Lumbosacral Epidural Lipomatosis: A Retrospective Matched Case-Control Database Study

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■ OBJECTIVE: **We present the largest known consecutive series of patients with epidural lipomatosis (EL) to characterize demographics and clinical symptoms of patients with EL on magnetic resonance imaging (MRI), and compare these characteristics against a matched control group.**

■ METHODS: **Patients evaluated for pathology requiring lumbar MRI imaging between September 2010 and September 2015 were retrospectively reviewed and included in this study if they were diagnosed with EL on a radiologic note during any visit to our medical center. One hundred ninety-nine patients fulfilled the study criteria and were included in the study cohort. A separate patient cohort of 199 unique, age- and gender-matched controls without lumbosacral EL was generated from a database of patients with lumbar MRI imaging during the same period.**

■ RESULTS: **Average age at diagnosis was 54.9 years (range, 25–84 years). One hundred thirty-three patients (66.8%) were men. On univariate analysis, patients with EL were more likely to have history of smoking (odds ratio [OR] 1.90, 95% confidence interval [CI] 1.23–2.94, $P = 0.004$), diabetes mellitus type 2 (OR 2.17, 95% CI 1.33–3.56, $P = 0.002$), or be on disability (OR 4.43, 95% CI 2.48–7.91, $P < 0.001$). Furthermore, patients with EL had significantly increased median body mass index compared with controls (36.7 vs. 29.4 kg/m^2; $P < 0.001$).**

■ CONCLUSIONS: **Patients with lumbosacral EL tend to be obese with a high incidence of type 2 diabetes mellitus, suggesting that this pathology may be a sequela of metabolic syndrome. Future research topics should include the pathogenesis of EL, as well as treatment outcomes of surgical versus primary care management.**

INTRODUCTION

First described in 1975,[1] epidural lipomatosis (EL) is hypertrophy of the adipose tissue in the epidural space often diagnosed on magnetic resonance imaging (MRI). This diagnosis must be differentiated from other pathologies, such as spinal angiolipoma, abscess, and other primary and secondary spinal tumors, that can appear similarly on routine imaging.[2] Epidural fat deposition can on rare occasions result in pain or neurological deficits due to compression of nerve roots and/or the spinal cord. Back pain and lower extremity weakness are the most common presenting symptoms, and other reported symptoms include numbness, paresthesias, radicular pain, and bowel or bladder incontinence.[3-6]

Causes of EL vary, although major causes all result in pathologic increases in spinal adipose tissue synthesis and deposition. Previous literature has suggested that 55.3% of cases with EL are attributable to exogenous steroid use and resulting adipose tissue hypertrophy. Endogenous steroid overproduction has also been implicated. Although obesity is also reported in several case

Key words
- Epidural fat
- Epidural lipomatosis
- Lumbar spine
- Lumbosacral spine
- Metabolic syndrome
- Obesity

Abbreviations and Acronyms
BMI: Body mass index
CI: Confidence interval
EL: Epidural lipomatosis
MRI: Magnetic resonance imaging
OR: Odds ratio

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Citation: World Neurosurg. (2016) 96:209-214.
http://dx.doi.org/10.1016/j.wneu.2016.08.125

Journal homepage: www.WORLDNEUROSURGERY.org

Available online: www.sciencedirect.com

studies as a risk factor for EL, to our knowledge there are no studies investigating the causal role of obesity-associated metabolic derangements including diabetes and metabolic syndrome. Furthermore, as many as 17% of cases cannot be attributed to any predisposing factor.[7]

Because EL is rarely recognized as the inciting cause of neurological deficits, much of the previous literature consists of isolated case reports and small case series. In the current study, we present the largest series of consecutive patients with EL. The aim of our study was to characterize patient demographics, clinical symptoms, and radiographic findings of patients who demonstrated EL on MRI, and to compare these patients against a matched control group.

METHODS

Institutional review board approval was received for this study. Patients evaluated for back pain and/or neurological deficits requiring lumbar MRI imaging between September 2010 and September 2015 were retrospectively reviewed. References to patient records were obtained from the neuroradiology department at a single large academic tertiary care referral center. Patients were included in this study if the key word "epidural lipomatosis" was listed as a diagnosis on a lumbar MRI radiologic note during any visit to our academic medical center. From these references, we were able to gather further information about each patient through chart review. Only patients with EL within at least 1 level of the lumbosacral spine were included in the present study. The MRI images were not subject to secondary review by another radiologist.

