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Extensive pulmonary haemorrhage in an Egyptian mummy

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Abstract We report on the morphological and trace element findings of several internal organs from an Egyptian mummy approximately dating from the year 950 B.C. according to ^{14}C-analysis. By use of a multidisciplinary approach we succeeded in discovering evidence for severe and presumably recurrent pulmonary bleeding during life. This was suggested by the finding of massive haemosiderin deposits in the lung and a selectively and markedly elevated level of iron in trace element analysis of the lung tissue. Furthermore, we observed an enhanced deposition of birefringent particles in the lung tissue, without significant fibrosis. The histological analysis of liver, stomach and intestine confirmed the macroscopic organ diagnoses without evidence of any major pathological processes. In addition, analysis for various drugs revealed a significant deposition of tetrahydrocannabinol (THC), nicotine and cocaine in several organs of the mummy. The concentration profiles additionally provide evidence for a preferential inhalation of THC, while nicotine and cocaine containing drugs seem to have been consumed orally.

Key words Paleopathology · Pulmonary haemorrhage · Parasitosis · Drugs

This manuscript is dedicated to Prof. Dr. M. Eder on the occasion on his 70th birthday

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Introduction

The detailed macro-, radio- and histomorphological analysis of Egyptian mummies following unwrapping has previously revealed some major pathological findings. These have significantly widened our knowledge and understanding of historic diseases and thus the circumstances of historic life [4, 5, 16–19]. Thus, a whole variety of distinct disorders, like parasitoses, tuberculosis or degenerative articular diseases, have been found repeatedly in mummies from ancient Egypt and from other places.

In the present report, we describe the pathological findings in an Egyptian mummy that had been unwrapped during the Munich Mummy Project [8]. This mummy shows distinct diseases of the respiratory system which may be closely related to the death of the individual and we are able to uncover some aspects of drug-related "therapy" by analysis of certain drugs found in the mummy's tissues.

Materials and methods

Description of the mummy

We have already described some aspects of the mummy [12]. Briefly, it had been brought to the Royal Bavarian Academy of Science in the 1820s by Dr. F.W. Sieber, a business man and private scientist from Prague. The exact source of the mummy is unknown, but according to a ^{14}C-dating it dates back approximately to 950 B.C. (21st Egyptian dynasty), but no further information is available about its previous history. Anthropological examination indicated that the mummy was that of an approximately 30–40-year-old man. The mummy had been kept in the Royal Bavarian Egyptologic State Collection and, after the First World War, in the State Collection for Egyptology in Munich until 1985, when it was unwrapped during the Munich Mummy Project [8]. Mummy unwrapping was decided upon since the state of conservation was poor; the head was completely missing due to damage during the Second World War (see Fig. 1). In the first descriptions of the mummy, no such destruction had been noted. In addition, some bandages were disrupted.

Following the removal of the linen bindings, several small packages were found in the chest cavity, containing naturally

