation of LEL (Fig 2b), and MRI classified as grade III according to Borré's classification.

Laminectomies and LEL resection were performed at L3–S1 (Fig. 3). The patient had immediate symptomatic relief and was able to walk normally after the surgery. The histopathological findings consisted of proliferation of mature adipocytes, and a diagnosis of LEL was made. In comparison of his subcutaneous fat tissue and EF tissue, the sizes of the lipid component of the subcutaneous and epidural adipocytes were 4723.3 ± 1422.1 mm^2 and 2325.0 ± 667.2 mm^2, respectively (Fig. 4). The composite karyotype was 46,X,-Y (Fig. 5).

Discussion

SEL is a condition that causes neural symptoms by the growth of mature adipose tissue without a capsule in the epidural space [2]. The pathogenesis of SEL is not yet clear. Frogel et al. [2] classified SEL into the following four categories: (1) exogenous steroid use, 55.3%; (2) obesity only, 24.5%; (3) endocrinopathy or endogenous steroid group, 3.2%; and (4) non-obese idiopathic group, approximately 17%. Depending on these classified causes, the predominant site of SLE tends to be different. Exogenous

steroid-induced SEL more often involves the thoracic spine, whereas idiopathic SEL more often involves the lumbar spine, i.e., LEL [2]. LEL is more likely to occur in older men and our cases were also all males over the age of 62. Our patients included 3 with exogenous steroid use (Category 1) and 3 with overweight only (Category 4).

MRI is the most useful diagnostic imaging tool for both LEL and spinal lipoma. Both LEL and lipoma are exhibited as hyperintensity masses on T1- and T2-weighted imaging. Therefore, it can be difficult to distinguish between LEL and lipomas [18–20]. Although lipoma, unlike LEL, is a mass lesion enveloped by a capsule identification of the capsule may be sometimes difficult [19]. Therefore, the terms *lipoma* and *lipomatosis* are sometimes applied ambiguously [20]. On the other hand, epidural hematoma, tumor, and abscess typically show signal hyperintensity on T1-weighted imaging and intermediate signal intensity on T2-weighted imaging, making differentiation from SEL less difficult [27].

It has been reported that there are no morphological differences between normal and epidural adipocytes in LEL [2]. However, there are few reports that have analyzed the size of epidural adipocytes in LEL [9, 28]. One case study showed adipocyte hypertrophy in an obese patient with idiopathic LEL [28]. Fujita et al. [9] also reported that epidural adipocytes in obese patients with LEL were significantly larger than those in patients with lumbar spinal stenosis (LSS). The mechanism was thought to be adipocyte hypertrophy associated with obesity in LEL. In the present study, the size of the epidural adipocytes was smaller than that of subcutaneous adipocytes in the same patient; this result is contradictory to the previous report. However, only epidural adipocytes were examined in the previous report. Differences in the methods of analysis may have led to the different results.

Typically, the diameter of adipocytes in normal-weight adults is 70–90 μm, and adipocytes do not usually exceed 130 μm [29]. If an adipocyte is assumed to be circular, the size should be approximately 3500–6500 μm^2 in a normal-weight adult, and adipocytes are not larger than 13,200 μm^2. In this study, the size of the subcutaneous adipocytes was found to be within the normal range. However, the size of the epidural adipocytes was significantly smaller than that of the subcutaneous adipocytes. This finding suggests that adipocytes in LEL are changed by exogenous and/or endogenous factors. One possible exogenous factor is the fact that epidural adipocytes are present in the spinal canal, which is an enclosed space. Barz et al. [30] reported that epidural pressure in patients with LSS increases substantially compared with individuals without stenosis. We have previously reported the detailed imaging findings and epidural pressure measurements in LEL [21]. We showed that epidural pressure is higher in LEL than in LSS. Furthermore, epidural pressure is higher than the subarachnoid space pressure in patients with LEL. Therefore, adipocytes in LEL might decrease in size because of high epidural pressure due to the proliferation of adipocytes in the enclosed space. As another possibility, adipocytes might be newly produced in LEL. Additionally, chromosomal aberrations are an endogenous factor that might influence cellular morphology and function.

