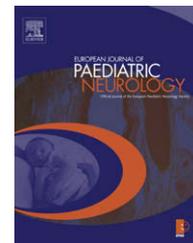




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## Special contribution

# Neural tube defect in a 4000-year-old Egyptian infant mummy: A case of meningocele from the museum of anthropology and ethnography of Turin (Italy)

Rosa Boano<sup>a,b,\*</sup>, Ezio Fulcheri<sup>c</sup>, Maria Cristina Martina<sup>d</sup>, Andrea Ferraris<sup>d</sup>, Renato Grilletto<sup>e</sup>, Rossana Cremonesi<sup>f</sup>, Federico Cesarani<sup>g</sup>, Giovanni Gandini<sup>d</sup>, Emma Rabino Massa<sup>a,e</sup>

<sup>a</sup>Department of Animal and Human Biology, University of Turin, Turin, Italy

<sup>b</sup>UMR 6578, Faculté de Médecine, Université de la Méditerranée, Marseille, France

<sup>c</sup>Section of Pathological Anatomy, Di.C.M.I., University of Genoa, Genoa, Italy

<sup>d</sup>Institute of Diagnostic and Interventional Radiology, San Giovanni Battista “Molinette” Hospital, University of Turin, Turin, Italy

<sup>e</sup>Museum of Anthropology and Ethnography of the University of Turin, Turin, Italy

<sup>f</sup>Complex Structure Neuro 3, San Giovanni Battista “Molinette” Hospital, Turin, Italy

<sup>g</sup>Complex Operational Structure for Radiological Diagnosis, Asti Hospital, ASL 19, Asti, Italy

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## ABSTRACT

This paper reports a paleopathological study of a severe neural tube defect in an ancient mummy, more specifically, a meningocele in an Egyptian infant from the XI dynasty (2100–1955 B.C.). This is one of the most ancient cases of meningocele in mummified human remains described in paleopathological literature.

Prehistoric and early historic examples of severe congenital defects of the vertebral column and neural tube are rare, because of the precarious preservation conditions of ancient human remains. Further, since the majority are only the skeletal remains, paleopathological and paleoepidemiological analysis based on the observation of bones is even more difficult. Hence, it is not easy to investigate this disease in the past in all its complexities and true diffusion.

The case presented here is peculiar, since it concerns a mummy with almost all soft tissues preserved, thus allowing us to describe the defect in an infant.

Only targeted, minimally invasive examinations were performed. An anthropological investigation with helical CT scan and histological analysis was used to diagnose the defect and identify post-mortem transformation processes.

The analyses confirmed the diagnosis of meningocele in an approximately six-month-old infant.

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\* Corresponding author. Department of Animal and Human Biology, Laboratory of Physical Anthropology, Via Accademia Albertina 13, 10123 Torino, Italy. Tel.: +39 0116704549; fax +39 0112364549.

E-mail address: [rosa.boano@unito.it](mailto:rosa.boano@unito.it) (R. Boano).

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## 1. Introduction

Neural tube defects comprise a group of congenital malformations that include spina bifida, a common and serious birth anomaly. The range of expression varies from major to minor: spina bifida cystica is the major form (meningocele and myelomeningocele) and spina bifida occulta is the minor form.<sup>1</sup> Both genetic and environmental factors have been involved in the etiology of the disease.

Many works on modern populations have been published on this issue, each time highlighting different important aspects, such as its incidence in different geographic areas, prevalence, investigation methods, classification and nomenclature, relations with various syndromes, relations with the environment, diet, and secular trends.<sup>2–6</sup> Barnes<sup>7</sup> has provided an excellent review of the developmental defects of the axial skeleton and the factors that influence their expression. Moreover, he has also provided us with a useful anthropological and paleopathological review.

