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CARACTERISTIQUES CLINIQUES ET BIOLOGIQUES DU SYNDROME METABOLIQUE ASSOCIE A LA LIPOMATOSE EPIDURALE

Une étude rétrospective monocentrique

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En présence des Maîtres de cette Faculté,
De mes chers condisciples
Et selon la tradition d'Hippocrate,
Je promets et je jure d'être fidèle aux lois de l'honneur
Et de la probité dans l'exercice de la Médecine.

Je donnerai mes soins gratuits à l'indigent,
Et n'exigerai jamais un salaire au-dessus de mon travail.

Admis dans l'intérieur des maisons,
Mes yeux ne verront pas ce qui s'y passe,
Ma langue taira les secrets qui me seront confiés
Et mon état ne servira pas à corrompre les mœurs ni à favoriser le crime.

Respectueux et reconnaissant envers mes Maîtres,
Je rendrai à leurs enfants l'instruction que j'ai reçue de leurs pères.

Que les hommes m'accordent leur estime
Si je suis fidèle à mes promesses.
Que je sois couvert d'opprobre
Et méprisé de mes confrères si j'y manque.

RESUME

Caractéristiques cliniques et biologiques du syndrome métabolique associé à la lipomatose épidurale : une étude rétrospective monocentrique

Contexte :
La lipomatose épidurale est une accumulation de tissus adipeux dans l'espace épidural, pouvant mener à des tableaux de lombosciatique ou de canal lombaire rétréci. Certaines anomalies métaboliques ont été incriminées dans la pathogénèse de la lipomatose idiopathique, mais les études menées sur de larges échantillons restent peu nombreuses.

Objectif :
L'objectif principal de cette étude était d'étudier les caractéristiques cliniques et biologiques des patients atteints de lipomatose épidurale, l'objectif secondaire d'étudier la fréquence du syndrome métabolique chez ces patients.

Méthode :
Dans cette étude rétrospective descriptive ont été inclus les patients atteints de lipomatose épidurale admis dans notre service de rhumatologie (consultation ou hospitalisation) entre mai 2003 et janvier 2020. Nous avons recueilli les caractéristiques démographiques, morphologiques (notamment indice de masse corporelle et tour de taille), les antécédents cardiovasculaires et maladies métaboliques, les traitements (antidiabétiques, hypolipémiants et corticoïdes), les signes cliniques rachidiens présentés et les données biologiques (notamment le profil glucidique et lipidique). Nous avons ensuite estimé la fréquence du syndrome métabolique selon la définition de la Fédération Internationale du Diabète.

Résultats :
Au total les données cliniques et biologiques de 117 patients ont été analysées. Soixante pour cent des patients étaient des hommes et 40% des femmes, l'âge moyen était de 62 ans. Concernant les antécédents, 25.6% des patients présentaient un diabète, 49.5 % présentaient une dyslipidémie et 64.9% avaient un antécédent d'hypertension artérielle. Sur le plan morphologique, 91.5% des patients étaient en surpoids ou obèses et, chez les 47 patients chez qui le tour de taille a été disponible, 97.8% présentaient une obésité abdominale. La recherche de syndrome métabolique a pu être réalisée sur 44 patients. Parmi ceux-ci, 34 (soit 77%) présentaient un syndrome métabolique.

Conclusion :
D'après notre étude, un pourcentage élevé de patients atteints de lipomatose épidurale pris en charge en rhumatologie, présente une obésité abdominale ou des désordres métaboliques tels qu'un diabète, une dyslipidémie ou une hypertension artérielle.

Mots clés : lipomatose épidurale, idiopathique, particularités cliniques, particularités biologiques, obésité, syndrome métabolique

ABSTRACT

Clinical and biological features of metabolic syndrome-associated epidural lipomatosis: a single-center, retrospective study

Background:
Epidural lipomatosis (EL) is an accumulation of adipose tissue in the epidural space that can lead to low back pain or lumbar spinal stenosis. Metabolic abnormalities have been incriminated in the pathogenesis of idiopathic EL, but studies conducted on large samples are lacking.

Objectives:
The primary objective of this study was to study the clinical and biological characteristics of patients with EL. The secondary objective was to study the frequency of metabolic syndrome in these patients.

Methods:
This retrospective descriptive study included patients with EL admitted to our rheumatology department (consultation or hospitalization) between May 2003 and January 2020. We collected demographic data, morphological data (including body mass index and waist circumference), cardiovascular and metabolic history, treatments (antidiabetic, hypolipidemic and corticosteroids), symptoms and biological data (including glycemic and lipid profile). We then estimated the frequency of metabolic syndrome according to the International Diabetes Federation definition.

Results:
A total of 117 patients' clinical and biological data were analyzed. 60% of patients were men and 40% were women, mean age was 62 years. Regarding the history, 25.6% of patients had diabetes, 49.5% had dyslipidemia, and 64.9% had a history of hypertension. Morphologically, 91.5% of patients were overweight or obese and, in the 47 patients in whom waist circumference was collected, 97.8% were displayed an abdominal obesity. The search for metabolic syndrome was performed on 44 patients. Of these, 34 (77%) had a metabolic syndrome.

Conclusion:
According to our study, a considerable percentage of patients with EL diagnosed in a rheumatology department have abdominal obesity or metabolic disorders such as diabetes, dyslipidemia or hypertension.

Keywords: epidural, lipomatosis, idiopathic, clinical features, biological features, obesity, metabolic syndrome

LISTE DES ABREVIATIONS

ADA = American Diabetes Association
a.k.a = Also known as
Alb = Albumin
ALP = Alkaline phosphatase
ALT= Alanine aminotransferase
ASAT = Aspartate aminotransferase
BMI = Body Mass index
CRP = C-Reactive Protein
CT = Computed tomography
DuS = Dural sac
EF = Epidural Fat
EL = Epidural lipomatosis
ESI = Epidural Steroid Injection
FBS = Fasting Blood Sugar
GGT = Gamma glutamyl-transferase
HBA1c= Glycated hemoglobin
HBP = High Blood pressure
HDL-C = High-density lipoprotein cholesterol
HU = Hounsfield units
IFG = Impaired fasting glycaemia
IGT = Impaired glucose tolerance
IL-6 = Interleukin 6
IM = intramuscular
IV = intravenous
LDL-C = Low-density lipoprotein cholesterol
LEL = Lumbar epidural lipomatosis
MRI = Magnetic resonance imaging
NAFLD = Nonalcoholic fatty liver disease
NASH = Non-Alcoholic Steatohepatitis
OGTT = Oral Glucose Tolerance Test
PAOD = Peripheral arterial occlusive disease
SFE = Société Française d'Endocrinologie = French Society of Endocrinology
TG = Triglyceride
TIA = Transient ischemic attack
TNF-α = Tumor necrosis factor-α
UA = Uric acid
WHO = World Health Organization

RESUME GENERAL DU TRAVAIL DE THESE

La lipomatose épidurale est une pathologie caractérisée par une accumulation de tissus adipeux non encapsulé dans l'espace épidural du canal rachidien. Bien que rare, elle peut entraîner une compression des structures neurologiques adjacentes et être responsable de tableaux de myélopathie, de lomboradiculalgie ou de canal lombaire étroit.
La lipomatose épidurale a été rapportée notamment chez des patients traités par corticothérapie au long cours ou avec un hypercorticisme endogène. Toutefois, de nombreux patients présentent une lipomatose dite « idiopathique », sans notion d'hypercorticisme exogène ou endogène. Des études récentes ont retrouvé un lien avec l'obésité et suggéré que la lipomatose épidurale pouvait être une manifestation du syndrome métabolique, corrélée à l'IMC, la circonférence abdominale, la graisse viscérale et à des dépôts de graisse hépatique.

Le syndrome métabolique est une association de facteurs cardio-métaboliques entraînant un risque augmenté de pathologie cardiovasculaire et de diabète de type 2, en prévalence croissante dans les pays développés. Il est reconnu que dans le syndrome métabolique, des dépôts ectopiques de graisse peuvent survenir dans différents organes dont le foie, le pancréas, le cœur, les muscles squelettiques. L'espace épidural pourrait potentiellement être une autre localisation cible de ces dépôts. Une meilleure compréhension des mécaniques impliqués dans la genèse de la lipomatose épidurale, notamment en cas de coexistence d'un syndrome métabolique, pourrait ainsi mener à des implications diagnostiques et thérapeutiques importantes.

L'objectif de notre étude était d'étudier les caractéristiques cliniques et biologiques des patients atteints de lipomatose épidurale admis dans un service de rhumatologie, ainsi que d'estimer la fréquence du syndrome métabolique chez ces patients.
Il s'agissait d'une étude rétrospective descriptive monocentrique, portant sur les patients atteints de lipomatose épidurale s'étant présentés dans le service de rhumatologie du Centre Hospitalo-Universitaire de Tours. Ces patients ont été admis en consultation ou hospitalisation entre 2003 et 2020 pour prise en charge de diverses affections rhumatologiques (lombosciatique ou canal lombaire étroit le plus souvent) et la découverte de la lipomatose épidurale a été généralement fortuite.
Des données cliniques et biologiques, retenues sur la base des connaissances de la littérature, ont pu être recueillies dans le but d'établir un profil de patient.
Il est à souligner que les modalités de recueil des données n'ont pas été identiques selon la période.
De mai 2003 à août 2010, les données ont été collectées à partir de dossiers de rhumatologie papiers par Mme Laetitia COTENTIN, alors interne au CHRU de Tours. A partir d'octobre 2010 et jusque janvier 2020, les dossiers ont été sélectionnés par moi-même, par recherche de mots clés dans un entrepôt de données informatique de l'hôpital, mettant à disposition les données issues du dossier médical informatisé du patient ou du codage des actes diagnostics ou thérapeutiques.

Cette étude descriptive devra bien sûr mener à des études analytiques de meilleur niveau de preuve, qui pourraient établir une potentielle association entre les facteurs métaboliques et la lipomatose épidurale.

TABLE DES MATIERES

INTRODUCTION

A. Background

Epidural lipomatosis (EL) is a rare medical condition defined by an excessive accumulation of unencapsulated fatty tissue in the epidural space surrounding the spinal cord. Diagnosis is often made by magnetic resonance imaging (MRI) and is reported in 1 to 2.5% of patients undergoing lumbar spine cross-sectional imaging (1).

