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## Case Report & Review of the Literature

# Ischiadic Nerve Lesion Due to Metastasis of a Non-Differentiated Urethra Carcinoma: Case Report and Review of the Literature

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## ABSTRACT

In clinical practice, we encounter mechanical lesions of the ischiadic nerve most frequently with a trauma of the pelvis circle or because of surgical injury in the alloplastic treatment of the hip joint. Other causes for nerve lesions are sporadic or even rare. To such ones also belongs compression of the nerve by metastasis of a urethra carcinoma to the gluteus maximus muscle. A typical manifestation of this nerve injury is a tibio-peroneal paresis with a preponderance in its peroneal component. The diagnostic process can be additionally complicated by a contemporaneous vertebrogenic syndrome with radiculopathy, the more so, when an intervertebral disc protrusion on imaging would be discovered. We present a case of a woman with a two-year history of an undifferentiated urethra carcinoma which has metastasized into the gluteus muscle and has produced a compression of the ischiadic nerve.

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## Introduction

The ischiadic nerve is the longest and most robust nerve of the human body. It stems from the sacral plexus and anatomically is created by ventral branches of spinal nerves L4-S3. It leaves the pelvis in the infrapiriform foramen and descends along the pelvitrochanteric muscles into the space between the tuber ossis ischii and the major trochanter, a region covered by the maximus gluteus muscle. In the extremity, it continues within the posterior part of the thigh, and usually above its entrance into the fossa poplitea it divides into its terminal branches, namely the tibial nerve and the common peroneal nerve. The height of

this bifurcation is very variable and can be anywhere between the sacral plexus and the lower part of the thigh [1, 2]. Due to its length and its close relation to some structures of the pelvis circle, the nerve is often exposed to a primary or secondary injury. In clinical practice, we come most frequently across traumatic mechanisms and iatrogenic interventions.

On the other hand, the rare causes of the ischiadic nerve lesions are metastases in the skeletal muscles, in particular, those from malignancies of the uropoietic system. Clinically the ischiadic nerve lesion presents with tibio-peroneal symptoms, predominantly in the peroneal branch. In differential diagnostics of oncological lesions, it is most important to

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differentiate them from vertebrogenic lesions with radiculopathy of the L5 and S1 roots. In the following case report, we demonstrate a female patient who suffered an ischiadic nerve lesion because of a metastasis of a non-differentiated carcinoma of the urethra into the gluteus maximus muscle.

### Materials and Methods

A 67-year-old woman was admitted to the department of neurology in July 2011 due to increasing pain in the lumbar region and its propagation along the lateral part of the lower extremity down to the calf. The first pain appeared in February 2011, and several days prior to admission the extremity became weak and an acroparesis set in. The history of the patient contained radical cystectomy with an uretero-ileostomy in 2009, followed by adjuvant chemotherapy by gemcitabine and cisplatin, due to a urethra carcinoma stage III, grade III. The last oncological examination evaluated the tumour to be in its remission.

On admission on the base of the neurological examination on June 28th, 2011, there were registered normal findings on the cranial nerves and upper extremities; on the right lower extremity the L2-S2 reflexes were extinct, dorsal flexion of the leg was weak and there was hypesthesia in the dermatoma L5. The patient stumbled and her gait was moreover modified by pain. In the foreground of her vertebrogenic examination there were muscular disbalance, mild disturbance of the vertebral column dynamics in the sagittal plane and the spinal processes of the thoraco-lumbar pass were sensitive when tapped.

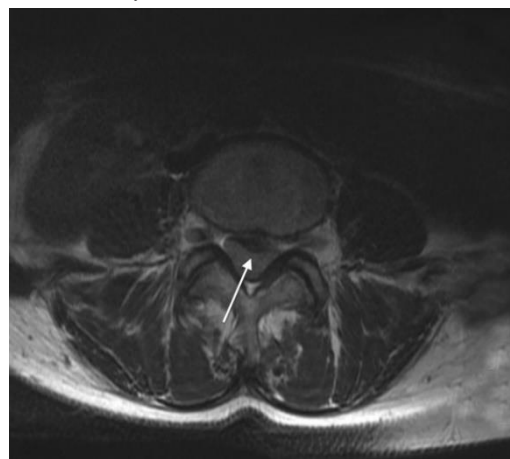
### Results

In our search for the aetiology, Computed tomography confirmed a medial intervertebral disc herniation L4-5 with paramedian propagation to the left and compression of the ventral aspect of the dural sac and the nerve roots (Figure 1). A compression fracture of the T10 vertebra was discovered as an additional finding. In laboratory tests only higher CRP level (12,7 µg/L) and elevated leukocytes (10,2x10/L) were assessed.



**Figure 1:** CT of the lumbar column, sagittal reconstruction. Prominence of the L4 disc into the spinal canal (white arrow).