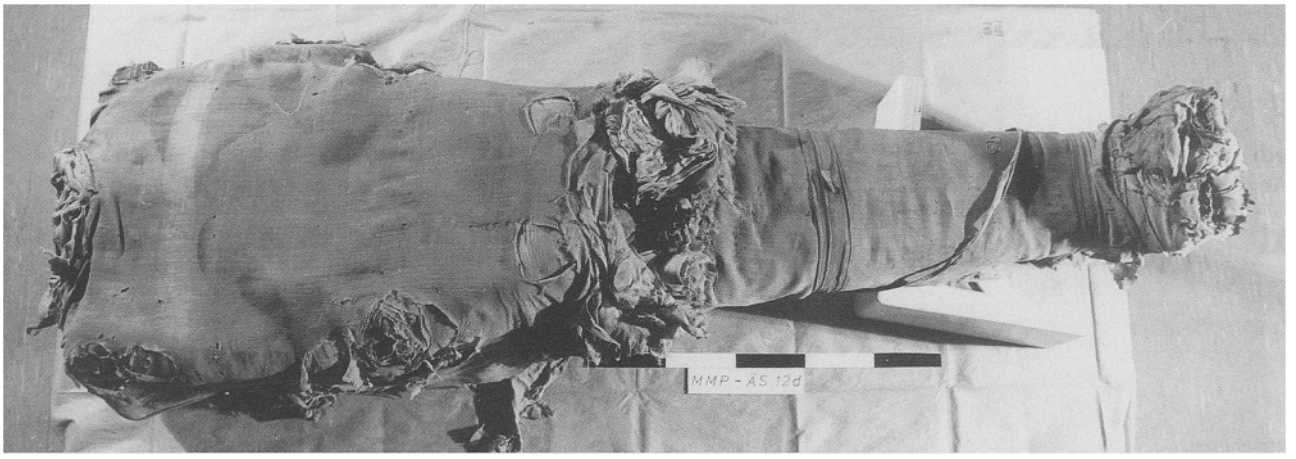

Fig. 1 Photograph of the mummy prior to its unwrapping. Note the missing head and the disruption of the bindings

mummified organs, which had also been carefully wrapped in separate linen bindings. Small divine figurines were present in four of these packages, which could be attributed to distinct organs. The figurines were the four sons of Horus, which had also previously been found by Smith and Dawson [15] in packages containing lung, liver, stomach and intestine (Fig. 2). A further macromorphological analysis of these organ remnants supported the organ diagnoses, although no secure diagnosis could be given, so that it was decided to perform a histomorphological investigation.

Histomorphological examination

We removed several tissue blocks from the inner parts of each organ package and a sample from the mummy's skin and rehydrated them according to previous protocols [14]. The rehydrated material was fixed in buffered 4–6% formaldehyde and embedded into paraffin. Subsequently, the paraffin material was used for the preparation of tissue sections as routinely performed. The following histochemical stainings were done in addition to the HE (haematoxylin-eosin) staining: elastic-van Gieson stain, Prussian blue, PAS, von Kossa, auramine-rhodamine and Ziehl-Neelsen staining.

Trace elemen analysis

Trace element analysis was done by ICP-AES (inductively coupled plasma atomic emission spectroscopy) as previously described [9]. This analysis was performed on the mummy's lung, liver, stomach and intestinal tissue. The resulting values were compared to an additional sample of soil that had been removed from the mummy's chest cavity.

Analysis of drug concentrations

We determined the concentrations of various drugs and drug metabolites, in skin, bone, tendon, lung, liver, stomach and intestines from the mummy. Thus, the concentrations of delta-9-tetrahydrocannabinol (THC), nicotine and cocaine alkaloids were analysed. The respective methods comprised radioimmunoassay and gas chromatography/mass spectrometry as previously described [1, 10, 12].

Results

Morphological analysis

The macroscopic organ diagnoses were confirmed by the histological analysis. Although condensed, the lung parenchyma was clearly identifiable by the focal presence of hyaline bronchial cartilage (Fig. 3a), collapsed airways, and blood vessel structures (Fig. 3b). Some of these blood vessels were so well preserved that any major intimal thickening could be excluded (see Fig. 3b and 4a). The bronchial cartilage was focally calcified (Fig. 3a).

As a major finding in the collapsed lung tissue we observed extensive disseminated deposits of a brown, grainy pigmented material that was notably confined to the collapsed airways in all our lung sections and that was obviously absent from the interstitial space of the lung parenchyma (Fig. 4a, b). The presence of large amounts of haemosiderin was evidenced in these deposits by a positive Prussian blue histochemical staining (Fig. 4b). Furthermore, we found occasional dark anthracotic pigment in the parenchyma as well as fine particulate conglomerates in the air spaces and in the parenchyma. The latter were partly birefringent in polarization microscopy and thus were assumed to represent silica containing particles (Fig. 4c). In some instances, these silica particles could clearly be localized in areas that were distinctly separate, at least in part, from the deposits of iron-positive material. There was no fibrous reaction around the haemosiderin nor associated with the birefringent deposits. In addition, we observed in some sections of the lung parenchyma occasional small round calcified particles that were surrounded by a PAS-positive material (Fig. 4d). These particles could not be attributed to any specific anatomical structure, like vessel walls etc. No haemosiderin deposits could be found in the immediate vicinity of these calcifications. Staining for acid fast bacilli (auramin-rhodamine and Ziehl-Neelsen-stains) was negative.