In rare cases, EL may compress nerve structures (spinal cord, nerve root or cauda equina) hence being responsible of clinical symptoms such as lower extremity numbness, radiculopathy, or reduction of walking distance.

EL is particularly seen in patients receiving exogenous steroids but has also been reported in patients with obesity or metabolic disorders. Although EL is a rare condition, a better understanding of its pathogenesis and risks factors could have potential diagnostic and therapeutic applications.

B. Anatomy of the spinal canal

The spinal canal, a.k.a vertebral canal, is the cavity formed by the vertebral column which contains the spinal cord and the spinal nerve roots branching off the spinal cord bilaterally.

It becomes progressively narrower from its superior part at the foramen magnum to its inferior part at the sacral hiatus. Two structural ligaments surround the vertebral canal, the ligamentum flavum and the posterior longitudinal ligament.

On cross-sectional plane, the epidural space is located between the spinal canal (posterior longitudinal ligament anteriorly, vertebral lamina and ligamentum flavum posteriorly) and the meninges. The outermost layer of the meninges, the dura mater, is closely associated with the arachnoid mater. The subarachnoid space is filled with cerebrospinal fluid and contains the vessels that supply the spinal cord. The innermost layer, the pia mater is closely attached to the spinal cord.

Thus, the epidural space consists on a circumferential space that contains epidural fat, loose connective tissue, small arteries, internal vertebral venous plexuses, lymphatics and spinal nerve roots. Loose fatty tissue is principally located in the posterior and lateral portions of the epidural space. The presence of fat in the epidural space is frequently observed in healthy subjects and is considered a mechanical protector for the Dural sac and nerve structures.

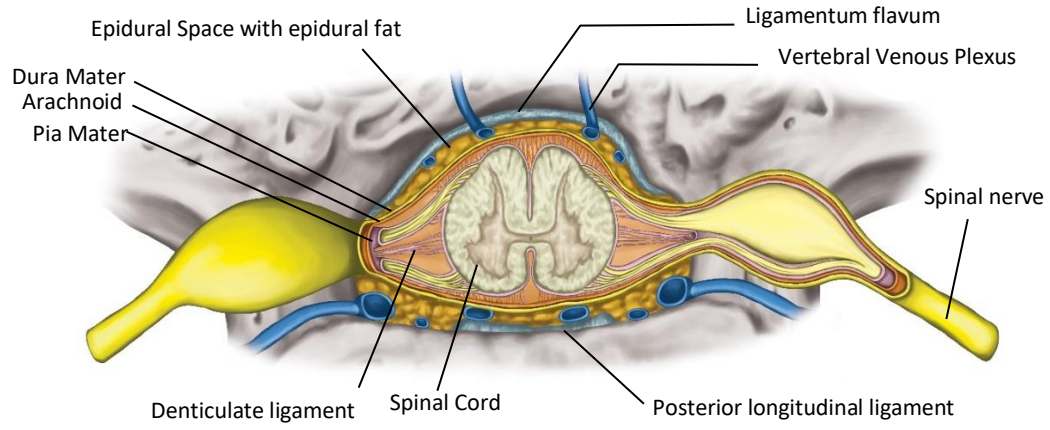


Figure 1. Anatomy of the spinal canal, Stihii, Shutterstock.com

C. Epidural lipomatosis

1. Definition and characteristics

As mentioned before, presence of fat in the epidural space is physiological. Pathological conditions related to adipose tissue include lipoma (encapsulated collection of adipocytes) or lipomatosis (secondary to adipocyte hypertrophy). EL is therefore characterized by the abnormal accumulation of unencapsulated adipose tissue in the epidural space.

Regarding its location, EL is rarely found at the cervical spine. In the dorsal spine, the most common site for fat deposition is from T2 to T10, and in the lumbar spine, it occurs more frequently at the L5/S1 level, then L4-L5 and L3/L4 levels (2).
EL was initially thought to be more frequent at the thoracic level. In fact, in their meta-analysis, Fogel *et al.* found that 45.8% of the reported case had a thoracic involvement, 43.6% had lumbosacral involvement and 10.6% had involvement in both thoracic and lumbosacral area. (3).
EL pattern depends on the underlying cause, dorsal location being more frequent in the cortico-induced form and lumbar or lumbosacral location in the idiopathic form (4).

EL is often separated into steroid induced EL and idiopathic (with no history of hypercorticism or corticoid treatment). A classification has been proposed with 5 main categories according to pathogenesis: exogenous steroid use, endogenous steroid hormonal disease, obesity, surgery induced, and idiopathic (4).
It should be noted that there is discordance in the literature regarding the definition of "idiopathic lipomatosis", some authors using the term to describe EL of unknown cause, and others using it to describe EL associated with obesity or other unknown causes. In our study, idiopathic lipomatosis encompasses cases associated with obesity and cases of unknown origin.

2. Imaging

Lipomatosis can be diagnosed on Computed tomography scan (CT scan) or Magnetic Resonance Imaging (MRI). MRI is recognized as the most sensitive and specific modality for EL evaluation. Lipomatosis can be diagnosed as a mass in the epidural space with T1 hypersignal and intermediate T2 signal. T1-weighted images allow measuring adipose thickness: an EF thickness exceeding 6 mm, 7 mm or 9.8 mm in the posterior epidural space, depending on the authors, is characteristic of EL.

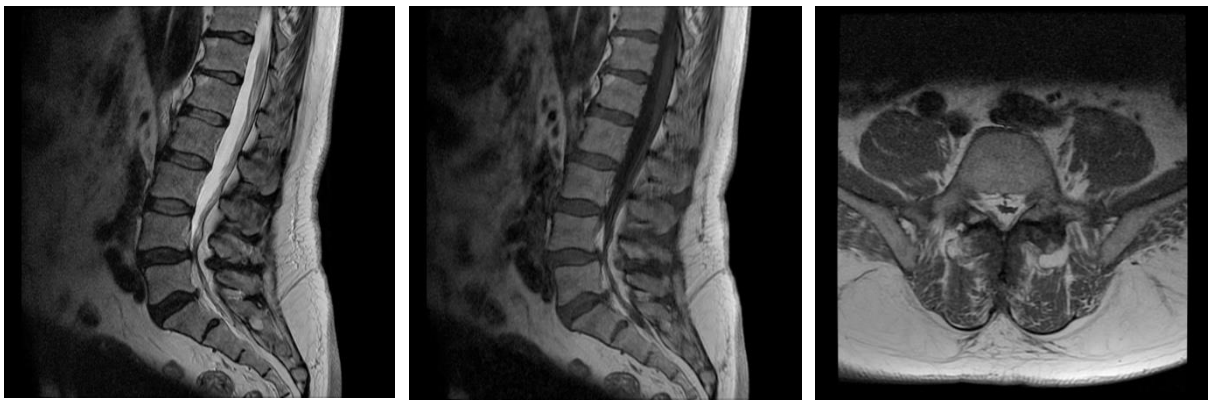


Figure 2. Epidural lipomatosis from L4 to S1 levels, associated with narrow posterior disc bulges at L4/5 and L5/S1, responsible of a narrowing of the dural sac. Case courtesy of Dr Matthew Lukies, Radiopaedia.org, rID: 57661

However, compared to absolute EF value, relative value of epidural fat (EF)/ anteroposterior diameter of the dural sac (DuS) may be a more accurate measure for diagnosing SEL (5).
Thus, Borre *et al.* (6) found that EL could be diagnosed if EF/ DuS exceeds 40%.
They suggested 4 MRI grades levels by measuring EF and DuS:

- LEL (lumbar EL) grade 0 (normal): EF/DuS index ≤ 40%;
- LEL grade I: EF/DuS index 41 – 50% (mild EF overgrowth);
- LEL grade II: EF/DuS index 51 – 74% (moderate EF over-growth);
- LEL grade III: EF/DuS index ≥ 75% (severe EF overgrowth).

In their study, grade I patients had no symptoms, grade II patients had symptoms in 14.5% of cases and grade III patients were all symptomatic. However, in this later group, 42.3% had concomitant abnormalities such as disk herniation, that could contribute to the symptoms.

In addition, the presence of EL can lead to different shapes of the Dural sac. In axial plane, the "Y sign" is often found, the thecal sac presenting a trifid aspect resembling the letter Y (7). This form owes to the presence of meningo-vertebral ligaments, fibro-elastic embryonic remnants connecting the dura mater and the ligamentum flavum. The Y sign, however, was found in less than half of the patients according to Borre *et al.* (6).

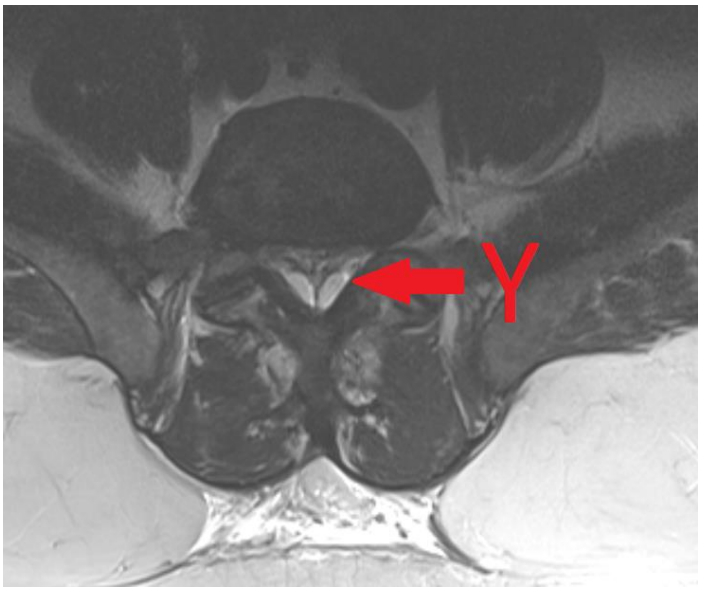


Figure 3. Y sign. Case courtesy of Dr Mauricio Macagnan, Radiopaedia.org, rID: 42993

3. Epidemiology

As said before, EL is reported in 1 to 2.5% of patients undergoing lumbar spine cross-sectional imaging. True prevalence of EL is however not well known.

The most common cause is glucocorticoid excess, mainly by the use of exogenous steroid which accounts for about 55% of cases (3), while endogenous Cushing syndrome may represent only 3% of cases. Idiopathic EL (obesity-associated and of unknown cause) would account for around 42 % of cases.

