

# Palaeopathological Diagnosis after 2500 Years. The Case of Imakhetkherresnet, Sister of Priest Iufaa

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**Abstract:** The aim of palaeopathological studies has been traditionally the determination of a diagnosis of any found pathological change. If based merely on skeletal evidence, most of them proved to be only tentative. Our case of the mature female Imakhetkherresnet, sister of the lector-priest Iufaa, having preserved scraps of soft tissue, enabled a precise diagnosis. Her skeletized mummy was discovered in Iufaa's unmolested tomb dating late 26<sup>th</sup> Dynasty at Abusir (Egypt) by the Czech Institute of Egyptology in 2001. A large smooth-walled cavity moulded by pressure of a relatively hard, globular and lobulated tissue mass was found inside the sacrum, growing in hour-glass shape outside it. By macroscopic and radiographic examination its diagnosis was *suggested*, while by histological analysis with histochemical tests and comparison with a recent case, the origin of the hollow could be "clinically" *determined*. It was caused by a benign tumour, originating in the nerve sheath, called *neurilemmoma* (*schwannoma*, *neurinoma*). This kind of tumour, occurring in the sacrum relatively rarely, was never before described in the palaeopathological literature.

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## Introduction

Palaeopathology starting in 19<sup>th</sup> century as a hobby of medical doctors interested in pathological changes of excavated human or animal skeletons was based solely on the macroscopic examination. Their diagnoses remain questionable. Following the discovery of X-rays by a German Conrad Roentgen, their use for pre- and historical skeletal studies ameliorated diagnostic possibilities, which became mostly tentative. Starting with trials to use microscopy by a Czech physiologist and laryngologist Jan Nepomuk Czermak in mid-19<sup>th</sup> century, the recent progress of histological techniques enabled to reach more exact, in our case “clinically” based diagnoses.

## Archaeological background

In 1994 an expedition of the Czech Institute of Egyptology, Charles University Prague, started investigation of a second large shaft tomb at Abusir near Cairo [1]. It contained an intact burial of the lector-priest lufaa, “overseer of King’s palace at Sais”. His mummy was lifted in 1998 and later studied [2, 3, 4, 5]. The tomb was dated late 26<sup>th</sup> Dynasty (before 525 B.C.)

During the 2001 season, the area east of lufaa’s tomb was investigated and two other smaller shafts R1 and R2 as well as a sanctuary between them were discovered (Figure 1). In the dead end of a 26 m long corridor descending to southwest from the 4 m deep bottom of shaft R2, two burials were found. First one lying in the very end of the corridor in a well preserved double wooden coffin was of a female Immakhetkherresnet, who was without a title. The second one deposited next to it to the east, whose coffin decayed by moisture, belonged to an anonymous male called “God’s father”. An S-shaped steeply descending shaft connected the corridor

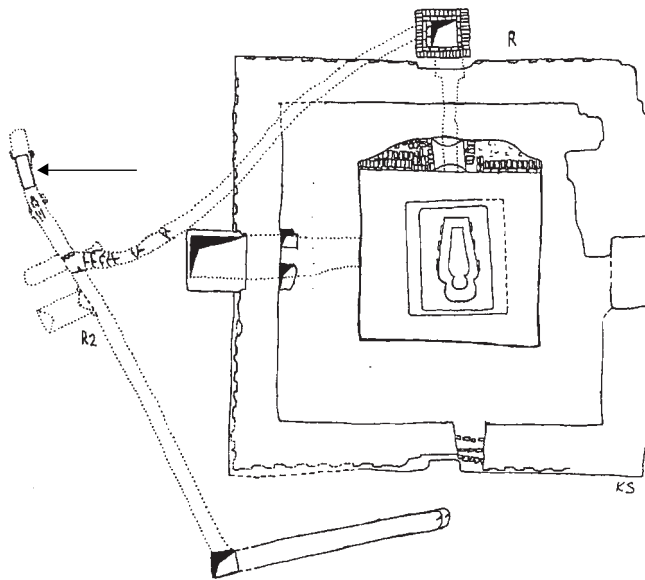


Figure 1 – Archaeological sketch-plan showing the Shaft-tomb of lufaa and the corridor descending from the bottom of Shaft R2. Immakhetkherresnet’s burial is marked with an arrow. (Author of Figure: Květa Smoláriková).

with the bottom of lufaa's Tomb. These burials belonged into the same time range as the Shaft-tomb of lufaa [6].