To the best of our knowledge, there are no reports on cytogenetic analysis in LEL. In this study, all patients showed solitary loss of the Y chromosome. In humans, the Y chromosome is one of two sex

chromosomes found only in males. The Y chromosome is functionally composed of three regions: (1) male-specific region of Y chromosome (MSY), (2) pseudoautosomal regions (PAR1 and PAR2), and (3) heterochromatin region on Yq. PAR is the lesion on Y and X chromosomes where homology remains, and heterochromatin region does not have a valid gene. The Y chromosome contains over 200 genes, of which at least 72 encode proteins. Some cells, especially those in elder men and smokers, lack a Y chromosome [31]. It has been found that men with a high proportion of hematopoietic stem cells in the peripheral blood that loss of the Y chromosome have been found to be at increased risk of non-blood cancer. [32]. Although the mechanism linking loss of the Y chromosome in peripheral blood and cancer mortality is not yet understood, these observations strongly suggest that the Y chromosome is involved in a wide variety of biological processes that have not yet been fully explored [32]. LEL occurs in middle and older age and is most often seen in men [33, 34]. Loss of the Y chromosome might partially contribute to the pathological mechanism or expression of LEL, although this may be an effect rather than a cause. To explore the role of the Y chromosome in LEL further, cytogenetic analysis in women with LEL will also be necessary.

In lipomas, various chromosomal aberrations such as 12q13-15 (65% of all cases), loss of 13q (10%), 6p21-23 (5%), and others (20%) have been reported [17]. With regard to the Y chromosome, only one case has been reported, i.e., t(Y;12) in a lipoma [35]; however, there are no reports of loss of the Y chromosome. Therefore, it is thought that there is no connection between lipomas and SEL based on cytogenetics. On the other hand, loss of the Y chromosome has been reported in various tumors, such as papillary renal cell carcinoma [36], urothelial bladder cancer [37], and hepatocellular carcinoma [38]. In this study, the size of epidural adipocytes was significantly smaller than that of subcutaneous adipocytes. In other words, the number of epidural adipocytes might be higher than the number of subcutaneous adipocytes. Therefore, although a mechanism for the pathogenesis of Y chromosome has not been elucidated, the Y chromosome might play a role in the pathogenesis of LEL.

The present study has several limitations. First, all patients evaluated with LEL were men, because LEL is more common in men. We have cytogenetic results for one woman, but the data cannot be presented here as they pertain to only one case. Second, cytogenetic analysis was performed only with epidural lipomatous tissue, not with subcutaneous lipomatous tissue. Therefore, we cannot definitively determine whether the loss of the Y chromosome is specific to EF in LEL. Third, the cohort was relatively small. Future studies examining larger sample sizes are needed.

Conclusions

We have identified morphologic changes and the loss of the Y chromosome in tissue samples from men with LEL. Epidural adipocytes were histologically smaller than subcutaneous adipocytes in each patient. Cytogenetically, a loss of the Y chromosome in epidural adipocytes was shown in all patients with LEL. In LEL, the loss of the Y chromosome may be related to morphologic changes in and proliferation of adipocytes. These findings suggest that LEL might be a benign tumor or tumor-like lesion in the spinal

canal. Additional studies with a larger number of patients with this rare condition are needed to explore further how the loss of the Y chromosome is related.

Declarations

Acknowledgments

We wish to thank Mr. Yoshiki Washizuka (technical assistant, Department of Orthopaedic Surgery) for his secretarial services.

Authors' contributions

TY and KS made substantial contributions to the conception and design. TY and YK were responsible for the acquisition or analysis and interpretation of the data. KW provided advice on the data analysis. TY, SS, and MH were involved in the surgical treatment. MK was involved in drafting the manuscript or revising it critically for important intellectual content. TY made a critical revision of the article for important intellectual content. All of the authors have read and approved the final manuscript.