D. Suspected risk factors of idiopathic EL

1. What we already know:

a. Steroid induced EL

The association between and endogenous hypercorticism, or more often corticosteroid use, is well known.
EL was first described in 1975 by Lee *et al.* in a patient who received corticosteroids after renal transplantation (8). Since then, it has been reported in patients receiving immunosuppressive therapy after organ transplantation and in patients requiring steroids for systemic disease.
As regards the pathogenesis, the exact underlying pathological mechanism of EL is unknown. Glucocorticoid receptor is present in adipose tissue and "hypercortisolism leads to accumulation of adipose tissue in a typical distribution on the face, neck, trunk, and mediastinum" (3). Spinal epidural fat, similarly to fat deposition seen in Cushing's syndrome, could expand because of steroids use.
The time course of EL progression is rarely documented. Clinically, the onset of symptoms seems to be gradual (9). However, no specific duration of exposure to corticosteroid has been linked to the development of EL.
Regarding epidural steroid injections (ESI), Jaimes *et al.* (10) showed a strong correlation between the number of epidural steroid injections and EL occurrence. One ESI delivery did not increase the patient's odds of developing EL., but after four ESI, the probability of developing EL was over 90%.

b. Idiopathic EL

Idiopathic EL is most often seen in obese adults and has been associated with hyperlipidemia, type 2 diabetes mellitus and metabolic syndrome.
In obesity, adipocyte hypertrophy may be responsible - at least in part - for the increase in epidural fat tissue. Moreover, obesity - especially abdominal obesity- is thought to cause a chronic inflammation which may, in turn, contribute to the overgrowth of adipose tissue in spinal canal (11).

c. Surgery-induced EL

Cases of EL have been described following spinal surgery. Greenish *et al.* (12) reported a case of EL after spinal decompression surgery, post-surgical MRI showing a lumbar EL which was not present pre-operatively. The patient did not have any injection of intrathecal steroids before or during surgery. Choi *et al.* (9) reported two cases of rapid progression of SEL after one or two epidural steroid injection, both with minimal EL before surgery, which notably increased after decompression surgery. These SEL patients developed neurologic symptoms after less than 5 months.
Surgery could therefore at least worsen a preexisting EL.

2. Definitions

a. Morphological parameters:

Waist circumference is measured in a standing position, midway between the lowest rib and the iliac crest at the end of a normal exhalation. A large waist circumference indicates abdominal obesity and is positively correlated with visceral adipose tissue that is more metabolically active than subcutaneous fat. The definition of abdominal obesity differs from one country to another. In France for instance, it is defined as a waist circumference greater than 94 cm for men and 80 cm for women, in the United States as a waist circumference greater than 102 cm for men and 88 cm for women, and in Japan as a waist circumference greater than 90 cm for men and 80 cm for women.

Waist-to-hip ratio is sometimes used to assess fat distribution. Hip circumference is measured in the standing position, around the largest part of the hips. A high ratio may be associated with higher risk of metabolic complications. Its standards vary according to ethnic groups, but the World Health Organization (WHO) sets a cut off of ≥ 0.90 for men and ≥ 0.85 for women, as an increased risk of metabolic complications.

Body mass index is an indicator used to assess the fatness of individuals between 18 and 65 years old. BMI is defined as the body mass divided by the square of the body height, and is expressed in units of kg/m² (BMI (kg/m2) = weight (kg) / height squared (m x m)).
BMI ranges are the following:

- BMI <18.5 kg/m²: thinness
- BMI ≥18.5 and < kg/m²: normal weight
- BMI ≥ 25 and <30 kg/m²: overweight
- BMI ≥ 30 and < 35 kg/m²: moderate obesity
- BMI ≥35 and <40 kg/m²: severe obesity
- BMI ≥40 kg/m²: morbid obesity

b. Blood glucose and blood glucose disorders

Diabetes, or diabetes mellitus, is a group of metabolic disorders characterized by a high blood sugar level over a prolonged period of time, caused either by insufficient production of insulin by the pancreas or by an inadequate response of the body's cells to the insulin produced.
The main types of diabetes mellitus are:
- Type 1 diabetes ("insulin-dependent diabetes mellitus"), characterized by a deficient insulin production due to a loss of beta cells in the pancreas caused by a autoimmune response,
- Type 2 diabetes, which begins with insulin resistance - a condition in which cells fail to respond to insulin properly - with a potential development of a lack of insulin as the disease progresses.

Type 2 diabetes is largely the result of excess body weight and physical inactivity.
Other causes include Gestational diabetes, Maturity onset diabetes of the young (MODY), genetic mutations, endocrinopathies, exocrine pancreatic defects, infections and drugs.

Impaired glucose tolerance (IGT) and impaired fasting glycaemia (IFG) are intermediate conditions in the transition between normality and diabetes. People with IGT or IFG are at high risk of developing type 2 diabetes.

Normal **fasting plasma glucose** level is ≤1.10 g/L (according to the French Society of Endocrinology). Non-diabetic fasting hyperglycaemia is defined as a blood glucose level between 1.10 and 1.26 g/L. Fasting plasma glucose ≥1.26 g/L on two occasions confirms the diagnosis for diabetes mellitus.

Oral glucose tolerance test (OGTT), performed after the intake of 75 g of glucose, is less common in current practice and has been replaced by fasting plasma glucose. Despite its limited use, it is still useful in situations that are difficult to interpret (elevation of fasting plasma glucose above normal but below 1.26 g/l, normal fasting plasma glucose with high postprandial plasma glucose). A blood sugar level at the second hour between 1.40 and 2 g/l indicates an impaired glucose tolerance (IGT).
A value of more than 2 g/L corresponds to a diabetes diagnosis.

Thus, a distinction can be made between normal subjects, hyperglycaemia in nondiabetic subjects (fasting blood glucose between 1.10 and 1.25 g/l), diabetics (fasting blood glucose greater than or equal to 1.26 g/l, or blood glucose greater than 2 g/l at the second hour of the OGTT) and glucose intolerant subjects (blood glucose between 1.40 and 2 g/l at the second hour of the OGTT)

Fasting blood glucose (g/L)	OGTT at H2 (g/L)	Diagnosis
1.1 to 1.25 g/L	-	Nondiabetic hyperglycemia
-	1.40 to 2 g/L	Glucose intolerance
≥1.26 g/L	> 2 g/L	Diabetes

Glycated hemoglobin (HbA1c) is a type of hemoglobin on which most monosaccharides (including glucose, galactose and fructose), spontaneously tend to bind with. HbA1c is known to reflect the average blood glucose level over the previous two to three months; it can be used as a diagnostic test for diabetes mellitus or as a marker for glycemic control in diabetic patients.

HbA1c (%)	Mmol/mol	
4.0% to 6.0%	20 to 42 mmol/mol	Normal
6.0% to 6.4%	42 to 47 mmol/mol	Pre-diabetes
6.5% or above	48 mmol/mol or above	Diabetes

Insulin is a peptide hormone produced by beta cells of the pancreatic islets. Insulin regulates the metabolism of carbohydrates, fats and protein by promoting the absorption of glucose from the blood into the liver, fat and skeletal muscle cells. In these tissues, glucose can be stored as glycogen via glycogenesis and/or fats via lipogenesis. Insulin plays an essential role in liposynthesis as it drives glucose into the cell, promotes the transformation of glucose into fatty acids, inhibits the triglyceride lipase responsible for lipolysis, neutralizes the lipolytic effect of cortisol and catecholamines, and stimulates the activity of lipoprotein lipase, responsible for lipogenesis.
The normal range of fasting insulinemia varies around 14 to 140 pmol/L. High insulinemia can result from a variety of metabolic diseases and conditions, including insulin resistance, early stages of type 2 diabetes, obesity, insulinoma, Cushing's syndrome and acromegaly.

C-peptide is a connecting peptide that links insulin's A-chain to its B-chain in the proinsulin molecule. Proinsulin produced in pancreatic beta cells breaks down to one molecule of insulin and one molecule of C-peptide. Both are released when blood sugar level gets high. C-peptide level are more stable in blood than insulin, which makes him a more reliable measure of insulin production. C peptide reflects insulin secretion but has also recently been shown to have its own biological effects.

Normal fasting C peptide level is around 0.3 to 1.5 nmol/L. Low C-peptide level can be a sign of type 1 diabetes or beta cell failure in type 2 diabetes. High C peptide can result from various conditions such as insulin resistance, type 2 diabetes, obesity, insulinoma and Cushing syndrome.

c. Lipid disorders

Dyslipidemia describes a wide range of conditions; the most common forms involving the following categories:

- Hypercholesterolemia with total cholesterol ≥ 2g/L
- High levels of low-density lipoproteins (LDL) ≥ 1.6 g/L
- Low levels of high-density lipoproteins (HDL) ≤ 0.4 g/L for a man and 0.5 g/L for a woman
- High levels of triglycerides ≥ 1.5 g/L

d. Hypertension

Arterial hypertension or high blood pressure is defined as systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg. There is an independent relationship between blood pressure value and cardiovascular and renal morbidity.

e. Cortisol disorders

Glucocorticoids are hormones that are produced by the zona fasciculata of the adrenal cortex, the most notable of which is cortisol. Like other steroid hormones, cortisol binds to an intracellular receptor which mediates its effects by changing gene expression. Among its many diverse effect, one of his major roles is to ensure an adequate response to stress.
Cortisol therefore increases blood sugar - through gluconeogenesis in the liver associated with decreased sensitivity of peripheral tissue to insulin, and promotes fat and protein breakdown.
As regards lipids metabolism, an acute increase in circulating cortisol promotes lipolysis whereas chronic circulated cortisol or exogenous corticosteroids stimulates lipogenesis and eventually induce central obesity.
Cortisol can be measured in blood, salivary or urine samples. It secretion varies according to the circadian rhythm. Normal values depend on the laboratory reference range, but are on average as follows:

- 8 am blood total cortisol: 275 to 685 nmol/L
- 4 pm blood total cortisol: 165 to 300 nmol/L
- Urinary free cortisol: 30 to 110 nmol/24h, varying depending on age and gender.

f. Other potential metabolic markers

Uric acid is a product of the metabolic breakdown of purine nucleotides and is a normal component of urine. High blood concentrations of uric acid are associated with gout and acid urate kidney stones. In recent years, a large body of evidence has been gathered, suggesting that hyperuricemia, defined as ≥ 360 µmol/L (60 mg/L), may play a role in the development and pathogenesis of metabolic, hemodynamic, and systemic conditions, including metabolic syndrome.

