Calcifying pseudoneoplasm of the neuraxis (CAPNON) associated with neurenteric cyst: an autopsy case showing unusual fatal outcome

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Case Report

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Abstract

Background

Calcifying pseudoneoplasm of the neuraxis (CAPNON) is a rare calcified tumefactive lesion that can occur in the brain or spine. Although the aetiology and natural course of CAPNON has not yet been fully established, recent study reported that many CAPNON cases have dual pathology, which may be associated with its aetiology.

Case presentation

A 53-year-old man with a history of an untreated brain mass was taken to a hospital by emergency transport. A computed tomography scan revealed an intracranial hypo-attenuated mass exhibiting mass effect. Several calcified foci were observed around the lesion. He suddenly showed tonic seizure after admission, therefore an emergency craniotomy was performed. However, he unfortunately died due to advanced cerebral oedema. Microscopic findings of the surgically obtained materials were consistent with neurenteric cyst (NC). Intracranial hard masses were found adjacent to NCs and the masses were composed of fibrous cartilage-like matrix with massive linear calcification and surrounding round-to-oval epithelioid cells.

Conclusion

CAPNON associated with NC was considered to be most appropriate diagnosis of present case. To the best of our knowledge, this is the first report of such case. The present case suggests that delay of treatment may cause a poor outcome, at least in CAPNON associated with NC. Careful investigation, including of the underlying pathology, may be essential for deciding treatment strategies for CAPNON.

Introduction

Calcifying pseudoneoplasm of the neuraxis (CAPNON) is a rare calcified tumefactive lesion that can occur in the brain or spine [1–3]. The growth of CAPNON is generally indolent, and the majority of reported cases show a benign clinical course after complete or subtotal surgical excision [2,3]. Therefore, the aetiology and natural course of CAPNON has not yet been fully established. A recent study reported that many CAPNON cases have dual pathology, which may be associated with its aetiology [1]. Here, we report a rare autopsy case of CAPNON that was completely free of any medical interventions in the critical period and was associated with a neurenteric cyst (NC), which is an endoderm-derived congenital lesion [4].

Case Report

A 53-year-old man complaining of head pain, systemic paralysis, and seizure in both legs was taken to Toyama Prefectural Central Hospital by emergency transport. Approximately 13 years previously, he had visited Toyama University Hospital because of hyposmia and headache. Imaging examination revealed a calcified mass in the left anterior cranial base (Fig. 1a–e). Although surgical treatment was proposed, he refused surgery and did not visit the hospital again. According to his family, his personality gradually changed and he had started to complain of several additional symptoms in the last few years, including dizziness, tinnitus, and neck pain. He had also shown abnormal behaviour in the last few months, such as suddenly screaming or talking to strangers. At the time of emergency transport, his consciousness was clear and conversation was possible. A computed tomography scan revealed an intracranial hypo-attenuated mass without enhancement, exhibiting mass effect (Fig. 1f–j). Additionally, several calcified foci were observed around the lesion. At midnight of the day he was hospitalized, he suddenly showed tonic seizure and anisocoria (2 mm and 4 mm on the right and left pupils, respectively); the neurosurgeon therefore decided to perform an emergency craniotomy. During surgery, a cystic lesion containing pus-like fluid and semisolid brittle whitish materials was observed (Fig. 2a). Partial resection of the lesion and internal and external decompression were performed. However, cerebral oedema progressed continuously despite intensive care, and he died 12 days after surgery.

Microscopic examination of the cystic lesion revealed a single layer of ciliated columnar epithelium without cellular atypia (Fig. 2b). These ciliated columnar cells were positive for cytokeratin 7 and 20 but negative for glial fibrillary acidic protein and S-100 (Fig. 2c-f) (Table 1). Cytological examination of the intra-cystic fluid identified no malignant cells. These findings are consistent with NC.

At autopsy, a large bone defect was observed in the midline of the anterior cranial fossa (Fig. 3a). The brain weighted 1542 g and exhibited severe encephalomalacia. Moreover, there were several hard masses, mainly in the left frontal lobe.