Ethics approval and consent to participate

This report was approved by the Ethics Committee, University of Toyama (Toyama, Japan), and clinical research number "21–22" was granted. All six patients provided written consent to participate in this study. All methods were performed in accordance with the relevant laboratory guidelines and regulations.

Consent for publication

Not applicable.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on request.

Competing interests

The authors declare that they have no competing interests.

References

1. Lee M, Lekias, J, Gubbay SS, Hurst PE (1975) Spinal cord compression by extradural fat after renal transplantation. Med J Aust 1:201-203. doi: 10.5694/j.1326-5377.1975.tb111328.x
2. Fogel GR, Cunningham PY 3rd, Esses SI (2005) Spinal epidural lipomatosis: case reports, literature review and meta-analysis. Spine J 5:202-211. doi: 10.1016/j.spinee.2004.05.252

3. Gupta R, Shah M, Reese CM (2011) Steroid induced spinal epidural lipomatosis-case report and review of the literature. W V Med J 107:20-22.
4. Sivakumar K, Sheinart K, Lidov M, Cohen B (1995) Symptomatic spinal epidural lipomatosis in a patient with Cushing's disease. Neurology 45:2281-2283. doi: 10.1212/wnl.45.12.2281
5. Toshniwal PK, Glick RP (1987) Spinal epidural lipomatosis: report of a case secondary to hypothyroidism and review of literature. J Neurol 234:172-176. doi: 10.1007/BF00314138
6. Badami JP, Hinck VC (1982) Symptomatic deposition of epidural fat in a morbidly obese woman. Am J Neuroradiol 3:664-665.
7. Selmi F, Davies KG, Sharma RR, Redfern RM (1994) Idiopathic spinal extradural lipomatosis in a non-obese otherwise healthy man. Br J Neurosurg 8:355-358. doi: 10.3109/02688699409029626
8. Haddad SF, Hitchon PW, Godersky JC (1991) Idiopathic and glucocorticoid-induced spinal epidural lipomatosis. J Neurosurg 74:38-42. doi: 10.3171/jns.1991.74.1.0038
9. Fujita N, Hosogane N, Hikata T et al (2016) Potential involvement of obesity-associated chronic inflammation in the pathogenesis of idiopathic spinal epidural lipomatosis. Spine 41:E1402-1407. doi: 10.1097/BRS.0000000000001646
10. Robertson SC, Traynelis VC, Follett KA, Menezes AH (1997) Idiopathic spinal epidural lipomatosis. Neurosurgery 41:68-74. doi: 10.1097/00006123-199707000-00015
11. Roy-Camille R, Mazel C, Husson JL, Saillant G (1991) Symptomatic spinal epidural lipomatosis induced by a long-term steroid treatment. Review of the literature and report of two additional cases. Spine 16:1365-1371. doi: 10.1097/00007632-199112000-00004
12. Kawai M, Udaka F, Nishioka K, Houshimaru M, Koyama T, Kameyama M et al (2002). A case of idiopathic spinal lipomatosis presented with radicular pain caused by compression with enlarged veins surrounding nerve roots. Acta Neurol Scand 1058:322-325. doi: 10.1034/j.1600-0404.2002.1c194.x
13. Guegan Y, Fardoun R, Launois B, Pecker J (1982) Spinal cord compression by extradural fat after prolonged corticosteroid therapy. J Neurosurg 56:267-269. doi: 10.3171/jns.1982.56.2.0267
14. Borré DG, Borré GE, Aude F, Palmieri GN (2003) Lumbosacral epidural lipomatosis: MRI grading. Eur Radiol 13:1709–1721. doi: 10.1007/s00330-002-1716-4
15. Hierholzer J, Benndorf G, Lehmann T et al (1996) Epidural lipomatosis: case report and literature review. Neuroradiology 38:343-348. doi: 10.1007/BF00596585
16. Kuhn MJ, Youssef HT, Swan TL, Swenson C (1994) Lumbar epidural lipomatosis: the "Y" sign of thecal sac compression. Comput Med Imaging Graph 18:367-372. doi: 10.1016/0895-6111(94)90007-8
17. Nielsen GP, Mandahi N (2013) Lipoma. In: Fletcher CDM, Bridge JA, PCW H, Mertens F (eds) WHO classification of tumours of soft tissue and bone. IARC, Lyon, pp 20-21
18. Zevgaridis D, Nanassis K, Zaramboukas T (2008). Lumbar nerve root compression due to extradural, intraforaminal lipoma. An underdiagnosed entity? J Neurosurg Spine 9:408–410. doi:

10.3171/SPI.2008.9.11.408

19. Loriaux DB, Adogwa O, Gottfried ON (2015) Radiculopathy in the setting of lumbar nerve root compression due to an extradural intraforaminal lipoma: a report of 3 cases. J Neurosurg Spine 23:55-58. doi: 10.3171/2014.11.SPINE14693
20. Schizas C, Ballesteros C, Roy P (2003) Cauda equina compression after trauma: an unusual presentation of spinal epidural lipoma. Spine 28:E148-151.
21. Yasuda T, Suzuki K, Kawaguchi Y et al (2018) Clinical and imaging characteristics in patients undergoing surgery for lumbar epidural lipomatosis. BMC Musculoskelet Disord 19:66. doi: 10.1186/s12891-018-1988-8
22. Konno S, Kikuchi S, Tanaka Y et al (2007) A diagnostic support tool for lumbar spinal stenosis: a self-administered, self-reported history questionnaire. BMC Musculoskelet Disord 8:102. doi: 10.1186/1471-2474-8-102
23. Kanamori M, Matsui H, Hirano N, Kawaguchi Y, Kitamoto R, Tsuji H (1993) Trumpet laminectomy for lumbar degenerative spinal stenosis. J Spinal Disord 6: 232-237. doi: 10.1097/00002517-199306030-00008
24. Schneider CA, Rasband WS, Eliceiri KW (2012) NIH Image to ImageJ: 25 years of image analysis. Nat Methods 9: 671-675. doi: 10.1038/nmeth.2089
25. Yasuda T, Perry KD, Nelson M et al (2009) Alveolar rhabdomyosarcoma of the head and neck region in older adults: genetic characterization and a review of the literature. Hum Pathol 40: 341-348. doi: 10.1016/j.humpath.2008.08.006
26. Simons A, Shaffer LG, Hastings RJ (2013) Cytogenetic Nomenclature: Changes in the ISCN 2013 Compared to the 2009 Edition. Cytogenet Genome Res 141:1-6. doi: 10.1159/000353118
27. Kumar, Y, Gupta N, Chhabra A, Fukuda T, Soni N, Hayashi D (2017) Magnetic resonance imaging of bacterial and tuberculous spondylodiscitis with associated complications and non-infectious spinal pathology mimicking infections: a pictorial review. BMC Musculoskeletal Disorders 18:244. doi: 10.1186/s12891-017-1608-z
28. Ohba T, Saito T, Kawasaki N, Maekawa S, Haro H (2011) Symptomatic spinal epidural lipomatosis with severe obesity at a young age. Orthopedics 34:233. doi: 10.3928/01477447-20110427-25
29. Sugihara H, Yonemitsu N, Miyabara S, Yun K (1986) Primary cultures of unilocular fat cells: characteristics of growth in vitro and changes in differentiation properties. Differentiation 31:42-49. doi: 10.1111/j.1432-0436.1986.tb00381.x
30. Barz T, Melloh M, Staub LP, Lord SJ, Lange J, Harry R Merk HR (2014) Increased intraoperative epidural pressure in lumbar spinal stenosis patients with a positive nerve root sedimentation sign. Eur Spine J 23: 985-990. doi: 10.1007/s00586-013-3071-3
31. McAuliffe ME, Williams PL, Korrick SA, Dadd R, Marchetti F, Martenies SE, Perry MJ (2014) Human sperm sex chromosome disomy and sperm DNA damage assessed by the neutral comet assay. Hum Reprod 29:2148-2155. doi: 10.1093/humrep/deu177