Our analgesic and myorelaxant infusions, combined with a protective regimen of motor activity, was not successful. Magnetic Resonance examination confirmed the previous CT finding (Figure 2). We have carried out electromyography, which has revealed a severe motor conduction, axonal type, disturbance on the right peroneus nerve; the F wave was absent, while the motor conduction on the left peroneus and the tibial nerve on both sides, including F waves, were normal. The findings in the tibial anterior muscle, the Medius gluteus muscle on the right as well as the fibrillations in the paravertebral muscles of the L4/5 segments supported the presumption of a neurogenic lesion of the root L5 right. We have abandoned our suspicion of a discogenic aetiology after attempting a periradicular corticoid instillation L4-5 from the right, which appeared to be of no clinical effect. Next, a lumbar puncture was carried out and the CSF analysis excluded any inflammatory aetiology. From July 7<sup>th</sup>, 2011, the patient suffered further weakening of the right lower extremity.



**Figure 2:** MR of the lumbar column in T2W image, axial scan. Medial disc herniation L4 with paramedian propagation to the left (arrow).



**Figure 3:** CT of the pelvis, coronal view with contrast. A mass lesion in the right gluteus maximus muscle, size 40x40x30 mm, with peripheral enhancement (arrow).

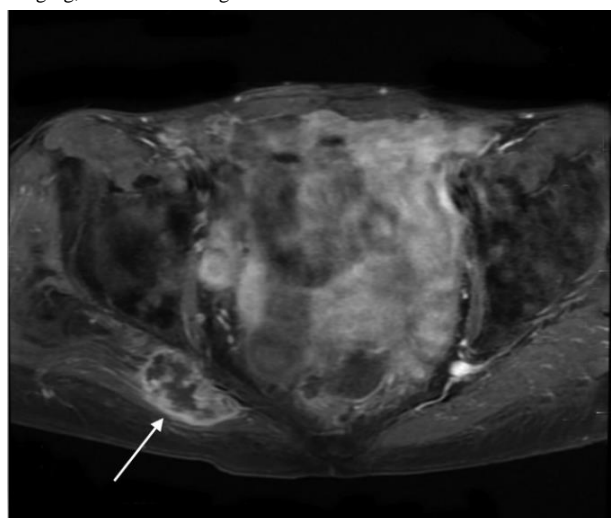
Our inspection showed evidence of a worsening paresis of dorsal flexion, as well as a new weakening of plantar flexion, in fact an image of a tibio-peroneal paralysis of the right lower extremity. Regarding the

oncological history of the patient, despite the declared remission of the tumour, an oncological screening was made. A skeletal scintigraphy and an ultrasound of the abdomen and pelvis excluded any metastatic spreading. After that we performed CT of the abdomen and pelvis including contrast application. The scans revealed an expanding mass in the right gluteus maximus muscle of a 40x40x30 mm diameter, which displayed a peripheral enhancement (Figures 3 & 4).



**Figure 4:** CT image of a tumorous mass in the right gluteus maximus muscle in axial view (arrow).

We attempted to suppress the neuropathic pain by plasters with fentanyl, and by indomethacin and amitriptyline. The patient was discharged from our neurologic department on July 15th, 2011 with a diagnosis, tibioperoneal paresis on the right, due to compression of the ischiadic nerve by a metastasis into the maximus gluteus muscle. A non-differentiated urethra carcinoma in anamnesis. We indicated a surgical examination and an inspection at her oncological department. In August 2011, the patient was admitted to the surgical department and her pelvis was examined by magnetic Resonance with GdTPA. It confirmed a tumorous mass in the right gluteus maximus muscle, sized 51x34x53 mm, pressing onto the ischiadic nerve (Figure 5). Since the last MR imaging, the tumour had grown.



**Figure 5:** T1W MR image of the tumor taken prior to surgery, axial view after contrast. This finding shows the growth of the lesion to a size 51x34x53 mm and a compression of the ischiadic nerve in the right.

On August 18<sup>th</sup>, 2011, a partial resection of the lesion was carried out in respect to the infiltration of the ischiadic nerve by tumorous masses. The histological analyses confirmed a metastasis of the non-differentiated urethra carcinoma. In the next two months, the patient underwent radiotherapy in a total dose of 50 Gy. The patient died in August 2012 and no autopsy was performed.

## Discussion

Injuries with fracture and luxation of pelvic bones or with a posterior luxation of the hip joint belong to the most frequent causes of the ischiadic lesions. Other harmful damage of the nerve arises with its compression by a haematoma, oedema, by femoral components, by an unnatural stretching, intraneural bleeding, by the extrusion of methacrylate or ischaemia at the alloplastic intervention of the hip-joint or with an erroneous application of an intramuscular injection into the gluteus region in persons with special inclination [3]. Besides the traumatic mechanisms and iatrogenic faults, the other causes of ischiadic lesions are sporadic or rare. In idiopathic neuropathies the genesis remains unknown [4]. Less frequent causes of this nerve lesions are the outer compression of the nerve by structural changes in the soft tissues with chronic overload (constrictive syndrome of the piriform muscle). Some lesions of the ischiadic nerve can be a consequence of ischaemia due to diseases of the low extremity vessels (vasculitis, atherosclerosis, thrombosis, vascular reconstructions) or due to vascular malformations (A-V malformations, venous angiomas, capillary haemangiomas) [5-8].