Microscopically, the hard masses were composed of fibrous cartilage-like matrix with massive linear calcification and partial ossification (Fig. 3b). NCs were also observed adjacent to hard mass lesions (Fig. 3c). Various pathological appearances containing collagen fibres and hyaline cartilage-like stroma were identified beneath the hard masses (Fig. 3d). Here, there were foci of granulation tissue, containing abundant lymphocytes and macrophages, and necrotic tissue with marked neutrophil infiltration (Fig. 3e). The hard masses were surrounded by round-to-oval epithelioid cells and giant cells (Fig. 3f). Immunohistochemically, these cells (Fig. 4a) were diffusely and strongly positive for vimentin (Fig. 4b), focally positive for epithelial membrane antigen (EMA, Fig. 4c), CD68 (Fig. 4d), and S-100 (Fig. 4e) but negative for somatostatin receptor 2 (SSTR2, Fig. 4f), pan-cytokeratin (Fig. 4g), and glial fibrillary acidic protein (GFAP, Fig. 4h). In contrast, the meningothelial hyperplastic lesion adjacent to the CAPNON was diffusely and strongly positive for vimentin (Fig. 4b), EMA (Fig. 4c), and SSTR2 (Fig. 4f) but negative for CD68, S-100, pan-cytokeratin (Fig. 4g), and GFAP (Fig. 4h). Immunohistochemical findings are summarized in Table 1. Many amyloid precursor protein-positive cells, indicating the presence of cell damage, were observed in the brain tissue (Fig. 4i) in addition to necrosis of the pituitary gland (Fig. 5).

Discussion

Supratentorial NC is rarely associated with calcification [4], and we were unable find any previous report of obvious mass lesions associated with NC. We consider that CAPNON associated with NC is the most appropriate pathological diagnosis of the present case; To the best of our knowledge, this is the first report of CAPNON associated with NC. The enlarged and newly appeared calcified lesions and the enlargement of the NC confirmed before surgery demonstrated that CAPNON development may have been associated with congenital NC in the current case. Prolonged and/or recurrent inflammation of NC and/or its secretion product in the present case might have contributed to the enlargement of NC itself, and might thus contribute to the occurrence and development of CAPNON. It is notable that synovial cysts are frequently associated with spinal CAPNON [1]. Therefore, investigations targeting cystic lesions may be important for examining the aetiology of CAPNON.

In the present case, slowly progressive cerebral oedema caused by the development of CAPNON and associated local inflammation may have gone beyond the irreversible level because of the long-term untreated period. Necrosis of pituitary glands is also associated with advanced brain oedema, and may cause pituitary apoplexy in the terminal phase. The present case demonstrates the importance of early surgical resection for CAPNON, even though the clinical course of CAPNON is essentially benign [1]. Careful investigation of the association between NC and CAPNON is needed, and complete resection of NC may be essential when NC is found beneath CAPNON.

Although we identified epithelioid cells that were positive for epithelial membrane antigen and vimentin, as shown in a previous report [3], the lesion should not be diagnosed as meningioma because these cells are also positive for various markers, including S-100, glial fibrillary acidic protein, nestin [5], and histiocytic markers such as CD68 and CD163 [6]. The immunohistochemical appearance of the present case, especially in the expression of SSTR2, which is the most sensitive and specific marker for meningiomas [7], was different from that previously shown in meningiomas. SSTR2 may thus be a useful marker for the differential diagnosis of CAPNON and calcified meningiomas. Interestingly, although the meningothelial cells are one of the possible candidates for the origin of CAPNON [1], the immunohistochemical results between CAPNON and meningothelial hyperplasia in this study were quite different. Thus, CAPNON may be a condition different from mere meningothelial hyperplasia and further investigation is needed to identify its origin and pathogenesis.

In conclusion, we reported a case of fatal CAPNON that was likely associated with NC; marked cerebral oedema related to prolonged local inflammation was evident in the brain. The present case suggests that no treatment may cause a poor outcome, at least in some CAPNON cases—and especially when CAPNON is associated with NC. Careful investigation, including of the underlying pathology, may be essential for deciding treatment strategies for CAPNON.

Abbreviations

CAPNONS: Calcifying pseudoneoplasm of the neuraxis; NC: Neurenteric cyst; EMA: Epithelial membrane antigen; GFAP: Glial fibrillary acidic protein

Declarations

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Authors' contributions

S Ichimata and N Nishida designed the study and performed the pathological observations. S Ichimata, Y Hata, and N Nishida participated in the autopsy. A Aikawa and S Ishizawa performed the pathological observations. D Sato and T Akai collected the clinical information. All authors were involved in writing the manuscript and had final approval of the submitted version.

Funding disclosure

None declared.

Data available statement

The data that support the findings of this study are available from the correspondence author upon reasonable statement.

Ethical approval

Ethical approval was obtained from the next kin and guardian. This study was approved by the Ethical Committee of Toyama University (I20200006) and was performed as per the ethical standards established in the 1964 Declaration of Helsinki, updated in 2008.

Conflicts of interest

The authors declare that they have no conflicts of interest.