The exclusion criteria included patients younger than 18 years of age or older than 85 years of age. Patients were further excluded if their clinical records did not contain sufficient basic demographic information such as age and gender, or if <1 month of follow-up was available. In addition, patients with vertebral fractures, spinal tumor, or history of spinal infection or prior lumbar spine surgery were excluded from our study. From the initial 363 patients retrieved from the database meeting our inclusion criteria, 164 patients were removed due to our exclusion criteria. In total, we identified 199 consecutive patients who fulfilled the study criteria, and were included in the final analysis. Follow-up time for the cohort was 24.8 ± 18.8 months (median, 19.9 months, range, 1.2–67.9 months).

A separate patient cohort of 199 unique, age- and gender-matched controls without lumbosacral EL was created from a database of references to patients who also had lumbar MRI due to back pain and/or neurological deficits during the same study period. As with the EL cohort, we again used these references to obtain further patient information through chart review. The purpose of this analysis was to compare the relative proportions of patients with given comorbidities or other characteristics in the EL study group to demographically similar controls. The same exclusion criteria as detailed previously were used for the control group. Matching was undertaken by using random number generation to select 199 individuals who had the same age and gender as patients in the study group until a patient who fit the same exclusion criteria was found. For example, if four 59-year-old men were in our study group, four 59-year-old men were randomly chosen from the pool of back MRI control scans taken during the study period and read by the same neuroradiology team.

Data Collection

Medical records were retrospectively reviewed for demographic details pertaining to age, gender, employment and disability status, and various medical comorbidities. Disability status was recorded based on whether or not the patient was approved for disability at any time during his or her treatment and follow-up. Body mass index (BMI) was recorded from the closest possible visit to the date of diagnosis of EL. BMI was further stratified using World Health Organization BMI classifications. A BMI of <18.5 was considered to be underweight, whereas BMIs ranging from 18.5–24.9, 25.0–29.9, 30.0–34.9, 35.0–39.9, and >40 were designated as normal weight, overweight, Obesity class I, Obesity class II, and Obesity class III, respectively. A positive smoking history was recorded if there was any history of smoking, even if the patient did not smoke at the time of evaluation. Other comorbidities that were investigated were diagnoses of diabetes mellitus and any endogenous steroid-producing disorder at the time of diagnosis of EL. This latter disease category includes diseases, such as polycystic ovarian syndrome, Cushing's syndrome, adrenal tumors, Grave's disease, and other conditions, that result in increased steroid hormone production. These variables were included in the investigation based on either prior case studies suggesting associations or anecdotal evidence from spine surgeons.[4,6-9]

Clinical details regarding pain and neurological deficits were also recorded. Pain was recorded if it was directly addressed in a clinic note near the time of diagnosis and if it pertained to the leg or lower back, both attributable to lumbosacral pathology. Lack of back or leg pain was only recorded if clinical notes explicitly denied these symptoms. Neurological deficit was further subdivided into categories of sensory deficit, motor weakness, or bowel and/or bladder incontinence. These symptoms were only documented from patients with neurological assessments recorded by a practitioner. Motor weakness was determined solely from recorded physical examinations assessing for full (5/5) motor strength. Sensation changes were determined to be positive with subjective patient discourse suggesting numbness, paresthesias, or allodynia, even if sensation testing by the provider resulted in indiscernible sensation deficits. Neurogenic claudication was recorded if specifically referenced by the provider.

Radiographic details from the radiologist's note diagnosing EL were recorded. These notes were dictated by fellowship-trained neuroradiologists at a large academic center and were not subjected to secondary review by another radiologist. A positive finding of spinal stenosis in the lumbosacral spine was included in the database if specifically recorded in a note written by the radiologist that interpreted the relevant clinical imaging. This was further stratified depending on if it was attributed to EL, degenerative pathology, or congenital stenosis. If stenosis or thecal sac compression due to EL were present, then overall stenosis severity was recorded using the exact terminology from the radiologist's note. Of note, a 2003 article by Borré et al[10] found that a similar grading system of mild, moderate, and severe (i.e., grade I–III)