### Material and Methods

The three mentioned individuals were mummified, as but owing to the humidity in the burial chamber and corridors, their flesh and wrappings mostly disintegrated. On the other hand, their almost complete skeletons have been well preserved.

According to several similar metric and descriptive features as well as occurrence of congenital anomalies they were found biologically related. Imakhetkherresnet was suggested to have been a sister of lufaa and this determination was proved paleographically by the same name of their mother [6]. The anonymous male seems to have been most probably their father [7].

The skeletal remains of Imakhetkherresnet are of an unequivocal female with gracile body build but without any signs of osteoporosis. Her muscular relief was relatively well developed. Medium deep sulci praeauriculares reveal her child bearing history. Progressed fusion of cranial sutures ( $C_2$ ,  $S_1$ ,  $L_{1-2}$  and pterion), the facies symphysialis of stage 8 [8], the smooth and slightly concave facies auriculares with a slight rim and the medium degree of osteophytosis of the spine and of degenerative arthritis of big joints suggest her age at death in the range of 35–45 years. Among her several pathological changes [9] the most interesting was a hollowed sacrum, It was investigated by macroscopical examination, standard X-rays, computed tomography and histology including immunohistochemical tests and comparison with a recent case [10, 11].

### Results of macroscopy

The sacrum of Imakhetkherresnet consists of six segments, including the sacralized fifth lumbar vertebra ( $L_5-S_5$ ) (Figures 2 and 3).

On the posterior side of its second segment (which in this case is  $S_1$ ), to the right between the crista sacralis media and the right foramen sacrale posterior, a large obliquely oval orifice is apparent (maximum diameter 25 mm). Its edge is regularly and smoothly rounded except in the right lateral lower section where it fused with the second right posterior foramen sacrale, destructing the upper half of its edge. This orifice leads into a large smoothly rounded cavity no.1 inside the bone which was hollowed by pressure of some relatively hard growing tissue. It penetrated from inside of the sacrum outside in a hour-glass manner (Figure 3).

A small and irregular secondary opening ( $10 \times 5$  mm) can be found in the same level left of the crista sacralis media. It resulted from breaking the compact bone thinned by pressure coming from another smaller cavity no. 2 inside the sacrum.

The anterior side of the third sacral segment (which in this case is  $S_2$ ) bulges anteriorly (about 2 mm) as the result of pressure coming from a biggest cavity no. 3 inside the bone. Its wall was also thinned to such an extent that it was secondarily perforated by an irregularly tipped opening ( $10 \times 12$  mm) (Figure 2).

The large completely smooth roundish and flat cavity, situated obliquely from right above to left down as traced by sounding inside the second and third segments, communicated largely with the canalis sacralis.

### Results of radiology

The spatial idea about the extent and form of the cavity inside the sacrum can be obtained by combination of the postero-anterior and lateral radiographs. It extends obliquely from the oval cavity no. 1 in the right medial quarter of the second segment (fused with the second right posterior foramen sacrale), across the mid-line to the left, merging with the biggest oval cavity no. 3 in the left medial quarter of the third segment (fused with the third left posterior foramen sacrale, Figure 4).

The striking length of the oblique excavation inside the sacrum is well apparent on the lateral projection (Figure 5), being more than twice longer (about 50 mm)



Figure 2 – Sacrum of Imakhetkherresnet in anterior view showing its composition of six segments and the perforation in the bulging anterior wall of the body of the third segment. (Author of Figure: Eugen Strouhal).



Figure 3 – Sacrum of Imakhetkherresnet in posterior view showing its composition of six segments, a large orifice right in the posterior wall of the body and a secondary perforation left in body of the second segment. (Author of Figure: Eugen Strouhal).

than its postero-anterior dimension (about 22 mm) and the transversal one (about 28 mm). In the left medial quarter of the second segment two small smoothly delineated hollows (nos. 2a and b) are apparent, the lower one appearing as oval, the upper one as semicircular. Presence of at least four well rounded lobes can be deduced from the lateral projection (Figure 5).

By computed tomography performed in the three basic directions planes the described cavities show inter-connections (Figures 6–8), revealing thus a hollow united with lobules.

Combining the results of macroscopy and radiology we were able to suggest the preliminary diagnosis of a neurilemmoma.

### Results of histology

Two tiny remnants of soft tissue have been preserved at the upper and lower edge of the oval orifice on right medial quarter of the posterior aspect of the second sacral segment. They were attempted for microscopical investigation.