The additional histological analysis of the other organs showed typical organ structures, however, with some post mortem destruction. There were no pathologi-

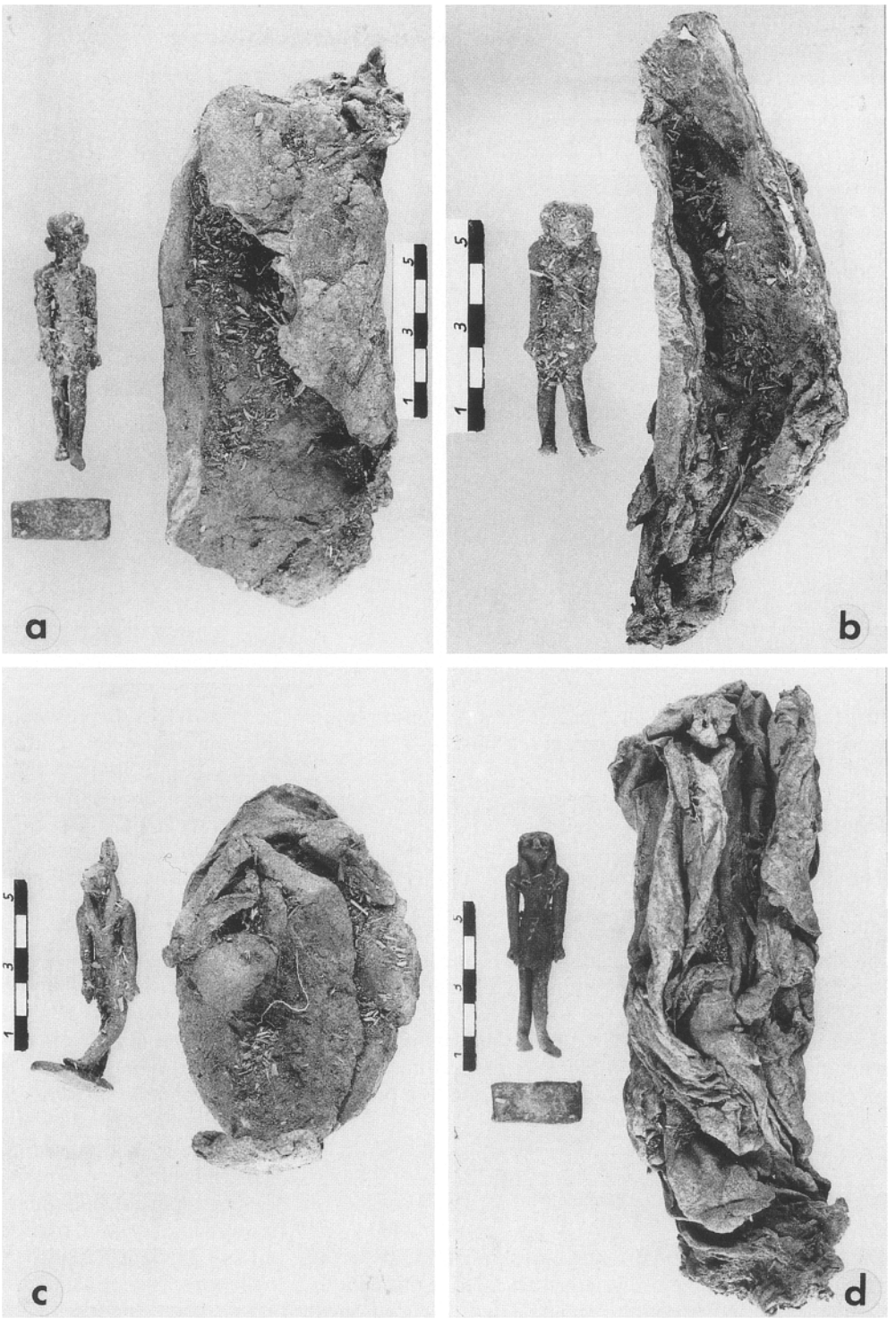

Fig. 2 Macroscopic aspects of the four organ packages found in the mummy's chest cavity. In each organ a small figurine of a son of Horus was found which allowed the attribution of each package to one certain organ. (**a**) The human-headed god Amset was found with the liver, (**b**) the baboon-headed god Hapi with the lung, (**c**) the jackal-headed god Kebehsenuf with the stomach and (**d**) the falcon-headed god Duatmutef with the intestines