There is a strong familial tendency to the development of neural tube defects, although genetic predisposition appears to require some exogenous factors for full defect expression. The strongest evidence points to maternal nutritional deficits, particularly of zinc, folic acid and selenium, which improves zinc absorption. All three nutrients are needed for genetic control and cell growth during morphogenesis. The incidence of these defects varies widely around the world and with time. For example, the highest incidences of spina bifida and anencephaly occur in northwestern Europeans as well as in some isolated Southern areas, such as in Egypt, where, zinc deficiency is endemic.<sup>7</sup>

The frequencies and geographical distributions of congenital malformations, like those of other diseases, have probably changed with time, partly due to micro-evolutionary factors, since diseases are often the consequence of environmental – artificial and natural – selection. Knowledge of past incidence and forms of congenital diseases provides insight into a population's normal and pathological genetic load, as well as a certain ability to predict current behavior and development of these diseases.<sup>8</sup>

Anthropology and paleopathology are valuable assessment tools for reconstructing the health status in past populations, but it is often difficult to obtain suitable data.

In the study of the spina bifida, the problem for paleopathologists is deciding what constitutes an abnormal condition in sacra, as many sacra have some evidences of incomplete development of the neural arch.<sup>9,10</sup>

Moreover, the interpretation of this type of congenital malformation in ancient human remains is limited because of precarious preservation conditions. Indeed, individuals with major neural tube defects die very early in infancy; immature biological remains are very fragile and are unlikely to be preserved. Moreover, skeletal defects are often undetected at birth, because of the incomplete ossification of immature bones. Consequently, paleopathological and paleoepidemiological analysis based on the observation of bones is often more difficult, frequently the incidence of spina bifida cystica is underestimated in ancient skeletal series.

The preservation of soft tissues, organs, and cells suitable for analyses is a major factor in the diagnosis. Significant advantages come from the study of mummified remains, since scientific analyses can provide complete documentation of the body and more exhaustive information about the expression of the defect.

Several cases of spina bifida with varying degrees of severity are often quoted in paleopathological literature, however they are most likely to be less severe cases of spina bifida occulta. This condition has been recognized in prehistoric and historic skeletal and mummy collections throughout the world and has been described by many authors.<sup>7,9–23</sup> References dealing with this defect are so common that a review would be beyond the aim of this paper. Conversely, very few cases of spina bifida cystica have been reported in ancient remains, even though the frequency of the pathology is high in some endogamous groups.<sup>7,9</sup>

With regard to ancient Egyptians, Barclay-Smith<sup>11</sup> described multiple anomalies in the vertebral column of a young female skeleton from the excavation of Sakkara dated 600–500 B.C. Other authors have described cases of spina bifida occulta.<sup>24–27</sup> However, very few studies have been published on mummies.<sup>28</sup>

This paper describes a case of meningocele in an Egyptian infant mummy from XI dynasty (2100–1955 B.C.). To date, it is one of the most ancient cases reported in paleopathological literature. Analyses carried out on the mummy provided data concerning the likely cause of death and post-mortem transformation processes.

## 2. Material

The mummy is from the XI dynasty (2100–1955 B.C.) and comes from the necropolis of Assiut in Middle Egypt. The specimen was dated based on complete and reliable excavation evidence. The body was discovered by the Italian Archeological Mission at the beginning of the 19th century during Assiut 4th Archeological Campaign (1911–1913) led by Ernesto Schiaparelli, Egyptologist of the Egyptian Museum of Turin (Italy), with the collaboration of Giovanni Marro, anthropologist of the Museum of Anthropology and Ethnography of Turin. Since its discovery, the mummy has been kept in the Museum of Anthropology and Ethnography.

The specimen is very interesting, because it is a complete natural mummy (Fig. 1); it was not discovered within a selected population sample or caste; on the contrary, it was part of a randomized sample.