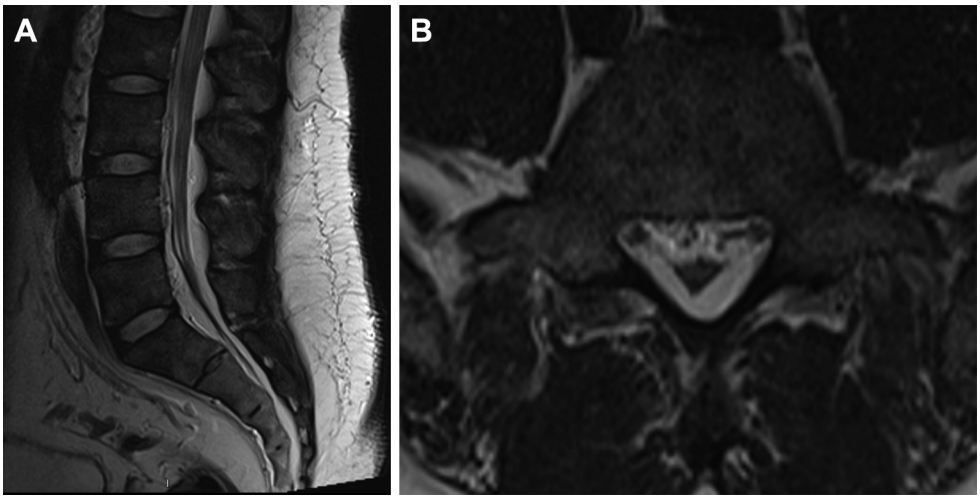

Figure 1. Representative images of 41-year-old male patient with epidural lipomatosis extending from L3 to S1. (**A**) T_2-weighted sagittal image; (**B**) T_2-weighted axial image at L5.

EL is a reliable and reproducible form of measurement with high interobserver and intraobserver reliability.

Details concerning each patient's treatment history were documented. Specifically, patient records were inspected for any history of epidural steroid injection or oral steroid use before the radiologic finding of EL. Treatment after the diagnosis of EL was characterized, including nonoperative management and specific surgical treatment aimed at decompressing the spinal cord at the level of EL. Surgical treatment was further stratified if it was intended for EL decompression or for other pathology. No other outcome measures were recorded.

Statistics

Demographics were compared between the study population and the control cohort with both Student's *t*-tests and Pearson χ^2 tests using matched cohort analysis. Logistic regression analysis was used to generate adjusted odds ratios (ORs) to determine demographics and comorbidities significantly associated with development of EL. Significance was established with probability values <0.01 to adjust for multiple comparisons. Statistical analyses were performed using STATA 11.0 (StataCorp, LP, College Station, Texas, USA).

RESULTS

Patient Demographics and Comorbidities

Images depicting a representative example of a 41-year-old male patient with lumbosacral EL are shown in Figure 1. Demographics for the 199 patients with EL included in this study are summarized in Table 1. Average age at diagnosis was 54.9 ± 12.4 years (median, 54 years, range, 25–84 years). One hundred thirty-three patients (66.8%) were men.

Demographic comparisons between the 2 groups are detailed in Table 1. On univariate, matched control analysis, patients with EL were more likely to have history of smoking (OR 1.90, 95% confidence interval [CI] 1.23–2.94, $P = 0.004$), diabetes mellitus type 2 (OR 2.17, 95% CI 1.33–3.56, $P = 0.002$), or be on disability (OR 4.43, 95% CI 2.48–7.91, $P < 0.001$). Furthermore, patients with EL had a significantly increased median BMI compared with controls (36.7 vs. 29.4 kg/m^2, $P < 0.001$). On multivariate analysis, disability status (adjusted OR 2.88, 95% CI 1.66–4.99, $P < 0.001$) and BMI (adjusted OR 1.13, 95% CI 1.09–1.17, $P < 0.001$) were correlated with EL pathogenesis.

Symptoms

Among the patients with EL, 90.1% reported back pain, whereas 76.3% reported leg pain. A neurological deficit was present in 28.7% of patients. Notably, 20.3% reported as having a sensation change, whereas 14.0% had a motor deficit.

Radiographic Findings

Central canal stenosis was observed in 190 (95.5%) of patients with EL (Table 2). Of these, 52 patients (26.1%) were noted to have severe stenosis. Of all patients with EL, spinal stenosis secondary to a degenerative pathology was noted on MRI in 85.4%.