cal findings in the liver tissue which showed typical lobular structures without any evidence of fibrotic tissue reaction, in the intestines or the stomach or the skin sample (not shown). There was no evidence for the deposition of any significant iron material (haemosiderin). In addition, no silica material or any other foreign material or calcifications could be found in the samples analysed from these organs.

Trace element analysis

This analysis revealed an approximately ten-fold increase in iron (88.4 mg/g) in the lung tissue in comparison to liver (2.0 mg/g) and to the soil (9.8 mg/g) that had been removed from the mummy's chest cavity (level of significance $P<0.0001$). All other elements tested seemed not be accumulated in any of the organs and the

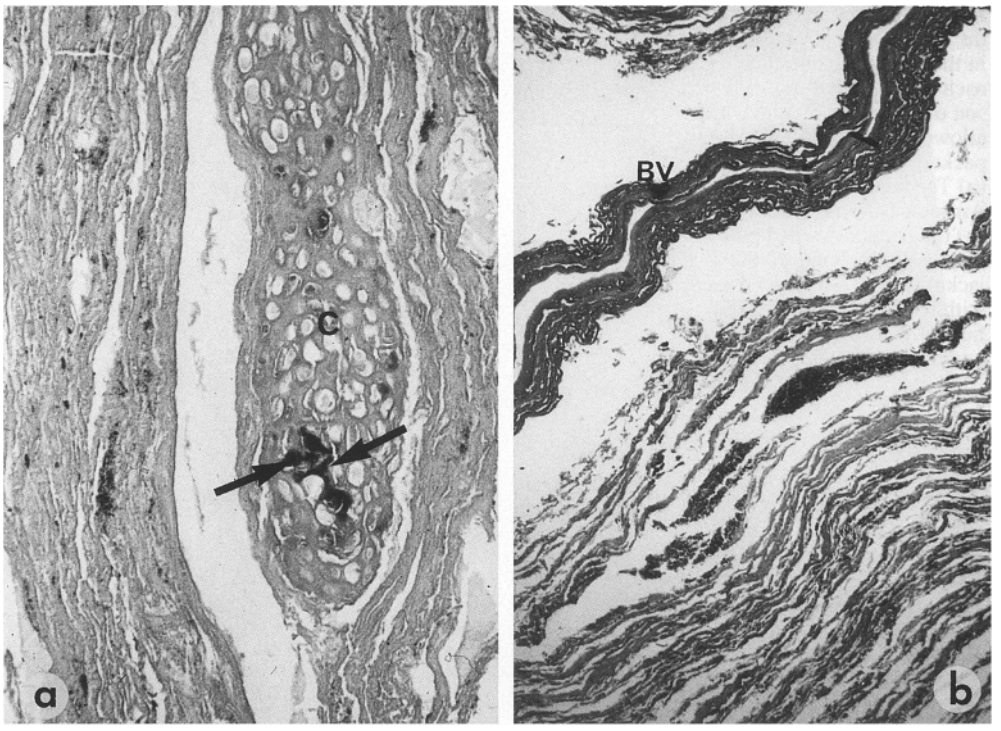

Fig. 3 Histological aspects of the lung following rehydration and paraffin embedding. (**a**) The lung is clearly identifiable by hyaline cartilage islands (*C*). Note focal degenerative calcification of the cartilage (*arrows*) (**b**) In some areas larger blood vessles (*BV*) are well-preserved in the lung tissue, while the parenchyma itself is condensed and collapsed. (**a**: HE, original ×400; **b**: elastica-van Gieson, ×100)

respective values were at the soil's range. Silica levels were not determined for technical reasons.