The mummy was found in an oval basket inside a grave dug into the mountain; the small corpse lay in a prone position, very unusual for its historical context, with the left arm extended along the body and the right one folded under the corpse near the pubic region; the head rested on the left cheek. The body had been huddled almost into a ball and heavily wrapped in linen bandages.<sup>26,29</sup>

The corpse is completely mummified except the head, which is almost totally free of soft tissues and is separated from the body because of poor preservation conditions. The



**Fig. 1 – Natural mummy from the XI dynasty (2100–1955 B.C.), necropolis of Assiut, Middle Egypt. The body (without head) is in prone position.**

external conditions of the body are quite good; a massive amount of fatty tissues is evident on the back and on the arms.

Estimated age-at-death is about six months on the basis of skull sutures (fontanellae), the morphology and development of deciduous teeth, and the development of the three parts of the temporal bones (pars petrosa, pars squama, tympanic ring).

There are no macroscopic signs of cultural treatment of the body (embalming).

In the lumbo-sacral region (Fig. 2), there is a well-defined, longitudinal, oval, almost kidney-shaped protrusion (55 mm long, 30 mm wide). The prone position of the body allows to directly inspect the lesion. There is a very thin tissue on both sides of the lesion, which probably completely covered it at the time of death, forming a kind of dome (cyst formation) that is now empty and partly destroyed. Accidental rupture due to past transport shows the extreme thinness of the wall, which is almost transparent and strongly curled, as if relaxed. In the central part of the lesion, the tissue is lined with fine depressions, all converging into a central crater-like area. Macroscopic observations reveal that the tissue of the dome are anatomically joined together to the side of the oval lesion. There is no unusual pigmentation or tufts of hair near the protruding skin-covered sac. There is no macroscopic evidence of nerves that could be referred to the cauda equina.

The ventral part of the body cannot be inspected since it sticks to hard sediment that forms a single solid block with the corpse.



**Fig. 2 – Detail of the lumbo-sacral region. A well-defined, longitudinal, oval, almost kidney-shaped protrusion is clearly visible. There is thin tissue on both sides of the lesion.**

The first scientific paper on this mummy was published in 1952 by G. Marro based on a macroscopic morphological analysis. Prof. Marro described the lesion in a sacral position and the resulting diagnosis was “rectal prolapse” in a newborn.<sup>29</sup>

A subsequent scientific review of the specimen proposed the diagnosis of “meningocele” on the basis of histological analyses.<sup>26</sup> The presence of a thick layer of sand adhering to the body has hindered more exhaustive radiological examinations of the lumbo-sacral region. However, recent CT and histological analyses have confirmed the diagnosis of meningocele in this approximately six-month-old infant.

### 3. Methods

A new examination was carried out to acquire complete documentation of the body based on a helical CT scan, histological analysis and a new anthropological investigation.

#### 3.1. CT scan examination

The study was carried out to evaluate the general conditions of the body under the superficial tissues, the skeleton, with particular attention to the morphology of the anterior and posterior arches of the vertebrae, identify any possible evidence of inner organs, inspect the ventral part of the body adhering to the hard sediment, and acquire information on the age-at-death, as determined by long bones measurement.

A helical CT scan was performed on the body (without the head). A multidetector CT unit (Lightspeed Qx/i; General Electric Medical Systems, Milwaukee, USA) was used with the following scan parameters: 120 kV, 200 mA, scan time 0.8 s, slice thickness 2.5 mm, reconstruction interval 1.25 mm, high speed modality, bone and standard algorithms. Post-processing, with evaluation of all the axial images and multiplanar and 3D reconstructions, was carried out at two workstations: Precision 530 with 2.5 Vitrea software (Vital Images, Fairfield, IA) and Sun Workstation (Advantage Windows 4.2, GE medical systems, Milwaukee, USA).