DISCUSSION

An exact mechanism for development of spinal EL is difficult to ascertain, suggesting that large demographic studies with appropriately selected control groups are needed to establish pathogenic factors. Our series of lumbar patients with EL is the largest to date, with 199 patients matched to 199 age and gender controls. To emphasize, these controls also had clinically required MRI for back pain and/or neurological deficits and fit the same exclusion criteria, although without a diagnosis of EL. We found that increased BMI and disability status were significantly correlated

Table 1. Demographics and Comparison With Control Cohort

	Study Groups		Matched Univariate Analysis		Multivariate Analysis	
Category	**EL (%)**	**Controls (%)**	**Odds Ratio (95% CI)**	***P* Value**	**Odds Ratio (95% CI)**	***P* Value**
No. of Patients	199	199	N/A	N/A	N/A	N/A
Mean age (SD)	54.9 (12.4)	54.9 (12.4)	N/A	1.00*	1.01 (0.99–1.03)	0.236
Gender						
Male	133 (66.8)	133 (66.8)	N/A	1.00	1.20 (0.71–2.01)	0.497
Female	66 (33.2)	66 (33.2)				
Smoking history	131 (66.2)	104 (52.3)	1.90 (1.23–2.94)	0.004	1.65 (1.00–2.72)	0.049
Diabetes	72 (36.4)	45 (22.6)	2.17 (1.33–3.56)	0.002	0.93 (0.54–1.59)	0.782
Endocrine condition	3 (1.5)	1 (0.5)	3.00 (0.31–28.84)	0.341	NI	
Previous oral steroid use	64 (32.2)	70 (35.2)	0.87 (0.57–1.33)	0.518	NI	
Previous ESI	53 (26.6)	55 (27.6)	0.95 (0.60–1.49)	0.816	NI	
Previous exogenous steroid	99 (49.8)	102 (51.3)	0.93 (0.61–1.43)	0.745	0.83 (0.51–1.35)	0.458
Previous statin use	91 (45.7)	69 (34.7)	1.66 (1.09–2.52)	0.018	1.21 (0.72–2.03)	0.476
Previous valproic acid use	3 (1.5)	2 (1.0)	1.50 (0.25–8.98)	0.657	NI	
Disability status	81 (40.7)	34 (17.1)	4.43 (2.48–7.91)	< 0.001	2.88 (1.66–4.99)	< 0.001
BMI (kg/m^2)						
Underweight	0 (0)	1 (0.6)	N/A	< 0.001†	1.13 (1.09–1.17)	< 0.001
Normal	7 (3.7)	37 (20.3)				
Overweight	22 (11.7)	68 (37.4)				
Obesity class I	45 (23.9)	35 (19.2)				
Obesity class II	54 (28.7)	23 (12.6)				
Obesity class III	60 (31.9)	18 (9.9)				
Median	36.7	29.4	Z = −8.743‡	< 0.001‡		

CI, confidence interval; N/A, not available; SD, standard deviation; EL, epidural lipomatosis; NI, not included; BMI, body mass index; ESI, epidural steroid injection.
*Student's *t*-test used to compare mean values.
†Pearson χ^2 test used to compare proportions.
‡Wilcoxon rank-sum test used to compare median values.

with a diagnosis of lumbosacral EL. In particular, for every point increase in BMI, there was a 13% increased likelihood of having EL, within our pool of analyzed patients. In patients with radiographically diagnosed EL, epidural fat collection contributed to canal stenosis in >80% cases (n = 160) and led to severe stenosis in >25% cases (n = 52). To highlight, only 14 (9%) of the patients with spinal stenosis was found to be primarily from EL. The remaining 146 (91%) of these patients also had other pathology contributing to the spinal stenosis, such as degeneration or intrinsic stenosis.

Prior literature on EL suggested that exogenous steroid use and endogenous steroid-producing conditions may be related to EL. A 2005 meta-analysis by Fogel et al[7] consolidated >100 patients from the literature and several cases from the author's institution to establish shared characteristics of the population of patients with spinal EL. In that study, exogenous steroid use was the most common association, with 55.3% of cases associated with a history of oral steroid use or epidural steroid injections. This is consistent with our finding that 49.8% of cases were preceded by some form of exogenous steroid exposure. In our study, however, exogenous steroid exposure rate was not significantly different from the control cohort (49.8% vs 51.3%, respectively). It is important to note, although, that our study was not specifically designed to examine this particular facet, and may have been underpowered, particularly as epidural steroid injections themselves were not quantified. The effect of endogenous steroid-producing conditions was more difficult to elucidate as such conditions were rare within our population of EL patients (3 patients, 1.5%). This was similar to the series of patients presented in a meta-analysis by Fogel et al[7] as only 3 patients in the previous literature were found to have EL due to Cushing's syndrome.[8,9,11]