Drug analysis

The determination of nicotine, cocaine and THC and/or their metabolites revealed significant amounts in all organs tested (skin, bone, tendon, liver, lung, stomach and intestines). The highest levels for nicotine and cocaine were found in the stomach, whilst significant amounts of THC were recognized in the lung tissue, as well as in skin/muscle. The detailed data are shown in Table 1. This maximum distribution points to an oral ingestion of nicotine and cocaine containing drugs, and to a preferential inhalation of THC.

Discussion

Detailed morphological and biochemical analysis of mummies from ancient Egypt has revealed significant information on living conditions and diseases during those times [4, 5, 16–19]. Thus, it has previously been shown that the inhalation of sand dust, particularly of silica crystals, are widespread findings in these mummies [5, 16]. In some of them, a fibrotic reaction of the lung parenchyma in terms of silicosis has been reported [16]. These observations have been interpreted as typical morphological findings of silica containing dust deposits due to sand dust inhalation during desert storms, a characteristic observation in recent populations of the Sahara and Negev deserts [2, 13]. The latter study [13] also clearly demonstrated the presence of silica crystals in the affected lung tissue by radiodiffraction analysis, so that it seems fair to assume that our historic patient suffered from the same condition, although we could not prove the presence of silica crystals in our patient by chemical or radiodiffraction methods.

As a further pathological finding, the histomorphological examination showed focal calcifications of the bronchial cartilage which usually occurs as a degenerative change in advanced age. This contrasts with the age estimation of the mummy by the usual anthropological methods which indicate a male individual of 30–40 years of age. One reason for this discrepancy may be the fact that the mummy's head was missing. Anthropological age determination using the skull is known to be more precise than that using the postcranial skeleton. Therefore, the histological findings may indeed indicate a more advanced age for this patient.

The report of pulmonary haemorrhage is based on the morphological and particularly the histochemical findings of extensive depositions of haemosiderin within the collapsed, but otherwise unremarkable lung alveoli. These haemosiderin deposits are confined to the lung and they are found in all different lung samples analysed. Furthermore, these findings are corroborated by trace element analyses that demonstrate an almost ten-fold increase in the parenchymal iron concentration when compared with the soil which had been obtained from the mummy's chest cavity and a fourty-fold increase when compared to other organs. These findings exclude the possibility that the lung tissue could have been merely contaminated with iron-laden soil, although chemical analysis had previously shown that desert sand contains