C-reactive protein (CRP) is a protein synthesized by the liver in response to pro-inflammatory factors released by macrophages and adipocytes. CRP is known as an objective marker of inflammation but has also been suggested as a risk marker for metabolic syndrome.
The normal values vary depending on the laboratory but is in general considered normal when inferior to 3 to 5 mg/L. Values between 3 (or 5) to 10 mg/L can be observed in some instances, among which obesity or smoking.

Liver function tests describe a panel of tests including total bilirubin, Aspartate aminotransferase (ASAT), Alanine aminotransferase (ALT), Alkaline phosphatase (ALP), Gamma Glutamyl transferase (GGT), Albumin. The normal ranges may vary according to laboratories. They are on average as follows: Total bilirubin < 20 µmol/L, ASAT < 30 UI/L, ALT < 35 UI/L, GGT < 55 UI/L, ALP < 80 UI/L, Alb 35-50 g/L. Elevated levels of liver enzymes are associated with to numerous medical conditions, including metabolic syndrome. Nonalcoholic fatty liver disease (NAFLD), whose presentation ranges from elevated liver enzymes to cirrhosis, is an emerging component of the metabolic syndrome.

f. Metabolic syndrome

Metabolic syndrome refers to the coexistence of several health disorders of lipid, carbohydrate or vascular origin associated with excess of weight in the same individual. These disorders increase the risk of type 2 diabetes, heart disease and stroke.

The exact clinical significance of the metabolic syndrome differs from one country to another. According to the International Diabetes Federation (IDF), metabolic syndrome is the combination of abdominal obesity (a waist circumference of more than 94 cm in men and 80 in women) and at least two of the following factors:

- Raised triglyceride levels: ≥ 1.5 g/L
- Reduced HDL cholesterol: < 0.4 g/L in men and 0.5 g/L in women.
- Raised blood pressure: ≥ 130 mmHg systolic blood pressure and 85 mmHg diastolic blood pressure.
- Raised fasting plasma glucose: ≥ 5.6 mmol/L (1g/L) (13)

E. Clinical consequences of epidural lipomatosis

EL is most often not symptomatic. In Theyskens' study (1), among 735 patients with lipomatosis on MRI, 23% were asymptomatic, 72% had non-specific spine-related symptoms, and only 5% had symptoms that could be specifically related to EL. This may relate to the usual moderate amount of fat tissue, to limited to have an effect on the Dural sac.

However, neurological symptoms can appear due to the compressive effect on neural structures (spinal cord, nerve root, cauda equina). The most common reported symptoms are back pain, myelopathy, radicular pain, paresthesia, hypoesthesia and paraparesis of the lower limbs, neurogenic claudication, and sphincter deficiencies (4).
The presentation depends on the location and degree of compression. When involving thoracic spine (preferentially in steroid induced forms), EL can lead to spinal cord compression with neurological impairment. In lumbar spine, most commons symptoms are consecutive to nerve root compression or lumbar spinal stenosis.

Clinical manifestations of spinal stenosis include neurogenic intermittent claudication, usually involving both lower limbs, reduced walking distance with symptoms that improve after sitting, squatting, lumbar spinal forward bending using a support ("shopping cart sign") and that worsen with extension of lumbar spine. It should be noticed that lumbar spinal stenosis is a degenerative condition in which coexistent spinal diseases such as changes in the discs, ligamentum flavum, and facet joints with aging may contribute to the narrowing of lumbar canal in addition to EL.
In the most severe forms, cauda equina syndrome may occur, characterized by severe low back pain, uni or bilateral radicular pain, muscle weakness of the lower legs, saddle anesthesia and bladder/bowel/sexual dysfunction.
It has been suggested that SEL causing neurological deficits occurs more frequently at thoracic than at lumbar spine. Moreover, idiopathic SEL induced neurological deficits seems extremely rare compared with cases resulting from corticosteroid therapy or endocrinopathy (14).

F. Study objective

The objective of this study was first to study the clinical and biological characteristics of patients with EL, then to estimate the frequency of metabolic syndrome in these patients.

METHODS

A. Characteristics of the study

We carried out a retrospective study on medical data including patients admitted in the department of rheumatology of the University Hospital of Tours, from May 2, 2003 to January 15, 2020.

B. Study population

1. Inclusion criteria

To be included, patients had to:
- Be hospitalized or seen during a visit
- Have a mention of “epidural lipomatosis” in their medical record, imaging report or medical coding

2. Exclusion criteria

Patients whose diagnosis was not confirmed by imaging (CT or MRI) were excluded.

3. Selection method

Medical data were collected from medical records (from 02 May 2003 to 11 August 2010) or by computerized search of keywords in a computerized data warehouse (from 19 October 2010 to 15 January 2020).

This warehouse contained medical reports or medico-administrative data (ICD-10 codes) from the Tours University Hospital. As electronic medical records have been introduced in the departments gradually, the digital data are exhaustive only from 2010 onwards, which explains the two-month gap between the hard copy and the computerized data collection.

C. Characteristics collected

<u>Clinical criteria collected were:</u>
1. Age, gender
2. Medical history of: diabetes, dyslipidemia, gout, hypertension, coronary artery disease, stroke, Peripheral Artery Occlusive Disease (PAOD)
3. Treatment by: insulin, oral antidiabetics, lipid-lowering agents, corticosteroids (oral, intravenous, inhaled, spine injection)
4. Symptomatology, i.e.: time since onset of symptoms, presence of low back pain, radicular pain, lumbar canal stenosis signs[1], walking distance
5. Morphological characteristics: weight, height, waist circumference, hip circumference, Body Mass Index (BMI)
6. Presence of hypertension or antihypertensive treatment

Biological criteria collected were :

7. Fasting blood glucose, Oral Glucose Tolerance Test (OGTT), Glycated hemoglobin (HbA1c), fasting C-peptide, fasting insulin
8. Total cholesterol, HDL-cholesterol, LDL-cholesterol, triglycerides
9. Cortisol levels at 8am and 4pm, urinary free cortisol
10. Uricemia, C-Reactive Protein (CRP), Albuminemia, Total bilirubin, Aspartate transaminase (ASAT), Alanine Transferase (ALT), Alkaline Phosphatase (ALP), Gamma-glutamyl transferase (GGT)

Other criteria collected:

11. Presence of metabolic syndrome [2]

Comments:

[1] Narrowed lumbar canal was defined as the presence of at least one of the following criteria: neurogenic intermittent claudication of the lower limbs aggravated by walking and ameliorated by stopping or sitting, worsening with lumbar extension and improvement with bending forward, "shopping cart sign"

[2] Diagnostic criteria for metabolic syndrome, according to the International Diabetes Federation (IDF) definition, include presence of abdominal obesity (=waist circumference greater than 94 cm in men and 80 in women) and at least two of the following factors: triglycerides ≥ 1. 5 g/L, HDL-cholesterol ≤ 0.4 g/L for a man and 0.5 g/L for a woman, raised blood pressure with systolic ≥ 130 mmHg and diastolic ≥ 85 mmHg, fasting blood glucose ≥ 5.6 mmol/L (1g/L).

D. Objectives

The primary objective of this study was to describe the clinical and biological features of patients with EL. The secondary objective was to investigate the percentage of metabolic syndrome in patients with EL.

E. Statistical analysis

A descriptive analysis of the collected data was performed.
Quantitative variables are expressed as means and standard deviation (SD) or as median and interquartile range. Qualitative variables are expressed as number of cases and percentage.

F. Ethical Framework

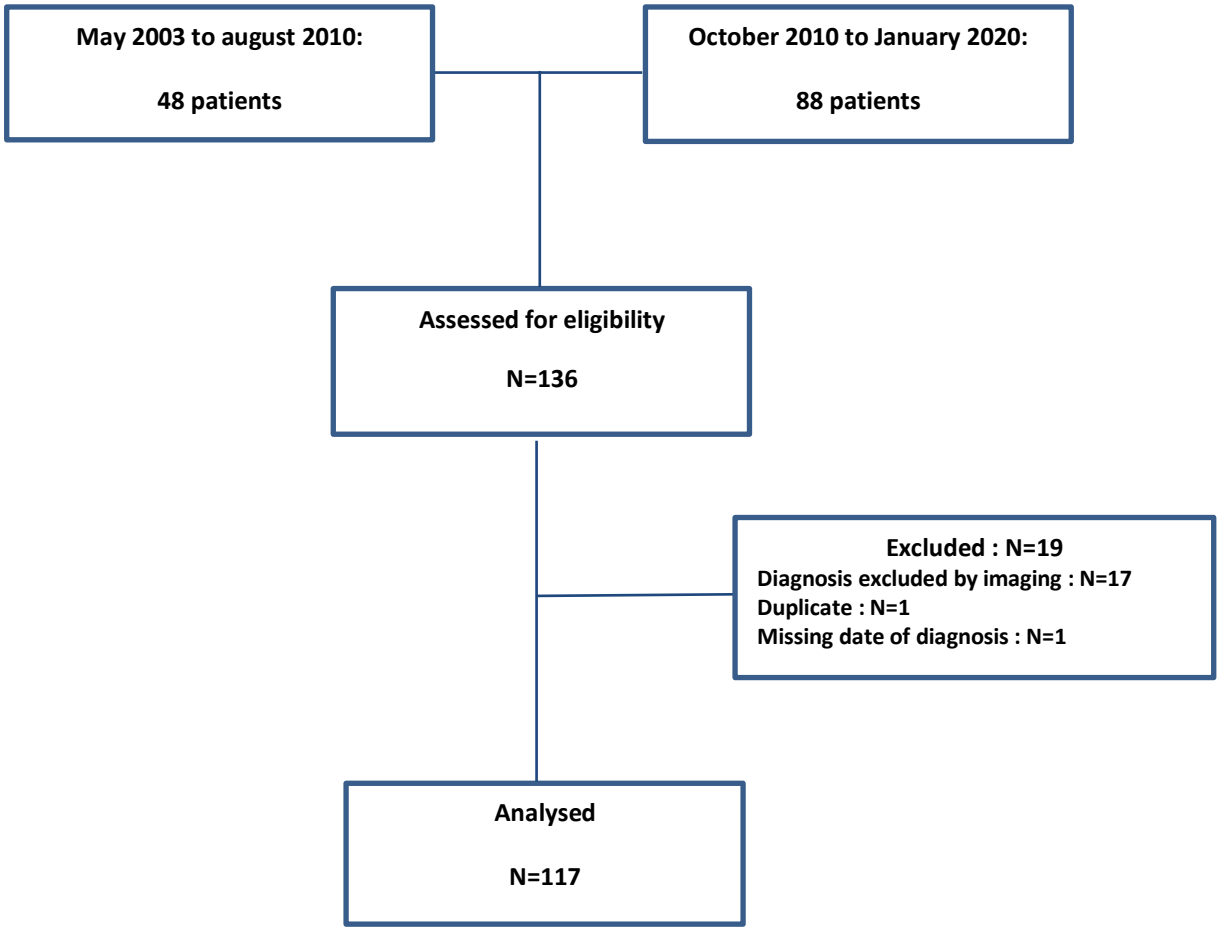
The study was declared to the National Data Protection Commission (CNIL) and conducted in compliance with personal data protection regulations.