Table 2. Radiographic Characteristics of Patients With Epidural Lipomatosis

	Category	Total (%)
Any stenosis	No	9 (4.5)
	Yes	190 (95.5)
EL stenosis	None	39 (19.6)
	Mild	37 (18.6)
	Mild—moderate	7 (3.5)
	Moderate	42 (21.1)
	Moderate—severe	22 (11.1)
	Severe	52 (26.1)
Other stenosis	Degenerative	170 (85.4)
	Intrinsic	6 (3.0)
	Neither (stenosis only due to EL)	17 (8.5)

EL, epidural lipomatosis.

Of other risk factors, obesity was a commonly observed comorbidity associated with EL. This is concordant with a study by Al-Khawaja et al[12] where 70% of patients with EL were found to be obese. We, furthermore, observed significantly increased BMI in patients with EL, compared with control patients, a relationship that persisted when adjusting for other factors during multivariate analysis. In addition to obesity, we found that diabetes mellitus type 2 was significantly increased in patients with EL on univariate analysis. At present, this is a relationship that has not been described in the literature.

The findings of increased rate of obesity and diabetes lead to a novel hypothesis that EL may be common in patients with metabolic syndrome.[13] In this condition, accumulation of proinflammatory visceral adipose tissue is associated with the development of metabolic derangement and insulin resistance. With these similar associations, EL may reflect an additional site of pathogenic fat deposition. Although a prospective natural history study would be necessary to confirm a causal relationship between metabolic syndrome and EL, this association does provide an interesting new perspective to the study of EL. We suggest that primary care physicians should consider EL as a possible contributing factor to back pain in patients with a concurrent diagnosis of metabolic syndrome. This provides additional impetus to control obesity, diabetes mellitus, and metabolic syndrome in the primary care setting before referring for surgical intervention. Furthermore, additional studies may be warranted to investigate the efficacy of medical versus surgical treatment of EL.

Regarding clinical symptomatology and radiographic findings, Jaimes et al[14] reviewed MRIs of 856 patients, finding 70 patients with varying degrees of EL and specific patterns of symptomatology. In terms of clinical symptoms, they found that sciatica was only caused by EL as the primary cause in 9 of 42 patients. Furthermore, EL was seen as a potential secondary cause of symptomatology in many patients. In our study, although degenerative pathology was responsible for most central canal stenosis, EL appeared to additionally contribute to central canal stenosis on MRI in 80% of the cases. Only 8 patients (4.2%) in our series underwent surgical decompression to specifically relieve stenosis caused primarily by EL. These data highlight the difficulty associated with ascribing particular symptoms (pain, neurological deficits) to EL alone, as many patients with this pathology may have an increased predisposition to having significant degenerative pathology at the same or adjacent levels that could contribute to spinal stenosis and subsequent symptomatology.

Our study has several limitations, many intrinsic to the format of the investigation as a retrospective database study. First, due to its retrospective, cross-sectional nature, it is impossible to demonstrate any relationship stronger than association between EL and the study variables. Furthermore, because our control subjects were chosen randomly from the total set of MRIs taken during the study period, the resultant group was very heterogeneous with respect to indication for lumbar spine MRI. In addition, we were unable to quantify the number of epidural spine injections, which may have limited our conclusions as we found no association between epidural spine injections and development of EL, although Jaimes et al[14] did establish this positive relationship. One final limitation of our study is that the findings of our study must and can only be generalized to patients who clinically required a lumbar MRI due to back pain and/or neurological deficits, as those were the only patients included.

CONCLUSION

This is the largest known consecutive series of age-matched and sex-matched patients with EL. Ascribing symptoms solely to the presence of EL is challenging given the frequent presence of other degenerative pathology. However, patients with lumbosacral EL tended to be obese with high incidences of diabetes mellitus type 2. We hypothesize that this diagnosis may be related to an overarching metabolic syndrome, with EL reflecting an additional site of pathogenic adipose tissue deposition, a novel association never before described in literature. Based on this study, future research topics should include the pathogenesis of EL, as well as treatment outcomes of surgical versus primary care management.

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Conflict of interest statement: The authors declare that the article content was composed in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Received 18 July 2016; accepted 30 August 2016

Citation: World Neurosurg. (2016) 96:209-214.
http://dx.doi.org/10.1016/j.wneu.2016.08.125

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