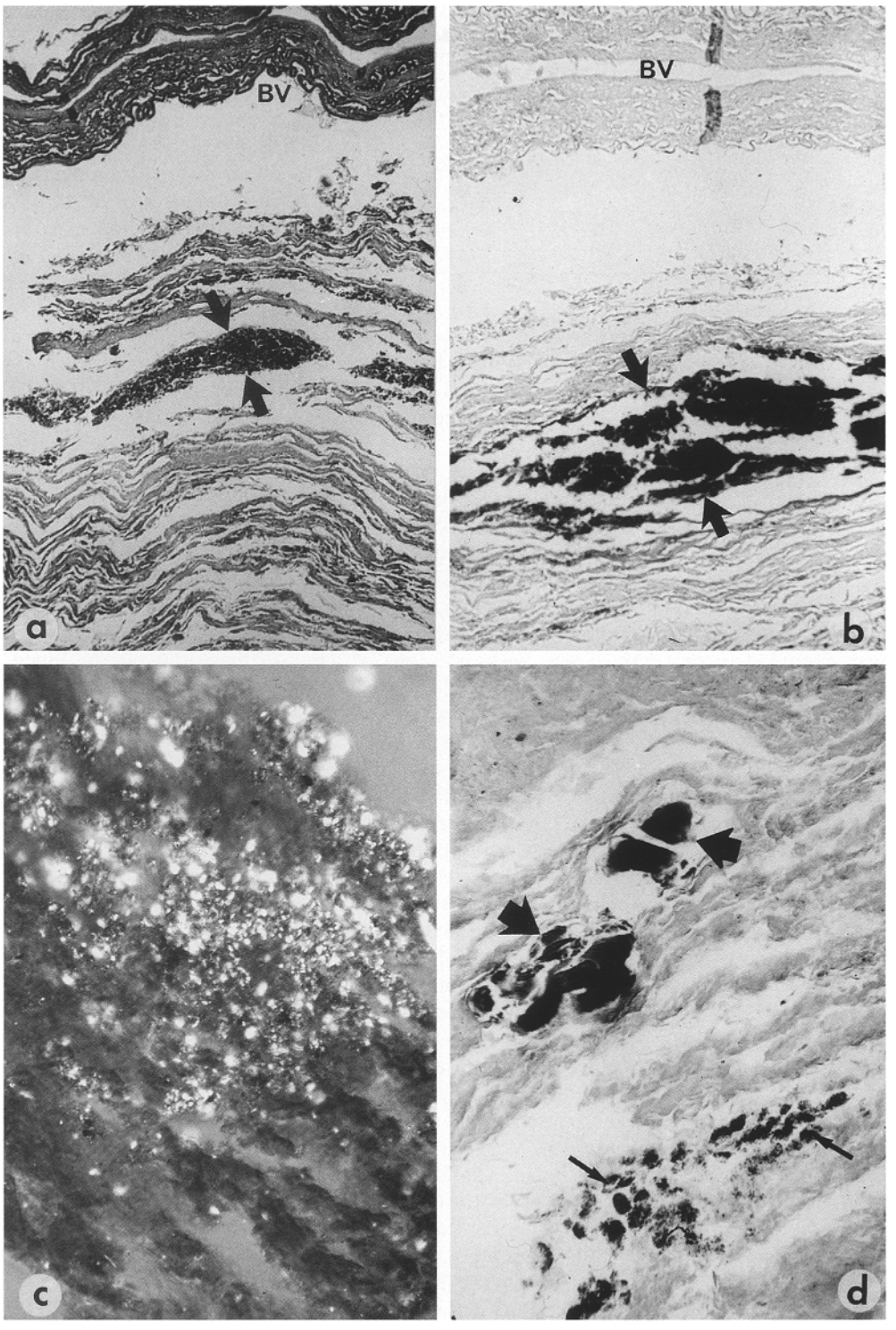

Fig. 4 Pathomorphological aspects of the mummy's lung tissue. (**a**) Within the collapsed small alveolar air spaces focal, grainy pigmented brown material is seen (*arrows*). Note the blood vessel at the upper margin (*BV*). (**b**) In a Prussian-blue histochemical staining the grainy material reacts strongly positive for iron (*arrows*). (**c**) In polarization microscopy occasional areas with birefringent conglomerates are found in the lung without significant fibrotic reaction, providing evidence for inhaled silica containing crystals. There is, however, no fibrosis. (**d**) Occasional small PAS-positive calcifications are seen within the lung parenchyma (*large arrows*). Note the deposition of dark anthracotic pigment at the lower half of the picture (*small arrows*) and stromal fibrosis. (**a**: elastica-van Gieson, original ×200; **b**: Prussian-blue, ×300; **c**: HE, polarized light, ×500; **d**: PAS, ×500)

2.6 to 4.6% ferric oxide (a divalent iron combination) [13]. In addition, the histochemical staining used in this study specifically reacts only with trivalent iron ions, but not with divalent ions as those found in the sand [3]. Furthermore, the different spatial distribution of haemosiderin and crystal deposits in the lung parenchyma clearly indicates that the "haemosiderin" was not simply an artefact of inhaled sand material.

According to these observations, it seems fair to speculate that our patient suffered from possibly recurrent pulmonary bleeding during life. To the best of our knowledge, there exists only one further report on pulmonary haemorrhage in an Egyptian mummy. In this report, Zimmermann [19] described an infant mummy with terminal intratracheal and pulmonary bleeding. Since he found acid fast bacilli in tissue sections of vertebral bone

Table 1 Concentrations of various drugs in different tissues of the mummy (all values: ng/g; mean±SD)

	Nicotine	Cocaine	Tetrahydrocannabinch
Bone	228±16	104±15	88±11
Skin/muscle	485±41	133±23	2686±265
Tendon	816±44	–	684±65
Lung	350±25	70±16	2090±312
Liver	887±51	461±62	306±42
Intestine	281±24	96±23	927±86
Stomach	1269±84	646±112	183±29

the dignosis of osseous and pulmonary tuberculosis was evident. Extensive histochemical stainings in our patient yielded no sign of mycobacterial infection in the lung. In addition, we observed no "fresh" bleeding residues in the bronchi of the specimen.