### 3.2. Histological examination

Histological examinations are useful to assess post-mortem transformation processes, types of mummification and embalming techniques, tissue preservation, and general characteristics. They also allow in specific to assess tissue degradation and detect infesting agents, such as fungi and bacteria, and inorganic or organic pollutants.<sup>30-33</sup> The histological analysis was performed on the skin of the left arm and on the thin tissue of the dome still present, at the side of the oval lesion. In the first case, we wanted to determine the preservation conditions of the tissues and the type of mummification. In the second case, we wanted to examine the cytological characteristics of the tissues of the dome associated with the lesion. No samples were taken of the central part of the lesion, for preservation reasons.

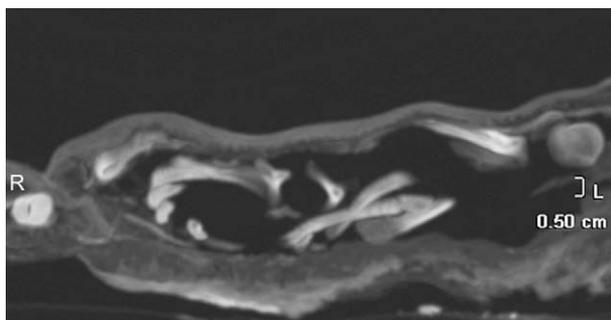
Small pieces (8-10 mm) of mummified tissue were sampled near extant fractures or lacerations without damaging the remains. The tissues were hydrated according to Sandison's method<sup>34</sup> and subsequent modifications<sup>35,36</sup> and then treated with hematoxylin-eosin, trichromic Masson's, Mallory's and Van Gieson's, and PAS staining.<sup>37</sup> The preparations were examined by conventional transmission light microscopy and polarized light microscopy.

## 4. Results

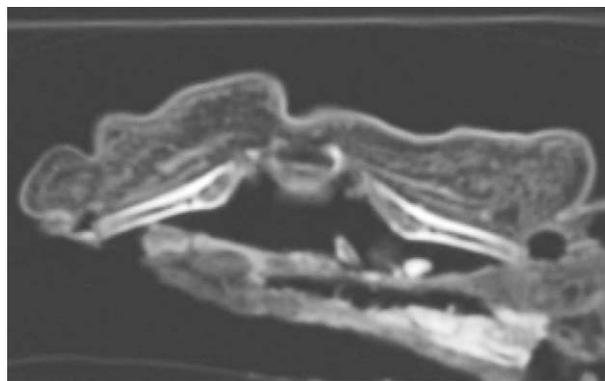
### 4.1. CT scan examination

From the evaluation of axial images, multiplanar and 3D reconstructions, poor general skeletal conditions were observed. Most of the bones, including some dorsal vertebrae, looked displaced. Post-mortem fractures of some ribs and of the right clavicle could also be observed. The thoracic and abdominal cavities appeared partially occupied by the displaced bones (Fig. 3). This is related to the fragility of the body, as seen in other investigated mummies of children.

In the axial images of the lumbo-sacral region, the skeletal disease involvement was recognized. In particular, a wide opening of the posterior arch could be observed and measured (6 mm), wider than those normally present in infant skeletons. The CT aspect is typical of an ossification defect of the sacral vertebrae (Fig. 4). The actual malformation extension could not be assessed because of displacement of part of the vertebrae.



**Fig. 3 – Axial CT scan of the chest. The thoracic cavity is partially occupied by displaced ribs and vertebrae. The inner organs – collapsed, and dehydrated – are not visible.**