32. Forsberg LA, Rasi C, Malmqvist N et al (2014) Mosaic loss of chromosome Y in peripheral blood is associated with shorter survival and higher risk of cancer. Nat Genet 46:624-328. doi: 10.1038/ng.2966
33. Al-Khawaja D, Seex K, Eslick GD (2008) Spinal epidural lipomatosis-a brief review. J Clin Neurosci 15:1323-1326. doi: 10.1016/j.jocn.2008.03.001
34. Chibbaro S, Mirone G, Nouri M, Di Emidio P, Polivka M, Marsella M, George B (2011) Dorsal epidural spinal lipomatosis. BMJ Case Rep: 2011. doi: 10.1136/bcr.09.2010.3365.
35. Liang CW, Mariño-Enríquez A, Johannessen C, Hornick JL, Dal Cin P (2011) Translocation (Y;12) in lipoma. Cancer Genet 204:53-56. doi: 10.1016/j.cancergencyto.2010.08.020
36. Kuroda N, Shiotsu T, Hes O, Michal M, Shuin T, Lee GH (2010) Acquired cystic disease-associated renal cell carcinoma with gain of chromosomes 3, 7, and 16, gain of chromosome X, and loss of chromosome Y. Med Mol Morphol 43:231-234. doi: 10.1007/s00795-009-0465-8
37. Minner S, Kilgué A, Stahl P et al (2010) Y chromosome loss is a frequent early event in urothelial bladder cancer. Pathology 42: 356-359. doi: 10.3109/00313021003767298
38. Park SJ, Jeong SY, Kim HJ (2006) Y chromosome loss and other genomic alterations in hepatocellular carcinoma cell lines analyzed by CGH and CGH array. Cancer Genet Cytogenet 166: 56-64. doi: 10.1016/j.cancergencyto.2005.08.022

Tables

Table 1. Clinical characteristics of patients with LEL

Case	Age/Sex	Past history	History of steroid administration	BMI (kg/m^2)	Site of LEL	Grade	Symptoms
1	64/M	None	None	26.1	L2-S1	III	L5 CES
2	79/M	None	None	26.2	L3-S1	III	L5 CES
3	77/M	None	None	27.1	L3-S1	III	L5 and S1 radiculopathy
4	70/M	Sudden deafness	270 mg over 9 days before age 8 y, continuous IV	25.5	L2-S1	II	L4 CES
5	77/M	Polymyalgia rheumatica	7.5 mg/day over 3 y, oral	26.2	L3-S1	III	L5 mixed CES
6	62/M	Interstitial pneumonia	1500 mg/day over 10 days before age 2 y, continuous IV	27.6	L3-S1	III	L4 CES

BMI, body mass index; CES, cauda equine syndrome; IV, intravenously; L, lumbar; LEL, lumbar epidural lipomatosis; S, sacral; y, years.

Table 2. Histopathology of subcutaneous fat and epidural fat

Case	Size of subcutaneous adipocytes (mean ± SD, μm^2)	Size of epidural adipocytes (mean ± SD, μm^2)	P value
1	6881.8 ± 2865.5	2439.9 ± 992.7	P<0.0001
2	7057.4 ± 3093.6	3130.8 ± 1111.4	P<0.0001
3	4865.5 ± 2120.8	2741.6 ± 1153.4	P<0.0001
4	5246.3 ± 2314.2	2643.8 ± 1413.6	P<0.0001
5	4723.3 ± 1422.1	2325.0 ± 667.2	P<0.0001
6	3899.9 ± 1355.0	2890.1 ± 1196.7	P=0.003
Overall	5485.6 ± 2584.1	2705.4 ± 1069.1	P<0.0001

SD, standard deviation.