RESULTS

A. Number of patients

During the study period, a total of 136 medical records (48 hard copy of medical report and 88 electronic records) were gathered. One record was excluded from the analysis because of missing date of diagnosis, one as a duplicate record, 17 were excluded due to several reasons essentially for diagnosis exclusion by imaging.
In total, the data of 117 patients were analyzed.

Figure 4. Flow chart



B. Clinical description

General characteristics

Our population had a mean age of 62 years. 60% of the patients were male and 40% female.

Morphological characteristics

Mean and median body mass index were respectively 32.3 kg/m² (6.07) and 31.9 kg/m² [27.32; 35.7]. In total, 30% patients were overweight, 61% obese.

Waist and hip circumference were collected in 47 patients. Mean and median waist circumference were respectively 109.2 cm (13.3) and 107 cm [100.25;120.5]. Waist-to-hip ratio was increased in 95.7% of patients. 97.8%of patients had abdominal obesity.

Medical history

25.6% of patients had diabetes and one patient had non-diabetic fasting hyperglycemia.

49.5% had dyslipidemia and 64.9% had a history of hypertension.

Furthermore, 26 (22%) had a history of cardiovascular events, namely 18 (15.4%) coronary artery disease, 7 (5.9%) a history of stroke and 1 (0.8%) an episode of transient ischemic attack (TIA), 8 (6.8%) a history of peripheral arterial occlusive disease (PAOD), 2 (1.7%) a history of mesenteric ischemia. Seven of them had a combination of several cardiovascular events.

History of corticosteroid treatment

47 patients (40.2%) had received corticosteroid treatment in the past.

14 (11.9%) received oral treatment. Among them, 3 (2.6%) patients received a short oral course of less than two weeks, one patient (0.8%) received two short courses of two weeks, two (1.7%) received a course of one month and seven (6%) received a course superior to three months. One patient (0.8%) received an oral course of prednisolone for an unknown duration.

Two patients (1.7%) received general corticosteroids by intravenous (IV) or intramuscular (IM) injection: one patient received a 10-day course of intramuscular methylprednisolone, one patient a course of intravenous methylprednisolone for a short period.

Twenty-five patients (21.3%) received corticosteroids spinal injection prior to hospitalization: 13 (11.1%) had previously received epidural steroid injections. The other sites of corticosteroid injections were facet joint injection (6%) and peri radicular injection (0.8%). 4 patients (3.4%) received infiltrations at different sites (1 patient both ESI and peri radicular, 2 patients both ESI and hiatus, 1 patient both ESI and Gluteus Medius).

One patient received several injections on his shoulder.

Regarding other routes of administration: 4 patients (3.4%) received inhaled corticosteroids for chronic obstructive pulmonary disease, 2 patients (1.7%) local nasal treatment, 3 patients (2.6%) long-term dermocorticoids.

It is noticeable that 4 patients received a combination of different routes (2 had both inhaled and oral corticosteroids, 1 had epidural injection and oral corticosteroids, 1 had dermocorticoid treatment and shoulder injections).

Table 1. Patients' demographics and clinical characteristics

Category	*Total* [a]	*Men*	*Women*
General characteristics			
Number of patients	N=117	N=70 (59.8)	N=47 (40.2)
Mean age	62 (11.7)	61.1 (11.2)	63.4 (12.5)
Age ≥75	13 (11.1)	5 (7.143)	8 (17)
65-74	40 (34.2)	22 (31.429)	17 (36.2)
50-64	49 (41.9)	32 (45.714)	16 (34)
<50	15 (12.8)	11 (15.714)	6 (12.8)
Comorbidity			
Diabetes	30 (25.6)	20 (28.6)	10 (21.2)
Dyslipidemia	58 (49.5)	39 (55.7)	19 (40.4)
Gout	11(9.4)	9 (12.8)	2 (4.3)
Hypertension	79 (67.5)	50 (71.4)	29 (61.7)
Coronary artery disease	18 (15.4)	16 (22.8)	2 (4.3)
Stroke	7 (5.9)	5 (7.1)	2 (4.3)
PAOD	8 (6.8)	8 (11.4)	0 (0)
Treatment			
Insulin	9 (7.6)	7 (10)	2 (4.3)
Oral antidiabetics	24 (20.5)	14 (20)	10 (21.2)
Lipid lowering agents	43 (36)	31 (44.2)	12 (25.5)
Corticosteroids	47 (40.2)	27 (38.5)	20 (42.5)
Morphological characteristics			
BMI	N=110	N=67	N=43
Mean BMI (kg/m^2)	32.31 (6.07)	31.99 (4.88)	32.8 (7.61)
Underweight	0 (0)	0 (0)	0 (0)
Normal	10 (9)	4 (5.97)	6 (14)
Overweight	33 (30)	22 (32.83)	11 (25.5)
Obese Class I (moderately obese)	36 (32.8)	24 (35.82)	12 (28)
Obese grade II (severely obese)	19 (17.2)	14 (20.9)	5 (11.5)
Obese grade III (morbidely obese)	12 (11)	3 (4.48)	9 (21)
Weight	91 (20.8)	95 (17.08)	85 (24.5)
Height	167 (11.57)	172 (7.89)	158 (10.85)
Waist circumference	N=47	N=31	N=16
Abdominal obesity [b]	46 (98%)	30 (97%)	16 (100%)
Waist circumference	109.2 (13.3)	112.2 (11.8)	103.6 (14.6)
Hip circumference	110 (12.87)	109.7 (11.7)	110.7 (15.2)
Waist-to-hip ratio	N=47	N=31	N=16
Mean waist-to-hip ratio	0.99 (0.07)	1.02(0.06)	0.93 (0.06)
Increased waist-to-hip ratio [c]	45 (95.7)	30 (97)	15 (94)

[a] *Values are expressed as means and standard deviation or as number of cases and percentage*

[b] *Defined as a waist circumference > 94 cm for men and > 80 cm for women*

[c] *Defined as a waist-to-hip ratio ≥0.90for men and ≥0.85 for women*

***Symptoms*:**
Mean time since onset of symptoms was 4.32 years (6.29), and median time 2 years [0.5 - 4], duration extending from 4 days to 21 years.
90.5% patients had low back pain, 82.9% had radiculalgia. 54 patients out of 82 (65.8%) had clinical symptoms of lumbar spinal stenosis. Walking distance was reduced, less than or equal to 500 m, for 60 out of 77 patients (77.9%).

C. Biological description

Glycemic parameters

Fasting blood glucose was increased (>1g/L) in 39.3% of patients and was above 1.1 g/L in 23.9% of patients. 11.9% had a value superior to 1.26 g/L.
When performed, OGTT test was out of range in 52.9% of patients. Glycated haemoglobin was increased in 35% of patients., Fasting C-peptide in 29% of patients, Fasting insulin levels in 13.2 of patients.

Lipidic parameters
Mean total cholesterol level was 2.20 g/L (0.586), mean LDL cholesterol level 1.359 g/L (0.52), and mean triglyceride level 1.84 g/L (1.20). They were increased in 67.3%, 33% and 51% of patients respectively. Mean HDL cholesterol level was 0.54 g/L (0.16), decreased in 25.6% of patients.
A total of 81.4% of patients had at least one affected lipid parameter. Considering only HDL-c, LDL-c, and TG, this was the case for 64% of patients.

Uricemia, CRP and hepatic parameters
Hyperuricemia was found in 46.4% of patients and CRP was increased in 42.2% of patients.
Regarding liver function tests results, values were out of range for total bilirubin, ASAT, ALT, ALP and GGT in 2.8%, 23.1%, 28.9%, 40.7%, and 51.9% of cases respectively. 65.7% of patients (69 out of 105) had at least one pathologically increased parameter.

Cortisolemia and cortisoluria
Cortisol levels at 8 am and 4 pm were measured in 57 and 51 patients and were increased in 7% and 15.7% of patients respectively, with mean value respectively 363 nmol/L (216.5) and 176 nmol/L (124.5). Urinary free cortisol was increased 25.9% of patients, with mean value 104.3 nmol/24h (119.9).

D. Presence of metabolic syndrome

Of the 44 patients for whom all the parameters were available, 34 (77%) met the criteria for metabolic syndrome, respectively 78.6% of men and 75% of women.

E. Therapeutic aspects

It should be noted that 67.9% patients (70 patients out of 103) received epidural injections following their admission, as a medical treatment for radicular pain.