Figure 4 – Postero-anterior radiogram of the sacrum disclosing the oval orifice of cavity in the right half of the second segment, two small lobes (nos. 2a and b) in its left half as well as the large cavity in the left half of the second segment continuing through the medial edge of the right half of the third segment. (Authors of Figure: Salima Ikram and Roxie Walker).



Figure 5 – Lateral radiogram of the sacrum revealing the large extent and the lobulated character of the merging cavities moulded by the tumour. (Authors of Figure: Salima Ikram and Roxie Walker).

The material was fixed in formalin (6%), dehydrated and sections for light microscopy were embedded in paraffin wax. For transmission electron microscopy embedding in epoxy medium Epon 812 was used.

In order to visualize details leading to diagnosis, we combined several blue toluidine stained semi-thin sections of Imakhetkherresnet's sample tissue with the red haematoxylin-eosin stained sections of a recent case of a benign tumour neurilemmoma (courtesy of the Department of pathological anatomy of the Medical faculty Pilsen). Imakhetkherresnet's tissue samples proved to contain features of a neurilemmoma. This is an encapsulated neoplasm possessing two pathognomic

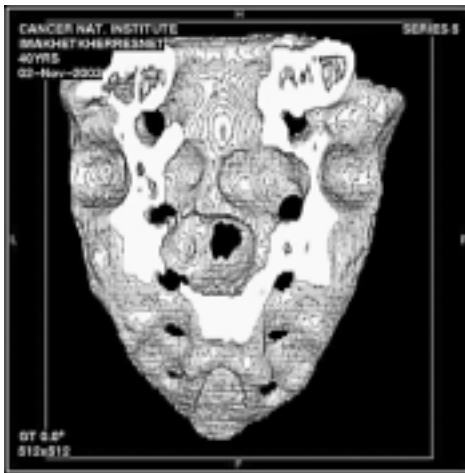


Figure 6 – CT section from middle of the postero-anterior series showing merging of cavities nos. 2a, 2b and 3. (Author of Figure: Fady Khattar).



Figure 7 – CT section from middle of the lateral series with united cavity no. 2, merging with cavity no. 3. (Author of Figure: Fady Khattar).



Figure 8 – CT section of the middle of the axial series with merged cavities nos. 3 (right) and 1 (left). (Author of Figure: Fady Khattar).

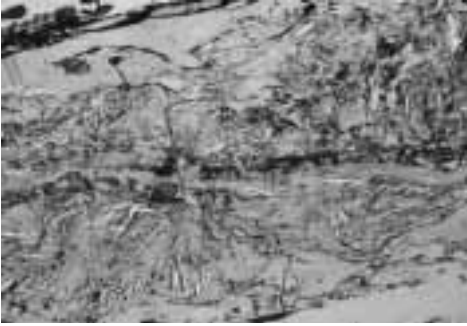


Figure 9 – Thin section stained with blue toluidin of the Imakhetkherresnet's tumour. Structure A: Verocay bodies with palisade and whorl-like arranged spindle-shaped cells (arrow-head) within a collagenous stroma.  $\times 200$ .

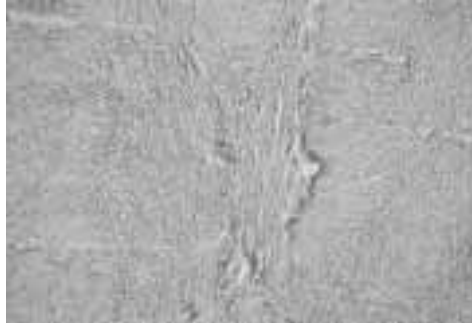


Figure 10 – Thin section stained by haematoxylin-eosin of a recent case of neurilemmoma. Structure A: Verocay bodies with spindle-shaped cells (arrow-head) within a collagenous stroma.  $\times 100$ . (Author of Figure: Alena Němečková).

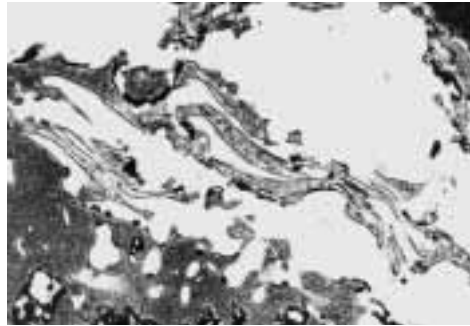


Figure 11 – Transmission electron microscopy (TEM) of the Imakhetkherresnet's tumor revealing in detail the disintegrated spindle-shaped cells.  $\times 6000$ . (Author of Figure: Alena Němečková).