Table 3. Cytogenetic data of patients with LEL

Case	Cause	Karyotype
1	Idiopathic	45,X,-Y[4]/46,XY,?t(15;16)(q24;p13.1)[1]/47,XY,+14[1]/46,XY[14]
2	Idiopathic	45,X,-Y[5]/46,idem, +5[1]/47,idem,+5,+12[1]/46,idem,+14[1]/46,idem,+21[1]/46,XY[11]
3	Idiopathic	45,X,-Y[4]/45,idem,?t(3;13)(q27;q12)[2]/47,idem,+4,+8[1]/47,XY,+3,der(10;12)(q10;q10),+18[1]/46,XY[12]
4	Secondary	45,X,-Y[7]/46,XY[13]
5	Secondary	46,X,-Y,+20[6]/46,X,-Y,+2[1]/47,Y,add(X)(p22.1),+7[1]/46,XY[12]
6	Secondary	45,X,-Y[5]/46,XY[16]

LEL, lumbar epidural lipomatosis.

Figures

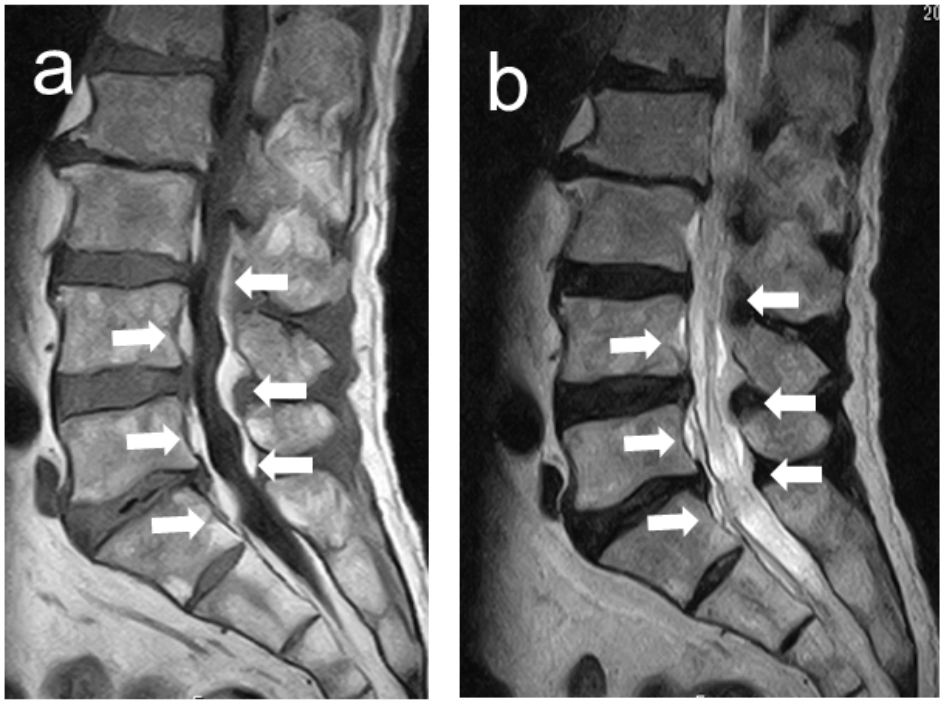

Fig. 1

Figure 1

Lumbar sagittal magnetic resonance imaging. a. T1-weighted sagittal image. b. T2-weighted sagittal image. Lumbar MRI reveals a high-intensity mass lesion on T1- and T2-weighted imaging consistent with epidural fat between L3 and S1. The dural sac is compressed by epidural fat on the ventral side and dorsal side (arrows).