Table 2. Patients' biological characteristics (1)

Catégorie	*Total* [a]	*Men*	*Women*
Fasting blood sugar	N= 117	N= 70 (60)	N=47 (40)
Fasting blood sugar (g/L)	1.07 (0.28)	1.11 (31.9)	1.00 (0.21)
<1 [b]	71 (60.7%)	38 (54.3)	33 (70.21)
<1.1 [b]	89 (76)	47 (67.1)	42 (89.4)
≥1.1 and <1.26	14 (11.95)	10 (14.3)	4 (8.5)
≥1.26	14 (11.95)	13 (18.6)	1 (2.1)
OGTT	N=17	N=11	N=6
T0 (g/L)	0.97 (0.10)	0.97 (0.11)	0.98 (0.08)
T120 (g/L)	1.38 (0.5)	1.34 (0.5)	1.57 (0.4)
T0 (g/L)			
<1.1	15 (88.2)	9 (81.8)	6 (100)
≥1.1 et <1.26	2 (11.8)	2 (18.2)	0
≥1.26	0 (0)	0 (0)	0
T120			
<1.40	8 (47)	7 (63.6)	1 (16.66)
≥1.40 et <2	7 (41.2)	3 (27.3)	4 (66.66)
≥2	2 (11.8)	1 (9.1)	1 (16.66)
HbA1c	N=60	N=41	N=19
HbA1c (%)	6.17 (1.03)	6.24 (0.98)	6.00 (1.13)
Increased HbA1c [c]	21 (35)	18 (43.9)	3 (15.8)
Peptide C	N=51	N=45	N=16
Peptide C (nmol/L)	1.32 (0.54)	1.36 (0.59)	1.25 (0.38)
Increased [d]	15 (29)	12 (26.6)	3 (18.7)
Fasting insulinemia	N=53	N=36	N=17
Fasting insulinemia (pmol/L)	87.67 (60.09)	92.6 (68.4)	77.11 (41.3)
Increased [e]	7 (13.2)	5 (13.8)	2 (11.7)
Cholesterol total	N=104	N=62	N=42
Cholesterol total (g/L)	2.20 (0.586)	2.11 (0.65)	2.34 (0.44)
Increased [f]	71 (67.3)	35 (56.5)	36 (85.7)
HDL chlolesterol	N=82	N=55	N=28
HDL chlolesterol (g/L)	0.54 (0.16)	0.51 (0.16)	0.60 (0.15)
Reduced [g]	21 (25.6)	14 (25.4)	9 (32.1)
LDL cholesterol	N=80	N=52	N=28
LDL cholesterol (g/L)	1.359 (0.52)	1.31 (0.55)	1.46 (0.44)
Increased [h]	20 (0.33)	12 (23)	8 (28.6)
Triglycerides	N=104	N=62	N=42
Trilglycerides (g/l)	1.84 (1.20)	1.98 (1.5)	1.64 (0.67)
Increased [i]	53 (51)	51 (82.3)	21 (50)

[a] *Values are expressed as means and standard deviation or as number of cases and percentage*
[b] *Definition of hyperglycemia varies according to the learned societies ,e.g. 1.0 g/L (5.6 mmol/L) according to the American Diabetes Association versus 1.1 g/L (6 mmol/L) according to the French Society of Endocrinology*
[c] *HbA1c ≥ 6%*
[d] *C peptide >1.5 nmol/L*
[e] *Fasting insulinemia>140 pmol/L*
[f] *Total cholesterol > 2g/L*
[g] *HDL-cholesterol <0.4 g/L for men and <0.5 g/L for women*
[h] *LDL cholesterol >1.6 g/L*
[i] *Triglycerides >1.5 g/L*

Table 3. Patients' biological characteristics (2)

Catégorie	*Total* [a]	*Men*	*Women*
8 am cortisolemia	N=57	N=41	N=16
8 am cortisolemia (nmol/L)	363 (216)	354.7 (224)	384.2 (200)
<275	19 (33)	14 (34.1)	5 (31.3)
≥275 and <685	34 (60)	24 (58.6)	10 (62.5)
	4 (7)	3 (7.3)	1 (6.2)
4 pm cortisolemia	N=51	N=36	N=15
4 pm cortisolemia (nmol/L)	176 (124.5)	173.3 (129.7)	184.5 (114.7)
<165	32 (62.7)	24 (66.7)	8 (53.3)
≥165 and <300	11 (21.6)	7 (19.4)	4 (26.7)
≥300	8 (15.7)	5 (13.9)	3 (20)
Urinary free cortisol	N=54	N=37	N=17
Urinary free cortisol (nmol/24h)	104.3 (119.9)	112.3 (133.6)	86.8 (83.8)
Increased UFC [b]	14 (25.9)	11 (29.7)	3 (17.6)
Uricemia	N=84	N=51	N=33
Uricemia (umol/L)	357.4 (102.7)	378.9 (104.3)	324.2 (92.3)
Increased uricemia [c]	39 (46.4)	25 (49)	14 (42.4)
CRP (mg/L)	N=109	N=63	N=46
Mean (mg/L)	10.06 (17.36)	10.9 (20.3)	7.2 (10.2)
Median	4.8 (2.65-8.6)	4.3 (2.05-9.45)	3.95 (2.5-8.05)
Increased CRP [d]	46 (42.2)	28 (44.4)	18 (39.1)
Albumin (g/L)	41.03 (5.1)	40.8 (5.6)	41.3 (4.5)
Total Bilirubin	N=107	N=62	N=45
Total Bilirubin (umol/L)	10.34 (4.54)	11.31 (4.7)	9.02 (3.9)
Increased [e]	3 (2.8)	1 (1.6)	2 (4.4)
ASAT	N=108	N=63	N=45
ASAT (UI/L)	27.2 (17.5)	30.2 (21)	23 (9.7)
Increased ASAT [f]	25 (23.1)	20 (31.7)	5 (11.1)
ALT	N=107	N=63	N=44
ALT (UI/L)	31.3 (21.1)	36.3 (23.3)	24.2 (15)
Increased ALT [g]	31 (28.9)	24 (38.1)	7 (15.9)
GGT	N=104	N=61	N=43
GGT (UI/L)	102.1 (110)	122.5 (126.3)	73.2 (74.9)
Median GGT	58.5 (36-127.5)	75 (42 – 149)	43 (26 – 86.5)
Increased [h]	54 (51.9)	37 (60.7)	17 (39.5)
ALP	N=108	N=63	N=45
ALP (UI/L)	78.6 (21.1)	78.3 (30.9)	79 (28.9)
Increased	44 (40.7)	26 (41.2)	18 (40)

[a] *Values are expressed as means with standard deviation, or when specified as median with interquartile range, or as number of cases and percentage.*
[b] *Urinnary Free Cortisol >110 nmol/24h*
[c] *Uricemia >360 umol/L*
[d] *CRP >5 mg/L*
[e] *Total bilirubin>20 umol/L*
[f] *ASAT>30 UI/L*
[g] *ALT>35 UI/L*
[h] *GGT >55 UI/L*
[i] *ALP> 80 UI/L*

DISCUSSION

According to our study, a high percentage of with EL admitted in a rheumatology department appear to present abdominal obesity (97.8%) or metabolic disorders such as diabetes (25.6%), dyslipidemia (49.5%) or high blood pressure (64,9%). In addition, metabolic risk markers such as uricemia, CRP and liver function tests values appear above normal value.
Moreover, a large majority of patents with EL display a metabolic syndrome (77%).

A. In the literature

Regarding obesity, most of the patients in our study were overweighted (30%) or obese (50%), and 97.8% had abdominal obesity. Obesity is a frequent comorbidity observed in patients with EL. Ishihara *et al.* (15) showed that EL was significantly correlated with body mass index, abdominal circumference and the presence of visceral fat. Moreover, a visceral fat area ≥ 100 cm^2 was independently associated with EL. In contrast, body fat percentage and subcutaneous fat did not show a correlation with epidural fat accumulation. In their study, Morishita *et al.* (16) analysed cross-sectional images (MRI and CT) of patients admitted with compression symptoms in the lumbar spinal canal and separated them into groups with and without EL. They found that EL group had a significantly larger abdominal circumference and BMI. Moreover, in men, the amount of visceral fat appeared significantly greater in patients EL than in the group without EL, while the area of subcutaneous fat did not differ significantly between the two groups. For women, both visceral and subcutaneous fat were significantly greater in the lipomatosis group. In a regression analysis, visceral fat appeared to be an independent factor in the pathogenesis of EL. The American case-control study by Yildirim *et al*. (17) found a significant correlation between an increased BMI and lipomatosis.

In our study there was a male predominance with 60% of male patients and 40% female, which is in agreement with the literature. Morishita *et al.* (16) showed that the "male" factor is not an independent factor in regression analysis. This male preponderance in EL may be explained, at least partially, by an accumulation of subcutaneous fat due to estrogen in women, whereas abdominal accumulation occurs preferentially in men.

Twenty-five percent of our patients had a former diagnosis of diabetes and glycaemia was increased in 39.3% of patients for fasting blood glucose, in 53% for HGPO, in 35% for HBA1c, in 29% for fasting C peptide and in 13.2% for fasting insulin. Regarding diabetes, studies found contradictory results: Ishihara *et al.* (15)showed no correlation between EL and the presence of type 2 diabetes, whereas Yildirim *et al.* (17) found a statistically significant association. Similarly, Morishita *et al.* (16) found significantly higher insulin levels in patients with EL, with no difference in HBA1c levels, though.

Hypertension was found in 64.9% of our patients. Hypertension was independently associated with EL in the study by Ishihara *et al.* (15), however the causal relationship between hypertension and EL remains unclear.
Regarding lipid profile, 49.5% of our patients had previously known dyslipidemia and 78.8% of patients had at least one lipid parameter out of range. Total cholesterol, HDL, LDL, Tiglycerides level were pathological in respectively 37%, 25.6%, 33%, 51% of our patients. In their study, Jaimes *et al.* (10) observed that triglycerides in were significantly elevated in the EL group compared to the control group. In the same way, Ishihara *et al.* found in a first study conducted on male patients (18) that hyperlipidemia was significantly associated with idiopathic EL. However, in a second study

conducted in male and female patients (15), no association was found between EL and triglyceride, HDL cholesterol levels or LDL cholesterol level. Likewise, Morishita *et al*.(16) found no significant difference in triglyceride, total cholesterol, HDL and LDL levels between EL patients and controls.

In our study, uricemia was increased in 46.4% of our patients and 9.4% had a history of gout.
Several studies showed an increase of mean uric acid levels in patients with EL, such as the study of Morischita *et al.* (16) or the one of Abe *et al.* (19) who both showed a uric acid significantly higher in patients with EL compared to control. Uric acid (UA) has been positively associated with obesity and metabolic syndrome (20). Obesity is known to reduce uric acid (UA) renal excretion. Moreover, some authors suggested that UA serum concentrations are independently related to leptin concentration (increased in obese patients) thus suggesting that leptin could be a pathogenic factor responsible for hyperuricemia in obesity (21).

CRP was increased in 42.2% of our patients, but elevation was rather moderate with a median value of 4.8 mg/L. Ishihara *et al.* (15) found no relationship between EL and CRP. Similarly, Abe *et al*. (19) found no significant difference in CRP values between EL patients and control.