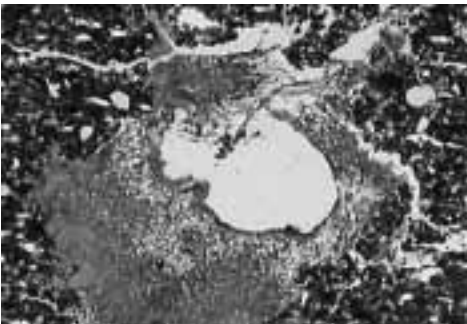


Figure 12 – Thin section stained with blue toluidin of the Imakhetkherresnet's tumor. Structure B: cells arranged in net-works, blood vessel (arrow-head), areas of hyalinisation.  $\times 200$ . (Author of Figure: Alena Němečková).



Figure 13 – Thin section stained by haematoxylin-eosin of a recent case of neurilemmoma. Structure B: a blood vessel with hyalin walls (arrow-head).  $\times 100$ . (Author of Figure: Alena Němečková).



tissue components labelled structure A (Antoni A) and structure B (Antoni B) which combine in variable proportions.

Structure A tissue of Imakhetkherresnet is mainly cellular and consists of bundles of spindle-shaped Schwann cells arranged in collagenous stroma and showing nuclear palisading, sometimes whorl-like. Parallel arrays of these palisades are known as Verocay bodies. They are set in a variably collagenous stroma (Figure 9).

The section of a recent case of neurilemmoma shows structure A tissue with closely packed spindle cells (Figure 10).

In Imakhetkherresnet's very strongly magnified transmission electron micrograph ultrastructural features are apparent. The disintegrating diagnostic spindle – shaped tumour cells lined by cell membranes are non-nucleated, but possess granules as the most characteristic component of these cells (Figure 11).

Structure B area of Imakhetkherresnet are also composed of spindle-shaped Schwann cells, but arranged in net-works, whose nuclei appear disintegrated. The myxoid or microcystic matrix is accompanied by blood vessels with thick hyaline walls and areas of hyalinisation (Figure 12).

The same structure B of a recent case consists also of myxomatous tissue with microcystic areas and dispersed Schwann cells. Blood vessels with hyaline walls are a characteristic finding (Figure 13).

### Results of immunohistochemistry

The neurilemmoma of the conventional type uses to be positive for S-100 protein. In our case it was negative.

Staining for glial fibrillary acid protein GFAP, variably positive, was found positive in the tissue of Imakhetkherresnet (Figure 14) as well in the tissue of the recent case (Figure 15).

The epithelial membrane antigen EMA, variably positive, proved to be positive in both tissues (Figures 16 and 17).

### Discussion

Two kinds of benign tumours derived from Schwann cells of the nerve myelin sheath are being currently discerned. First is *neurilemmoma* (*schwannoma*, *neurinoma*), a solitary, nodular hamartoma, mostly located on retroperitoneal spinal nerves. In distinction to them, a *neurofibroma* can be located on any peripheral nerve. If appearing solitary, also neurofibroma is usually benign. In multiple occurrences, they are part of the syndrome of *neurofibromatosis*. Malignant degeneration of any of them causes *neurofibrosarcoma* (*malignant schwannoma*) [12]. Osseous localisations of solitary lesions of the two above-mentioned benign tumours are known in long bones, jaws, and sacrum (neurofibroma also intradurally in the spinal canal).

Up to date palaeopathological literature reported only two probable cases of neurofibromatosis, first one in lumbar vertebral bodies of an adult Anglo-Saxon [13]), second one in skull, pelvis and spine of an early 19<sup>th</sup> century British male [14]. On the other hand, the authors of the Cambridge Encyclopaedia



of Human Paleopathology stated, that they “were unable to identify other reports of either neurofibromas or neurofibrosarcomas”, not mentioning any reports on neurilemmomas, whose absence in the record can be presumed [12].

In pathological anatomical studies, neurilemmoma is described as a globular, well delimited, roundish and rather hard tumour (thus able to produce intraosseous cavities by pressure). Under cut, it is grey, sometimes dotted with cystoid cavities [15]. An older but detailed description suits well to our find: “Macroscopically neurinoma appears as well delimited tumorous knot of globular or egg shape, nut to apple size, rarely of larger dimensions. Its surface is tuberous or lobulated. In some localisations, especially in the spinal channel, it can be of an hour-glass shape... This peculiar shape originates by growth of part of the tumorous matter through foramen intervertebrale, while the other part remains deposited intradurally” [16]. The same occurred in our case. (However, the same shape can also be attained by a neurofibroma or a ganglioneuroma).