The nervus ischiadicus lesions can be elicited also by primary tumours of neural structures, like schwannoma, neurofibroma, neurofibrosarcoma, or tumours of the neighbouring structures (lipoma, liposarcoma, lymphoma) [9]. Metastases to the skeletal muscles can also be considered, but they are rare [10, 11]. This was confirmed by a retrospective study, covering a period of 1990-2010, which has revealed only 461 such cases [11]. Most metastases to the muscles originate from bronchogenic carcinoma (25,2%), followed by metastases from gastrointestinal malignancies (21%), reproductive organs (9,3%), breast and kidneys (8,2%), some of unknown origin (6,1%), uroepithelial carcinoma (5%), sarcoma (4,8%), thyroid carcinoma (3,7%) and others (2,8%). According to this study, the metastases were mostly localized in the muscles of the thigh (22,1%) and minimally in the muscles of the head, neck, and shoulder (3,5%).

It has been found that some carcinomas metastasize into some locations. Breast carcinoma metastasizes, compared with other tumours, more often into the extraocular muscles; for the spread of bronchogenic carcinoma, typical locations are in the muscles of the upper and lower extremities; for colorectal carcinoma in the abdominal wall. In the gluteal and lower extremity muscles, the prevailing source of metastases is carcinoma of the stomach [11]. Nagao in 2004 reported a hitherto single case of an ischiadic nerve injury due to a gluteus muscle metastasis in a man with a urine bladder adenocarcinoma [10]. Several instances of metastatic ischiadic lesions due to a paraneoplastic lumbosacral plexopathy (LSP) are also reported in the literature [12]. Another paper of 2014 also deals with a possibility of perineural spreading of bladder carcinoma via the hypogastric and splanchnic

nerves over the lumbosacral plexus into the nerves of the lower extremity and spinal nerves [13].

Primary urethra carcinomas affect females more frequently and they are rare. Tumours in the distal part of the urethra are well-differentiated and less malignant as tumours of the proximal part or of the whole of the urethra, which, on the contrary, are of low differentiation. Carcinomas of transitional epithelium (60%), adenocarcinomas (20%), non-differentiated carcinomas (10%), sarcomas (8%) and melanomas (2%) prevail in women. Except for melanoma, the histology of the tumor has no substantial influence on the prognosis. In our patient, the non-differentiated carcinoma affected the whole urethra including its orifice into the bladder, without penetration into the periurethral musculature. Metastases into the regional lymph nodes were not detected. Tumours of the urethra usually metastasize into the regional lymphatic nodes, while the haematogenic dissemination creating distant metastases in the lungs, liver, bones, and brain is rare [14]. Carcinomas in men vary in their frequency of afflicting the segments of the urethra as well as in tumor typology [15]. Advanced primary urethral cancer by high-grade urothelial carcinoma (so called sarcoma-like variant), has also been described as a highly interesting Clinical Case [16].

As a complication of urethral carcinoma, a stricture of urethra can occur, and it can be proved using ultrasonography [17]. As an exceedingly rare entity, a glomus tumor of urethra in a male was described [18]. In veterinary medicine, urethral and low bladder carcinomas from transitional cell, were described in dogs (*Canis lupus f. familiaris*), followed by radiotherapy and in the cats (*Felis silvestris f. catus*) [19, 20]. The urinary bladder and urethra stem from the urogenital sinus and present an anatomical and functional unit. The single metastasis in our patient confirms the possibility of propagation of carcinoma of the urethra not only via the lymphatic and vascular network, but also perineurally, as it is in the case of carcinoma of the bladder [13]. The history with clinical examination, accompanied by electromyography is in most cases sufficient to assess the location and severity of the ischiadic injury. In differential diagnosis, it is necessary to distinguish a radicular lesion (L5, S1) due to discopathy, damage of the sacral plexus in the small pelvis and inflammatory neuropathies (CIDP). In cases with an atypical clinical course, and unclear history, or with simultaneous discopathy, tumor or other illness, the diagnostics is often difficult and require not only imaging methods (US, CT, MRI) but also examination of the cerebrospinal fluid.

Lesions of the ischiadic nerve and its distal branches belong to the most frequent neuropathies of the lower extremity. The aetiology of such ischiadic disturbances is manifold. In clinical practice we come across iatrogenic and traumatic causes. In rare cases, we can include metastases in the skeletal muscles. Next to the unique case of a metastasis of a urine bladder adenocarcinoma in the gluteal muscle, published in 2004, we present an analogous case of ischiadic nerve affliction by a metastasis of a non-differentiated urethra carcinoma [10]. An occurrence, which to our best knowledge, has never been described in literature before. Assigning the aetiology to an ischiadic lesion is important for the choice of treatment and for estimate of the prognosis. One of the typical manifestations of the ischiadic lesion is a neuropathic pain, which we attempted to influence pharmacologically (tricyclic antidepressants, antiepileptics, lidocaine plasters). Surgery is a method of choice in nerve

compressions. In instances of a tumorous infiltration of the nerve, the extent of the intervention is limited, and the treatment needs often to be combined with actinotherapy.

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## Conflicts of Interest

None.

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