Liver function tests were out of range in 65.7% of our patients, mainly for GGT (increased in 51.9% of cases). EL has been associated with hepatic fat accumulation and liver dysfunction. Abe *et al.* (19) found an association between lipomatosis and liver density on CT scan (44.67+/- 5.06 HU for the EL group versus 56.7=/- 8.46 HU for the control group ; p=0.03), a density <40 HU being synonymous of hepatic steatosis. Gamma-GT levels were also significantly increased in the lipomatosis group (58.6 +/- 5.39 versus 28.1 +/- 2.62, p=0.01).
Nonalcoholic fatty liver disease (NAFLD) is the most common chronic liver disease worldwide.
Non-Alcoholic Steatohepatitis (NASH) is the most severe form of NAFLD, ranging from isolated liver enzyme elevation to cirrhosis. The link between NASH and metabolic syndrome is increasingly mentioned, and NASH could be considered as the liver manifestation of a metabolic disorder.
GGT elevation is usually the first biologic marker of metabolic syndrome and associated liver steatosis. The correlation between the presence of EL and fatty liver disease suggests an association between EL and systemic fat depositions.

In our study, 77% of patients for whom data were available met the criteria for metabolic syndrome.
Thus, EL may be a manifestation of the metabolic syndrome. This is suggested by the high frequency of patients with abdominal obesity and type 2 diabetes in our study. The Japanese retrospective study by Ishihara *et al.* (15) showed that EL was significantly correlated with the presence of metabolic syndrome (Odds radio 3.9, p<0.01, 95% CI 1.5-9.8). A visceral fat area ≥ 100 cm^2 (OR 4.8, 95% CI=1.5-15.3) was also independently associated with EL. It is known that metabolic syndrome is associated with visceral fat rather than subcutaneous fat.

The literature suggests that hypercorticism or exogenous corticosteroid use (oral or by epidural injection) may be related to EL, with more than 50% of cases associated with a history of oral or injectable corticosteroid use. Exogenous steroid use is constantly reported as the most significant risk factor for developing SEL. In our study, 40% of patients had a history of corticosteroid treatment: 12% received oral treatment (6% more than 3 months), 22% had previous epidural steroid injection. The biological cortisol parameters were increased in some patients (in 7%, 16%, 26% of patients respectively for 8 am, 4 pm cortisolemia, 24h cortisoluria). But it is important to note that our study was not specifically designed to examine this specific point, no correlation was made between a

history of corticosteroid therapy and the presence of EL, and epidural spinal injection were not quantified. Theyskens *et al.* (1) showed that corticosteroid was significantly and independently associated with the presence of EL whether it is systemic corticosteroid use (OR: 2.59, 95% CI: 1.69–3.99), or epidural corticosteroid injections (OR: 3.48, 95% CI: 2.82–4.30) in multivariate analysis.
It is noteworthy that in Yildirim *et al.* study, no significant difference was found in exposure to exogenous corticoids between cases and controls (49.8% versus 51.3% respectively) (17).

(Appendix 1)

B. OBESITY, INFLAMMATION AND LIPOMATOSIS

The pathogenesis of idiopathic lipomatosis is thought to be associated with obesity and metabolic syndrome. The positive correlation between BMI, abdominal fat and EL may suggest a link between obesity and EL. As mentioned before, excessive deposition of triglycerides in adipocytes leads to cellular hypertrophy which may be responsible - at least in part - for the increase in epidural fat tissue. However, chronic inflammation associated with obesity could also be involved in the pathogenesis of EL.

In obesity, hypertrophic adipocytes express pro-inflammatory cytokines, i.e. tumor necrosis factor-α (TNF-α) and interleukin 6 (IL-6), which stimulate CRP synthesis by the liver, predisposing to a pro-inflammatory state (11) (22).
Moreover, adipocytes also secrete large amounts of adipokines (such as adiponectin and leptin) that have important, and opposite, effects on inflammation and metabolism.
Adiponectin is known for its anti-inflammatory effects, and its positive metabolic effect on insulin sensitivity. Hypoadiponectinemia has been associated with increased levels of fasting blood glucose, triglycerides, and decreased HDL-c. Despite the increased secretion of adiponectin by visceral fat, serum level of adiponectin appears to be reduced in obese subjects. This decreased level of adiponectin in obesity is unclear but it has been suggested than the increased expression of IL-6 and TNF-α are responsible for inhibiting and reducing the adiponectin production and secretion (22).
Leptin is known for its function in regulating homeostasis and energy, especially with its effects on hunger and alimentary behavior. But it has also recently been identified as a mediator of inflammatory response, with proliferative and anti-apoptotic effect on immune cells and with positive regulation of the production of proinflammatory cytokines (23).
It can thus be suggested that obesity-induced inflammation itself promotes metabolic disorder.

Fujita *et al.* (11) showed that in patients with EL, adipocyte size appeared significantly larger than in controls (2846.8 vs. 1699.0 µm2, P = 0.017), as did TNF-α and IL-1β expression levels (respectively 2.59-fold increase, P = 0.023 ; and 2.60-fold increase, P = 0.015). There was however no significant difference in the levels of adiponectin, leptin, IL-6 and IL-8 between EL patients and controls.

How chronic inflammation associated with obesity could be involved in the pathogenesis of EL is not fully understood. The excess of nutrients in adipocytes could promote chronic low-grade inflammation accompanied by the production of inflammatory cytokines, which could themselves promote insulin resistance, thus worsening insulin metabolism and adipocyte functions.

C. STRENGTHS AND LIMITATIONS

The current study has some strengths that might be mentioned: it was conducted on a large number of EL patients presenting with symptoms. Collection of data was exhaustive, including morphological, clinical and biological data while mainly focusing on metabolic factors.
However, there were several limitations. First, given its retrospective design, our study may suffer from several biases including selection biases and missing data. In addition, because no control group was available, we could not study the respective effect of potential factors of EL.
Moreover, the study was conducted in symptomatic patients, mainly with lumbar EL, which cannot be extrapolated to patients with thoracic EL. In the late case, EL is often secondary to corticosteroids - with clinical features dominated by myelopathy and paraplegia.
Additionally, we did not focus on imaging (MRI or CT-scan) nor did we measure epidural fat, visceral fat area or subcutaneous fat area.

D. PERSPECTIVES

We believe that this work paves the way to further studies to decipher the links between metabolic factors exposure, clinical features, and imaging in EL.

In terms of clinical practice, a better understanding of the pathophysiological mechanisms of EL could have important diagnostic and therapeutic implications.
In terms of diagnosis, EL should be suspected in patients with spinal symptoms and metabolic syndrome. Control of metabolic factors in subjects at risk could possibly limit the progression EL and its neurological consequences. In addition, screening for risk factors could be considered in any patient with incidental EL.
In terms of therapeutic implications, treatment of EL currently ranges from conservative treatment to surgical excision. Indication may actually depend on the pathogenesis of EL. Fogel *et al.* (3) found that in corticosteroid EL patients, laminectomy and medical management seem to have roughly the same success rate (around 77% of success rate from improved symptoms to complete recovery), whereas in obese patients conservative medical treatment involving weight loss seems more efficient (81.8% success rate versus 66.7% in the surgically managed group).

In EL accompanying the metabolic syndrome or obesity, correction of metabolic abnormalities with control of comorbidities (weight loss in case of obesity, management of diabetes or metabolic syndrome) may improve symptoms (15). Weight loss and physical activity in obese patient is a critical factor to reduce not only fat cell size, but also insulin sensitivity and also inflammation (24).
Several cases report presented successful medical treatment in obese patients with EL.
In the case described by Maillot *et al.* (25) of a patient with idiopathic lipomatosis associated with obesity, a hygienic-dietary management with a hypocaloric diet and reduction in alcohol consumption led to an improvement of the lumbar clinical symptoms, a concurrent reduction in weight, and also to a reduction in lumbar epidural fatty tissue on imaging. Similarly, Beges *et al.* (26) described an obese patient with EL who received a weight-reduction program which allowed an improvement in both symptoms(bilateral radiculalgia with lower limb weakness) and lipomatosis lesions on imaging. In the case report by Trungu *et al.* (27), conservative treatment by weight loss resulted in complete disappearance of neurological symptoms and MRI lesions of lipomatosis.

As regards surgical management, classically by laminectomy, associated with removal of epidural fat, the indication should only be given as a second line after medical treatment or in the presence of severe neurological symptoms (28). This is especially true since the contribution of EL to lumbar symptoms may be difficult to assess in patients who may have concomitant degenerative lesions that may themselves be responsible for lumbar stenosis.

CONCLUSION

According to our study, a considerable proportion of patients with symptomatic EL present metabolic disorders (diabetes, dyslipidemia or high blood pressure), abdominal obesity and metabolic syndrome. This finding should increase the clinicians' awareness when dealing with lumbar symptoms.

DECLARATION

Ethics approval and consent to participate:
This study was conducted in compliance with personal data protection regulations and declared to the National Data Protection Commission (CNIL) in accordance with the provisions of the law "Informatique et Libertés" (law of January 6, 1978 as amended). Patients admitted before 2016 received written information. After 2016, the University Hospital Center of Tours provides the patients a systematic information of the potential use of their medical data for research and evaluation in an anonymous and regulated manner, subject to patient non-objection.

Consent for publication:
Not applicable

Availability of data and materials:
Data were extracted from paper medical records of from the eCDC and DPP (computerized medical record) platform from the Tours University Hospital.

Competing interests:
The authors declare that they have no competing interest.

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REFERENCES

1. Theyskens NC, Paulino Pereira NR, Janssen SJ, Bono CM, Schwab JH, Cha TD. The prevalence of spinal epidural lipomatosis on magnetic resonance imaging. Spine J. juill 2017;17(7):969-76.

2. Park SK, Han JM, Lee K, Cho WJ, Oh JH, Choi YS. The Clinical Characteristics of Spinal Epidural Lipomatosis in the Lumbar Spine. Anesth Pain Med. oct 2018;8(5):e83069.

3. Fogel GR, Cunningham PY, Esses SI. Spinal epidural lipomatosis: case reports, literature review and meta-analysis. The Spine Journal. mars 2005;5(2):202-11.

4. Kim K, Mendelis J, Cho W. Spinal Epidural Lipomatosis: A Review of Pathogenesis, Characteristics, Clinical Presentation, and Management. Global Spine Journal. sept 2019;9(6):658-65.

5. Ge Y, Yang X, You Y, Xuan Y, Yan G. Comparison of relative and absolute values of magnetic resonance imaging in the diagnosis of spinal epidural lipomatosis. J Spinal Cord Med. juill 2019;42(4):502-7.