Progressive degenerative changes of neurilemmoma, initially focal, are common. They consist of hyalinization, haemorrhage, cystic changes and calcification called *ancient schwannoma* [17].

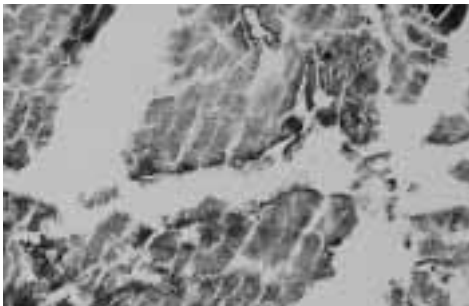


Figure 14 – Positive results of the GFAP test in the Imakhetkherresnet's tumor.  
(Author of Figure: Alena Němečková).

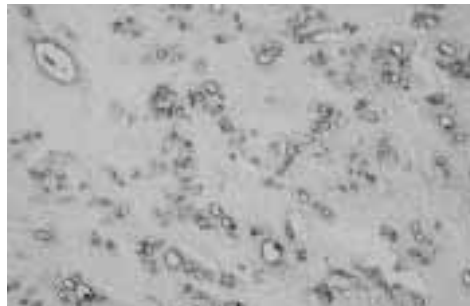


Figure 15 – Comparison of positive results of the GFAP test in a recent case of neurilemmoma.  
(Author of Figure: Alena Němečková).



Figure 16 – Positive results of the EMA test in the Imakhetkherresnet's tumor.  
(Author of Figure: Alena Němečková).



Figure 17 – Comparison of positive results of the EMA test. (Author of Figure: Alena Němečková).

Neurilemmoma can occur in the mandible, vertebrae and sacral bodies [18]. Among all tumours which can be found in the spinal channel neurilemmomas account for 25%, while meningiomas for 30%, gliomas for 15–20% and tumorous metastases for 10–25%. They mostly afflict the thoracic area, less and evenly the cervical and lumbar sections, while the sacral part is involved only rarely [19].

Among modern case reports sacral neurilemmomas are not very often reported and series of collected cases are not numerous. Thus 13 cases eroding the anterior aspect of the sacrum [20], 21 cases of giant intrasacral schwannoma (similar in size to our case) [21], 12 cases with intraforaminal neurinomas in the lumbosacral space [22], 23 cases together with a case of giant schwannoma causing lumbosacral radiculopathy [23], 30 cases together with 6 new giant cases [24] and 25 reported cases plus 3 newly found ones [25] were reviewed. Additional reports on about a dozen of further single cases can be also found in the literature.

Age range of the patients fall mostly between 30 and 50 years. No clear-cut sexual predilection has been observed [12, 20, 23].

Symptoms like low-back pain, dysesthesiae and weakness of legs, hypo- and paresthesias, constipation, and incontinence, predating clinical diagnosis by an average of 5.2 years, occur often [20, 23, 24]. A 57-year-old woman with a giant schwannoma of the cauda equinea had a full 10-year history of low back pain [26]. In other cases minimal symptomatology in relation to radiographic findings was observed [21, 25]. In spite of histologically benign tumour, it can be sometimes neurologically devastating [20]. Recorded reports on its malignant change are, however, very rare [17].

## Conclusion

The described large smoothly walled cavity was according to the microscopical proof hollowed out by a neoplastic process originating in a Schwann cell of the myelin sheath of a nerve (in this case belonging to the plexus sacralis), called neurilemmoma or schwannoma (in older literature also neurinoma). Its intraosseous location can produce a lobulated cavity by pressure.

Imakhetkherresnet's tumour surely grew for several years until it reached its big size with a lobulated character and penetrated into the foramina sacralia posteriora. We may suppose that it could have produced gradually a painful radicular syndrome by pressure on the sacral plexus and/or by obstruction of the foramina sacralia posteriora. It was for sure not the direct cause of Imakhetkherresnet's death, except indirectly.

Imakhetkherresnet's tumour found the in rarely occurring localisation inside the sacrum is the first one ever described in the palaeopathological literature.

Our description of a find of an intrasacral neurilemmoma which yielded a rare opportunity to be analysed histologically, can be in the same time considered a first quasi "clinical" and sound paleopathological diagnosis.

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