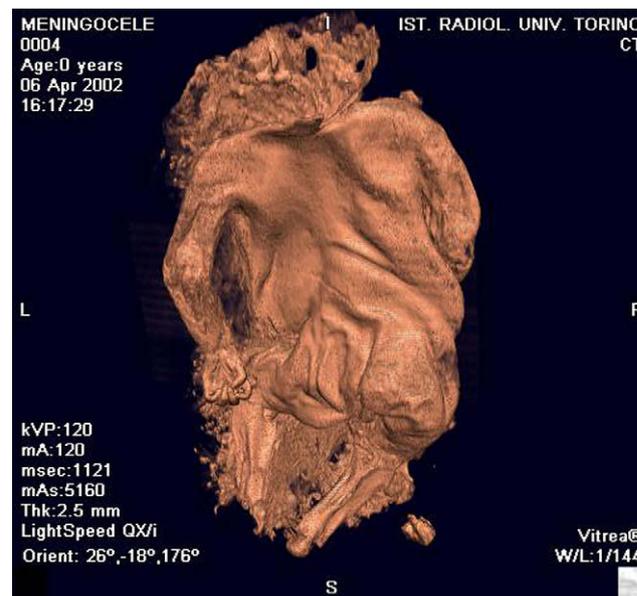


**Fig. 4 – Axial CT scan of the lumbo-sacral region. A wide opening (6 mm) in the posterior arch of the first sacral vertebra is visible, confirming skeletal involvement of the disease.**

In line with a natural mummification process of the body, no embalming materials were found. The inner organs were not visible, most likely for their small volume at the moment of death and their subsequent volume loss due to dehydration.

The presence of sand and debris did not affect the evaluation, nor the reconstruction of the skeleton and of the most superficial parts of the body (Fig. 5).

A virtual removal of the materials (sand and debris) adherent to the ventral part of the body was attempted by post-processing procedures used in previous studies by our group for the virtual removal of bandages in completely wrapped mummies.<sup>38,39</sup> However, the insufficient difference in density between the soft, dehydrated tissues and the debris,



**Fig. 5 – 3D volume rendering reconstruction of full body spiral CT data. The details of the dorsal surface are accurately shown. The skin defect in the site of the meningocele can be clearly identified.**

the strong adhesion between the two structures, and the likely severe degradation of soft tissues, did not allow any sufficiently accurate evaluation of the ventral surface.

Long bones were measured to acquire further information on the age-at-death. The femur length (84.9 mm) (Fig. 6) suggested an age of approximately six months, in agreement with the development of skull bones and deciduous teeth.

#### 4.2. Histological examination

Post-mortem transformation processes were analyzed by histological examination of the skin of the arm. All skin layers are perfect; the epidermis and dermis are very well preserved throughout their thickness. The exfoliating corneal layer, a well close-knit spinous layer, and the melanocyte-rich basal layer are all clearly evident in the epidermis (Fig. 7); the derma is firm. The adipose tissue is very well preserved in the hypodermis.

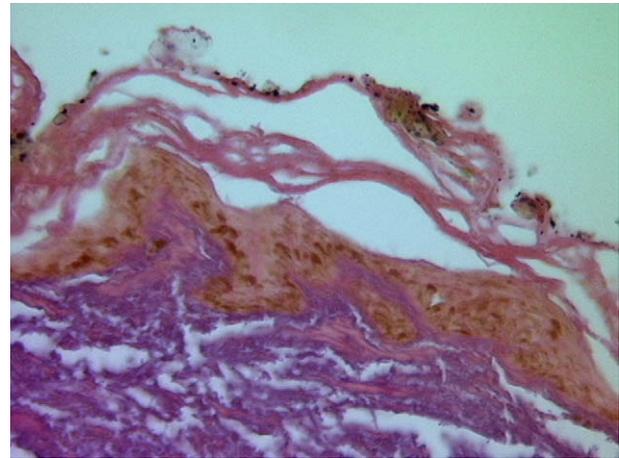
Histological analysis of the tissue of the dome covering the lesion has identified skin tissue characterized by the total absence of epidermis (epidermolysis). The tissue sample of the dome taken from the base side of the lesion features subcutaneous tissue with bundles of thin collagen fibres that are easily separated. A dense membrane attributable to the dural sac can be observed (Fig. 8). The tissue sample of the dome taken from the upper side of the lesion consists of a thin and dense membrane attributable to the dural sac and identical to the previous one. A thin vascular network was observed here (Fig. 9). Epithelial, muscular, as well as glandular structures could not be identified, nor were any fatty or nervous tissues detected.