6. Borré DG, Borré GE, Aude F, Palmieri GN. Lumbosacral epidural lipomatosis: MRI grading. Eur Radiol. 1 juill 2003;13(7):1709-21.

7. Kuhn MJ, Youssef HT, Swan TL, Swenson LC. Lumbar epidural lipomatosis: the « Y » sign of thecal sac compression. Comput Med Imaging Graph. oct 1994;18(5):367-72.

8. Lee M, Lekias J, Gubbay SS, Hurst PE. Spinal cord compression by extradural fat after renal transplantation. Med J Aust. 15 févr 1975;1(7):201-3.

9. Choi K-C, Kang B-U, Lee CD, Lee S-H. Rapid progression of spinal epidural lipomatosis. Eur Spine J. juin 2012;21(Suppl 4):408-12.

10. Jaimes R, Rocco AG. Multiple epidural steroid injections and body mass index linked with occurrence of epidural lipomatosis: a case series. BMC Anesthesiol. 15 août 2014;14:70.

11. Fujita N, Hosogane N, Hikata T, Iwanami A, Watanabe K, Shiono Y, et al. Potential Involvement of Obesity-Associated Chronic Inflammation in the Pathogenesis of Idiopathic Spinal Epidural Lipomatosis. Spine. 1 déc 2016;41(23):E1402.

12. Greenish D, Watura K, Harding I. Spinal epidural lipomatosis following bilateral spinal decompression surgery. BMJ Case Rep. 15 févr 2019;12(2).

13. Alberti KGM, Zimmet P, Shaw J. The metabolic syndrome—a new worldwide definition. The Lancet. 24 sept 2005;366(9491):1059-62.

14. Ishikawa Y, Shimada Y, Miyakoshi N, Suzuki T, Hongo M, Kasukawa Y, et al. Decompression of idiopathic lumbar epidural lipomatosis: diagnostic magnetic resonance imaging evaluation and review of the literature. J Neurosurg Spine. janv 2006;4(1):24-30.

15. Ishihara S, Fujita N, Azuma K, Michikawa T, Yagi M, Tsuji T, et al. Spinal epidural lipomatosis is a previously unrecognized manifestation of metabolic syndrome. The Spine Journal. 1 mars 2019;19(3):493-500.

16. Morishita S, Arai Y, Yoshii T, Sakai K, Hirai T, Okawa A. Lumbar epidural lipomatosis is associated with visceral fat and metabolic disorders. Eur Spine J. 1 juill 2018;27(7):1653-61.

17. Yildirim B, Puvanesarajah V, An HS, Novicoff WM, Jain A, Shen FH, et al. Lumbosacral Epidural Lipomatosis: A Retrospective Matched Case-Control Database Study. World Neurosurgery. 1 déc 2016;96:209-14.

18. Ishihara S, Fujita N, Yagi M, Tsuji T, Michikawa T, Nishiwaki Y, et al. Idiopathic Spinal Epidural Fat Accumulation Is Associated With Hyperlipidemia. Spine (Phila Pa 1976). 15 avr 2018;43(8):E468-73.

19. Abe T, Miyazaki M, Ishihara T, Kanezaki S, Notani N, Kataoka M, et al. Spinal epidural lipomatosis is associated with liver fat deposition and dysfunction. Clin Neurol Neurosurg. oct 2019;185:105480.

20. Chen L, Zhu W, Chen Z, Dai H, Ren J, Chen J, et al. Relationship between hyperuricemia and metabolic syndrome. J Zhejiang Univ Sci B. août 2007;8(8):593-8.

21. Fruehwald-Schultes B, Peters A, Kern W, Beyer J, Pfützner A. Serum leptin is associated with serum uric acid concentrations in humans. Metabolism. juin 1999;48(6):677-80.

22. Ellulu MS, Patimah I, Khaza'ai H, Rahmat A, Abed Y. Obesity and inflammation: the linking mechanism and the complications. Arch Med Sci. juin 2017;13(4):851-63.

23. Fantuzzi G, Faggioni R. Leptin in the regulation of immunity, inflammation, and hematopoiesis. Journal of Leukocyte Biology. 2000;68(4):437-46.

24. Bianchi VE. Weight loss is a critical factor to reduce inflammation. Clin Nutr ESPEN. déc 2018;28:21-35.

25. Maillot F, Mulleman D, Mammou S, Goupille P, Valat J-P. Is epidural lipomatosis associated with abnormality of body fat distribution? A case report. Eur Spine J. févr 2006;15(1):105-8.

26. Beges C, Rousselin B, Chevrot A, Godefroy D, Vallee C, Berenbaum F, et al. Epidural lipomatosis. Interest of magnetic resonance imaging in a weight-reduction treated case. Spine (Phila Pa 1976). 15 janv 1994;19(2):251-4.

27. Trungu S, Forcato S, Raco A. Spinal Epidural Lipomatosis: Weight Loss Cure. World Neurosurg. 2019;125:368-70.

28. Mallard F, Buni M, Nolet PS, Emary P, Taylor JA, Moammer G. Lumbar spinal epidural lipomatosis: A case report and review of the literature. Int J Surg Case Rep. janv 2021;78:71-5.

ANNEXES

Appendix 1: Comparative table

Parameter	Our study	In the literature
Gender	Male preponderance *60% men and 40% women*	***Morishita et al. (16)*** « Male » factor is not an independant factor
Obesity	Increased obesity and abdominal obesity *30% of patients overweight* *50% obese* *97.8% abdominal obesity*	***Ishihara et al. (15)*** EL is significantly correlated with BMI, abdominal circumference and the prevalence of visceral fat ***Morishita et al. (16)*** EL group has a significantly larger abdominal circumference and BMI versus control group ***Yildirim et al. (17)*** There is a significant correlation between increased BMI and lipomatosis
Diabetes	Increased glycemic parameters *25% diabetic patients* *Fasting blood glucose increased in 39.3% of patients, OGTT in 53% of patients, HBA1c in 35% of patients, fasting C peptide in 29% of patients and fasting insulin in 13.2% of patients*	***Ishihara et al. (15)*** No correlation between EL and the presence of type 2 diabetes ***Yildirim et al. (17)*** Statistically significant association between EL and type 2 diabetes ***Morishita et al. (16)*** Significantly higher insulin levels in patients with epidural lipomatosis, HBA1c levels no significantly different
Hypertension	Increased blood pressure *64.9% of patients with high blood pressure*	***Ishihara et al. (15)*** Hypertension is independently associated with EL
Dyslipidemia	Increased dyslipidemia *Dyslipidemia in 49.5% of patients. Total cholesterol, HDL-c, LDL-c, TG pathological in respectively 37%, 25.6%, 33% and 51% of patients*	J***aimes et al.*** (10) Triglycerides significantly increased in the EL group compared to the control group ***Ishihara et al. (18)*** Idiopathic spinal epidural fat accumulation is associated with hyperlipidemia
Metabolic syndrome	High prevalence of metabolic syndrome *77% of patients*	***Ishihara et al. (15)*** EL is significantyl correlated with the presence of metabolic syndrome
Uricemia	High prevalence of hyperuricemia *46.4% of patients*	***Morishita et al. (16)*** Uric acid significantly higher in patients with EL ***Abe et al. (19)*** Higher uricemia in the EL group compared to control
CRP	Moderate elevation in a percentage of patients *(42.2%)*	***Ishihara et al. (15)*** No correlation between EL and CRP ***Abe et al.(19)*** No correlation between EL and CRP
Liver balance disturbances	High prevalence of abnormal liver function tests *65.7% of patients, mainly GGT elevation*	***Abe et al. (19)*** Gamma-GT levels significantly increased in the EL group
Glucocorticoid excess	*40% of patients with history of corticosteroid treatment, 12% oral treatment (6% more than 6 monthes), 11% previous ESI*	***Theyskens et al. (1)*** Corticosteroid treatment significantly and independently associated with of EL (systemic corticosteroid or epidural injections)

Vu, le Directeur de Thèse

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DOIZE Heidi
40 pages – 3 tableaux – 4 figures – 2 annexes

Résumé :

Contexte: La lipomatose épidurale est une accumulation de tissus adipeux dans l'espace épidural, pouvant mener à des tableaux cliniques de lombosciatique ou de canal lombaire rétréci. Certaines anomalies métaboliques ont été incriminées dans la pathogénèse de la lipomatose épidurale, mais les études menées sur de larges échantillons restent peu nombreuses.
Objectifs: L'objectif principal de cette étude était d'étudier les caractéristiques cliniques et biologiques des patients atteints de lipomatose épidurale, l'objectif secondaire d'étudier la fréquence du syndrome métabolique chez ces patients.
Méthode: Dans cette étude rétrospective descriptive ont été inclus les patients atteints de lipomatose épidurale admis dans notre service de rhumatologie (consultation ou hospitalisation) entre mai 2003 et janvier 2020. Nous avons recueilli les caractéristiques démographiques, morphologiques (notamment indice de masse corporelle et tour de taille), les antécédents cardiovasculaires et maladies métaboliques, les traitements (antidiabétiques, hypolipémiants et corticoïdes), les signes cliniques rachidiens et les données biologiques (notamment le profil glucidique et lipidique). Nous avons ensuite estimé la fréquence du syndrome métabolique selon la définition de la Fédération Internationale du Diabète.
Résultats: Au total les données cliniques et biologiques de 117 patients ont été analysées. Soixante pour cent des patients étaient des hommes et 40% des femmes, l'âge moyen était de 62 ans. Concernant les antécédents, 25.6% des patients présentaient un diabète, 49.5 % présentaient une dyslipidémie et 64.9% avaient un antécédent d'hypertension artérielle. Sur le plan morphologique, 91.5% des patients étaient en surpoids ou obèses et, chez les 47 patients chez qui le tour de taille était disponible, 97.8% présentaient une obésité abdominale. La recherche de syndrome métabolique a pu être réalisée sur 44 patients. Parmi ceux-ci, 34 (soit 77%) présentaient un syndrome métabolique.
Conclusion: D'après notre étude, un pourcentage élevé de patients atteints de lipomatose épidurale pris en charge en rhumatologie présente une obésité abdominale ou des désordres métaboliques tels qu'un diabète, une dyslipidémie ou une hypertension artérielle.

Mots clés : lipomatose épidurale, idiopathique, particularités cliniques, particularités biologiques, obésité, syndrome métabolique

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