The reason for this possibly recurrent bleeding remains unclear. However, some causes for such lung bleeding can be excluded. In particular a cardiac cause can be excluded, this usually leads to chronic pulmonary hypertension and the appearance of "heart-failure cells" in the lungs (iron-containing macrophages). This disease is also associated with pulmonary arteriosclerosis which was excluded in our case. There were no signs of any circumscribed infiltrate (such as Aspergillus associated or other pneumonias) and the careful inspection of the mummy's chest wall provided no evidence for any traumatic event like blunt chest trauma, which may have led to parenchymal haemorrhage. Similarly, where were no signs of "vasculitis" neither by perivascular scarring nor by any vascular destruction. The histomorphological investigation of the other organ samples revealed no further pathological abnormality. We cannot exclude the possibility that the blood had been aspirated from other sources, following haematemesis or skull trauma, although in acute blood asphyxiation it is unlikely that a conversion of the divalent haemoglobin iron to the trivalent haemosiderin iron would have happened so rapidly. Although we are aware of the fact that no secure diagnosis on this patient can be presented, we speculate that the focal calcifications in the lung parenchyma may be causally related to the lung bleeding.

One possible cause is parasitosis. There are previous reports on parasitic infections in historic individuals which were diagnosed by morphological findings of calcified parasitic remnants. One argument for such a pathogenetic process in our case is the histochemical staining of the few small calcifications within the pulmonary parenchyma showing a peripheral PAS-positive zone (which may resemble a cuticulum) and surrounding fibrosis. However, there are some arguments against such a process: in the other organs analysed no such calcifications were seen, the PAS-staining pattern is not specific for parasites and other diseases, like histoplasmosis or other fungi, have to be taken into consideration. The observation of residues of the haemorrhage in many areas of the lung argues much more in favour of a "systemic" cause, rather than circumscribed calcifications and the co-existence of calcifications and haemosiderin does not imply cause and effect. In summary, the exact nature of the calcifications and that of the bleeding remain obscure.

From our analysis of the concentrations of various drugs in different mummy tissues, we may speculate about historic therapeutic measures. We observed significant amounts of all three substance classes in the mummy's tissues, especially of THC, as well as of drugs containing cocaine and nicotine [12]. These findings are in accord with previous observations on bone samples from other Egyptian mummies [10], although the exact nature of the drugs is unclear with respect to cocaine and nicotine consumption [see 11]. Since we found significant concentrations of tetrahydrocannabinol in the lungs, showing values ranging above those of the other internal organs, it is fair to assume that this drug was mainly incorporated by inhalation. This assumption is supported by medical papyri describing smoking ceremonies with hashish [7]. This could also explain the high concentrations of THC in skin/muscle due to post-mortem smoking ceremonies. The concentrations of drugs containing cocaine and nicotine were found to be highest in the stomach and the intestine, which points to oral ingestion of these substances. Since we had also observed significant concentrations of cotinine, the major metabolite of nicotine [12], and since nicotine is rather quickly metabolized into cotinine in vivo, these observations point to consumption of nicotine in life. In this regard, it is an interesting observation that recent analyses on the nicotine content of various vegetables yielded significant amounts of nicotine in some plants [6] which may have been used as therapeutic drugs. Since we also found these drugs in other organs although at much lower levels, it cannot be ruled out that some contamination had occurred during the embalming procedure, although we had tried carefully to remove tissue samples from the inner areas of the organs.

In summary, our findings indicate extensive haemosiderin deposition within the mummy's air spaces providing evidence for haemorrhage during life. Although the exact source of this bleeding remains uncertain, we speculate that the extensive pulmonary haemorrhage contributed to the final fatal outcome in this historic patient. Furthermore, the detection of various drugs provides evidence that multidrug therapy was given to relieve his pain.

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