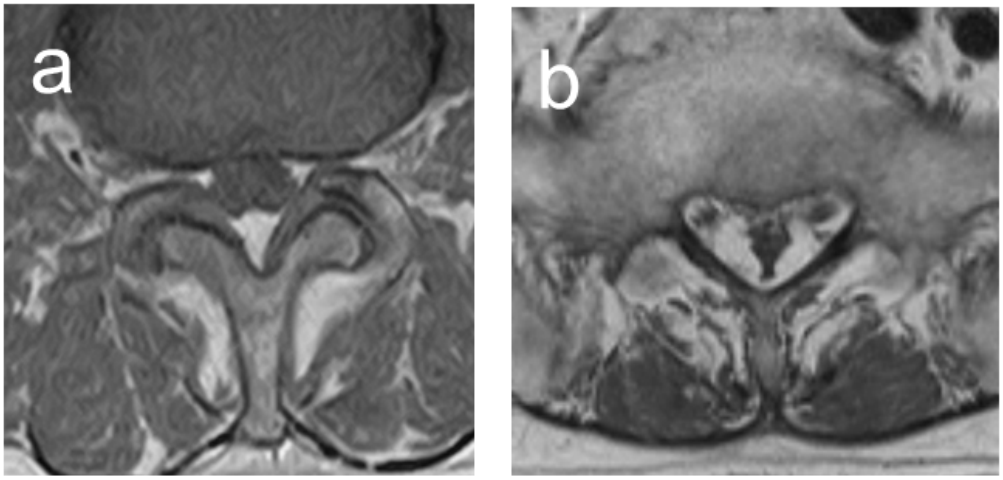

Fig. 2

Figure 2

Lumbar axial magnetic resonance imaging. a. T1-weighted image at the level of L4-5. The producing polygonal deformation of the dural sac is shown due to extradural adipose tissue. b. T1-weighted image at the level of L5–S1. The diamond-shaped deformation of the dural sac is shown due to circumferential extradural adipose tissue. MRI grade is III.

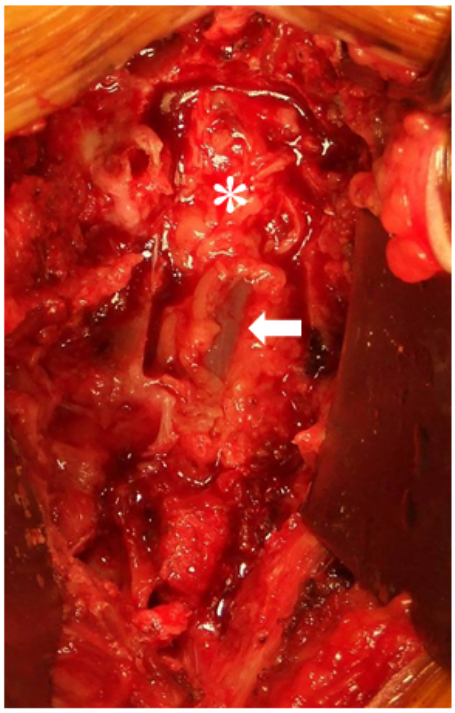

Fig. 3

Figure 3

Intraoperative findings. Lumbar epidural dorsal fat is shown following removal of lamina and ligamentum flavum. The proliferation of epidural fat tissue is recognized (asterisk), and the dura mater becomes thin (arrow).