## 5. Discussion

The role of CT in the non-invasive evaluation of the inner structures of the mummified bodies was confirmed also in



**Fig. 6** – Electronic measurement of the femur was performed. According to these measurements and the evaluation of the mandible and skull bones, the estimated age-at-death is 6 months.



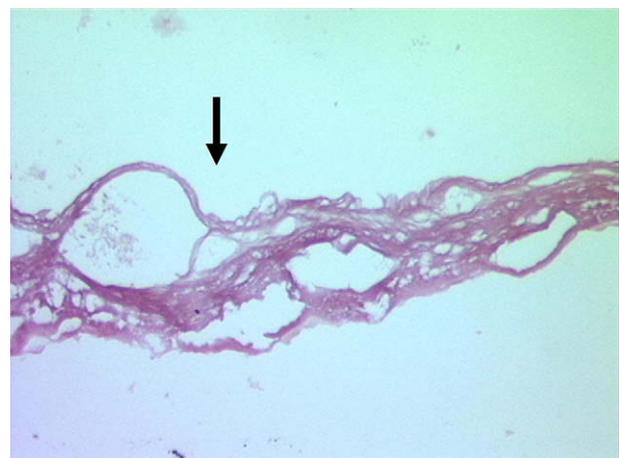
**Fig. 7** – Skin specimen of the left arm. The exfoliating corneal layer, a well close-knit spinous layer, and the melanocyte-rich basal layer are all clearly evident in the epidermis. The derma is firm. Hematoxylin-eosin, 10 $\times$ .

this study. Important information on the skeletal conditions and bone malformation were achieved from the evaluation of axial scans and multiplanar reconstructions.

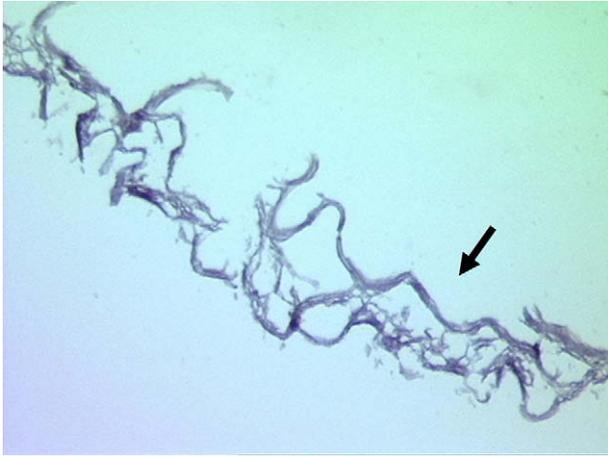
Detailed information on the appearance and position of the bones could not be gathered from conventional X-ray images performed in the past due to the superimposition of sediments. In particular, it had been impossible to evaluate the posterior arch of the vertebrae and measure the opening.

The electronic measurement of the long bones contributed to determining the age-at-death.

3D reconstructions were highly iconographic and rich in details, but CT evaluation of superficial tissues did not allow to obtain any additional information from direct inspection alone.



**Fig. 8** – The tissue sample of the dome taken from the base side of the lesion: subcutaneous tissue with bundles of thin collagen fibres. A dense membrane referred to the dural sac can be observed (arrow). Hematoxylin-eosin, 25 $\times$ .



**Fig. 9** – The tissue sample of the dome taken from the upper side of the lesion: dural sac. The tissue features a thin and dense membrane that can be referred to the dural sac (arrow) identical to the one shown in Fig. 8. On the opposite side, a fine vascular mesh is evident. No epithelial structures are detectable. Hematoxylin–eosin, 25×.