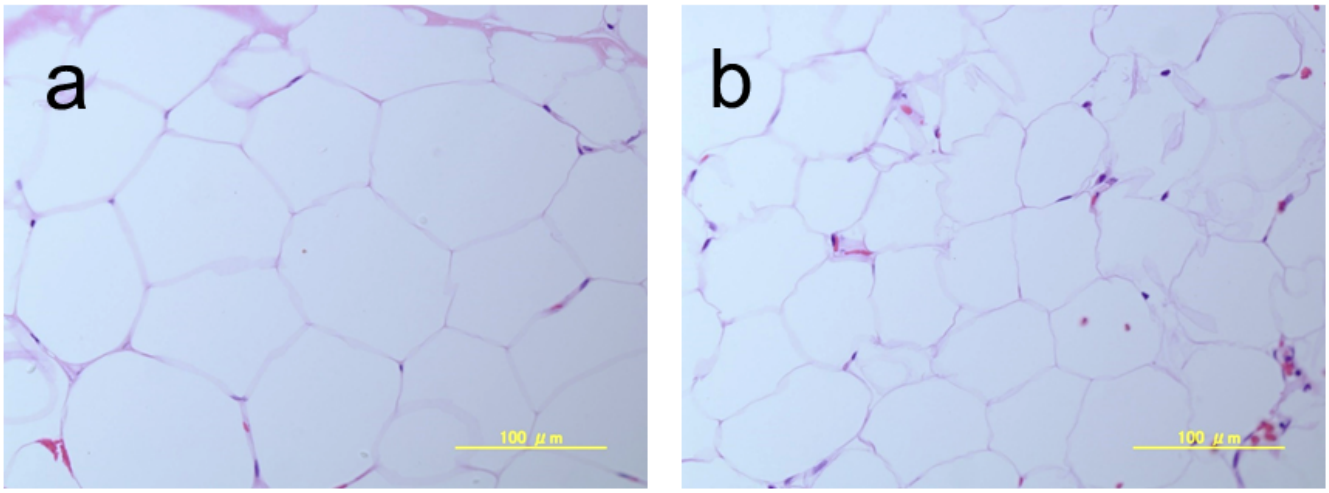

Fig. 4a

Figure 4

Histopathological findings. a. Subcutaneous fat tissue. Lipid droplet is large and uniform. b. Epidural fat tissue. Lipid droplet is small and slightly heterogeneous. It does not display nuclear atypia and there is no increased mitosis, hyperchromasia, or multinucleation of adipocyte. Lipoblasts were not identified.

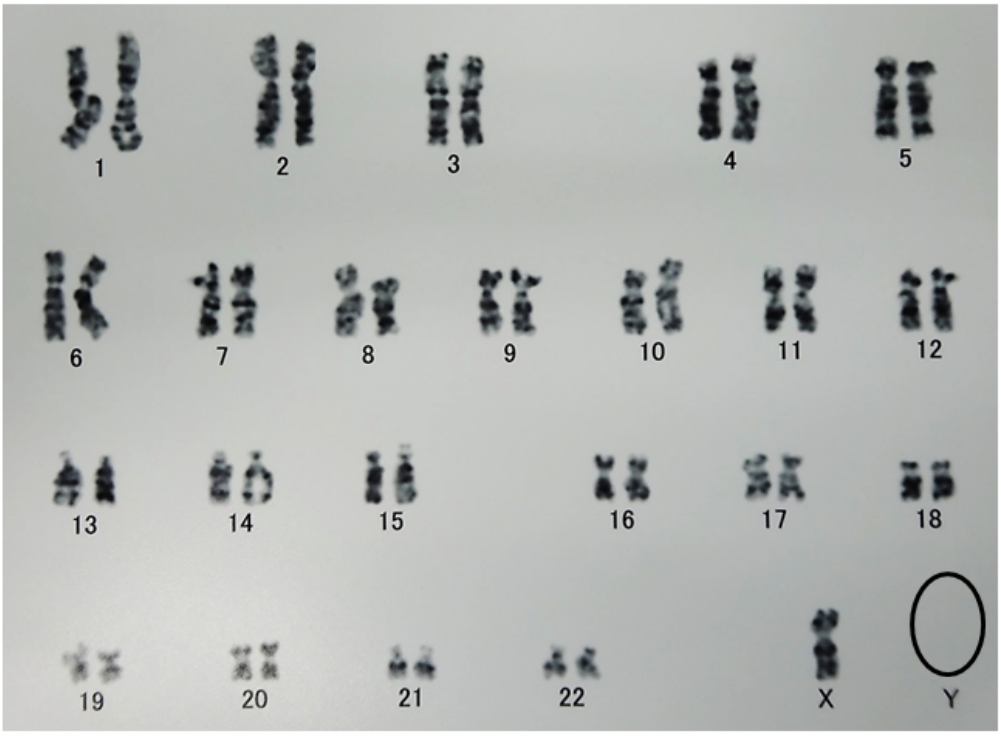

Fig. 5

Figure 5

Representative karyotype Karyotype shows loss of chromosome Y (circle).