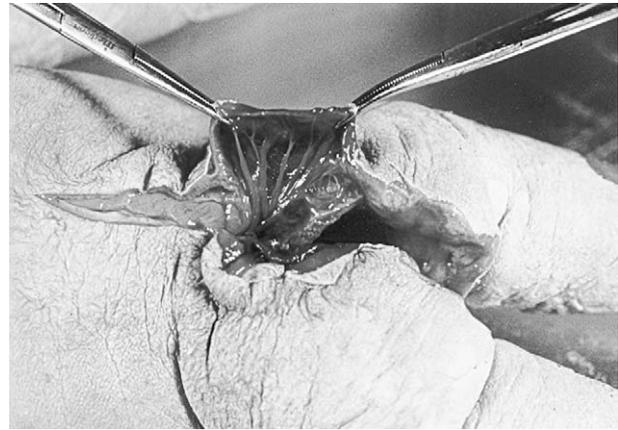
Macroscopic observations reveal that the tissue of the dome are anatomically joined together to the side of the oval lesion. There is no unusual pigmentation or tufts of hair near the protruding skin-covered sac. Nor were any nerves to be referred to cauda equina detected. All these features strongly confirm a meningocele diagnosis. This case was compared with a myelomeningocele case diagnosed in a modern subject during post-mortem examination (Fig. 10). Macroscopic evidence is totally different, especially for the absence of the nervous system in the paleopathological case.

The histological analysis of the arm skin revealed an integral epidermal layer. No cases of bacterial and fungal contaminations were observed. Rapid and natural mummification in the hot sterile sand of the desert has contributed to excellent preservation.

The histological analysis of the tissue of the dome covering the lesion revealed epidermolysis. The absence or presence of epidermolysis depends on the amount of water in the tissues. The dehydrated skin of an older individual is less likely to undergo epidermolysis, whereas massive epidermolysis is likely to take place quite early in the highly hydrated skin of an infant. Even the thickness of the cell layers of flat epithelia and their keratinization (which varies depending on the body surface of the anatomical region) have a strong impact on epidermolysis onset. Hence, epidermolysis depends on many variables that differ from individual to individual.

In the paleopathological case, the skin of the dome would have undergone epidermolysis even under optimal preservation conditions, because it was very thin and delicate (in fact, autopsies show that the skin in this delicate anatomical region deteriorates easily).

As we have seen in other cases, there is a strong correlation between the para-physiological condition of an individual before death and his mummification. Likewise, pre-mortem



**Fig. 10** – Myelomeningocele diagnosed in a modern subject during a post-mortem examination on a term fetus. Nervous system elements are clearly visible.

pathological conditions strongly affect the speed of mummification and related transformation processes.<sup>40</sup>

The histological analysis also helped us identify the defect, leading to the diagnosis of meningocele.

A myelomeningocele diagnosis was ruled out by the absence of nervous tissues. Since there were no elements of teratomatous tissue growth, a differential diagnosis of cystic teratoma of the sacrum was also excluded.

## 6. Conclusion

Anthropology and paleopathology are valuable assessment tools for an innovative approach to the biological–naturalistic study of congenital malformations. These disciplines provide a historical understanding of malformations. They take conceptual and technological tools from pathological anatomy that is then used to analyze ancient lesions and infer their clinical meaning. They also provide a broad geographic and time picture of congenital malformations, from proto-history to our more recent past.

Knowledge of the past incidence and forms of congenital diseases provides knowledge of a population's normal and pathological genetic load, as well as a certain ability to predict the current behavior and development of these diseases.

Paleopathological documentation methods and the development of correct diagnostic procedures for ancient specimens are essential to increase the value of the data and their use for epidemiological purposes.

The description of this case is, in our opinion, a significant historic and biological document which, for its ancient nature and good preservation conditions, has no parallel yet in paleopathological literature. It gives an important and valuable contribution to our biological archive, with regard to aspects that are very important today in both medical and social fields.

In conclusion, we wish to stress the medical–scientific importance of anthropological, anatomic, and pathological anatomy museum collections which, also due to the ever more common use of minimally invasive and more accurate imaging techniques, are offering new, attractive investigation opportunities.

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