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Figures

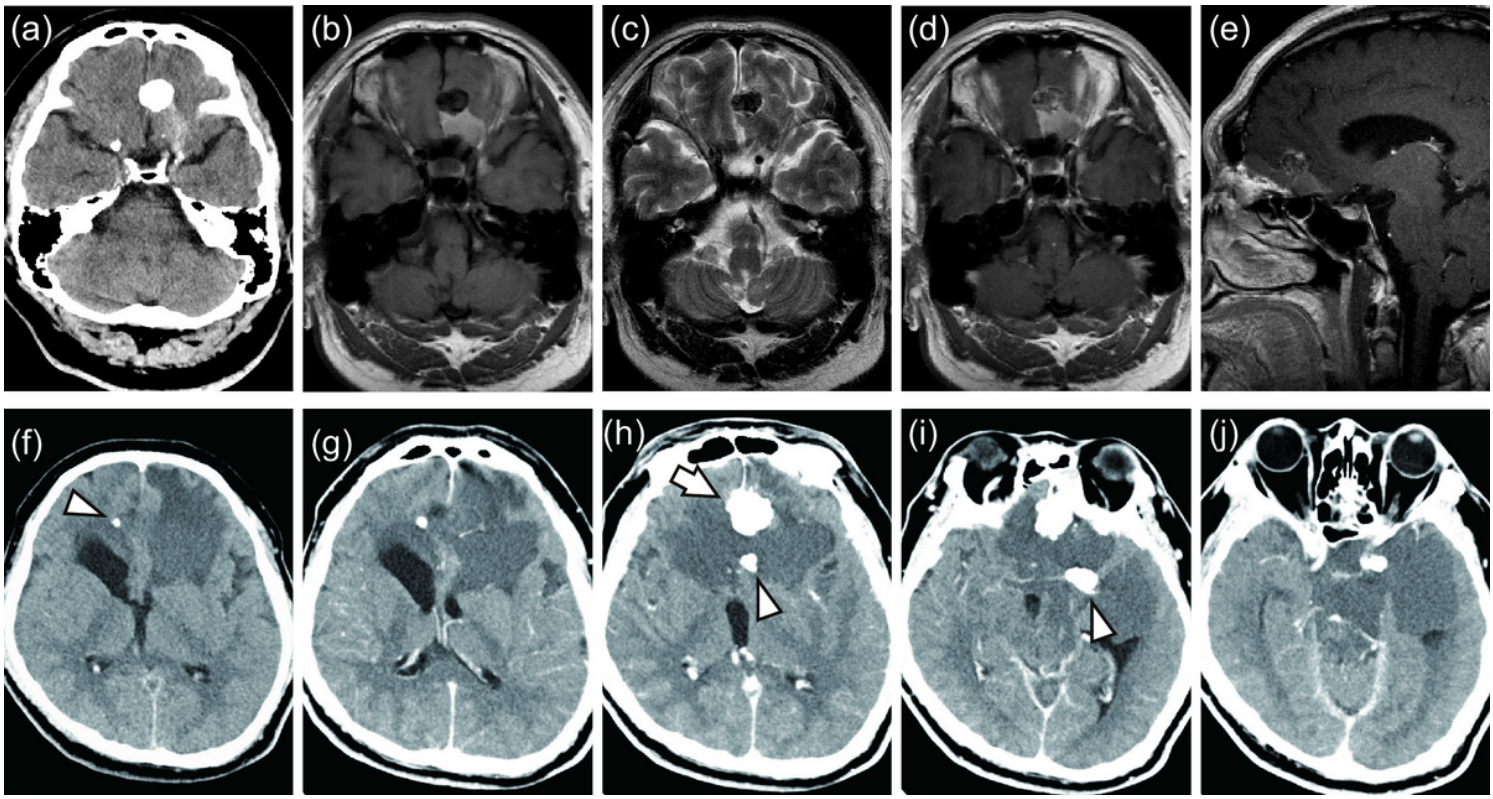

Figure 1

Representative findings of imaging examinations (a–j). (a–e) Findings at the first examination. (f–j) Findings approximately 13 years after the first examination. (a, f) Non-enhanced computed tomography (CT) scan, (b, c) non-enhanced magnetic resonance imaging (MRI) scan, (d, e) gadolinium-enhanced T1-weighted MRI scan, (g–j) contrast-enhanced CT scan. (a) An iso- to hyper-attenuated lesion with calcified nodule in the left anterior cranial base. The lesion was hyperintense compared with the cerebrospinal fluid on a T1-weighted scan (b) and hypointense on a T2-weighted scan (c). (d, e) The rim of both the non-calcified and calcified areas exhibited mild enhancement. (f–j) An intracranial hypo-attenuated mass without enhancement ranging from the left frontal lobe to the left temporal lobe, right frontal lobe, chiasmatic cistern, and prepontine cistern, exhibiting mass effect and midline shift. Enlargement of the pre-existing calcified lesion (arrow) and newly appeared calcified lesions (arrowheads) were observed.

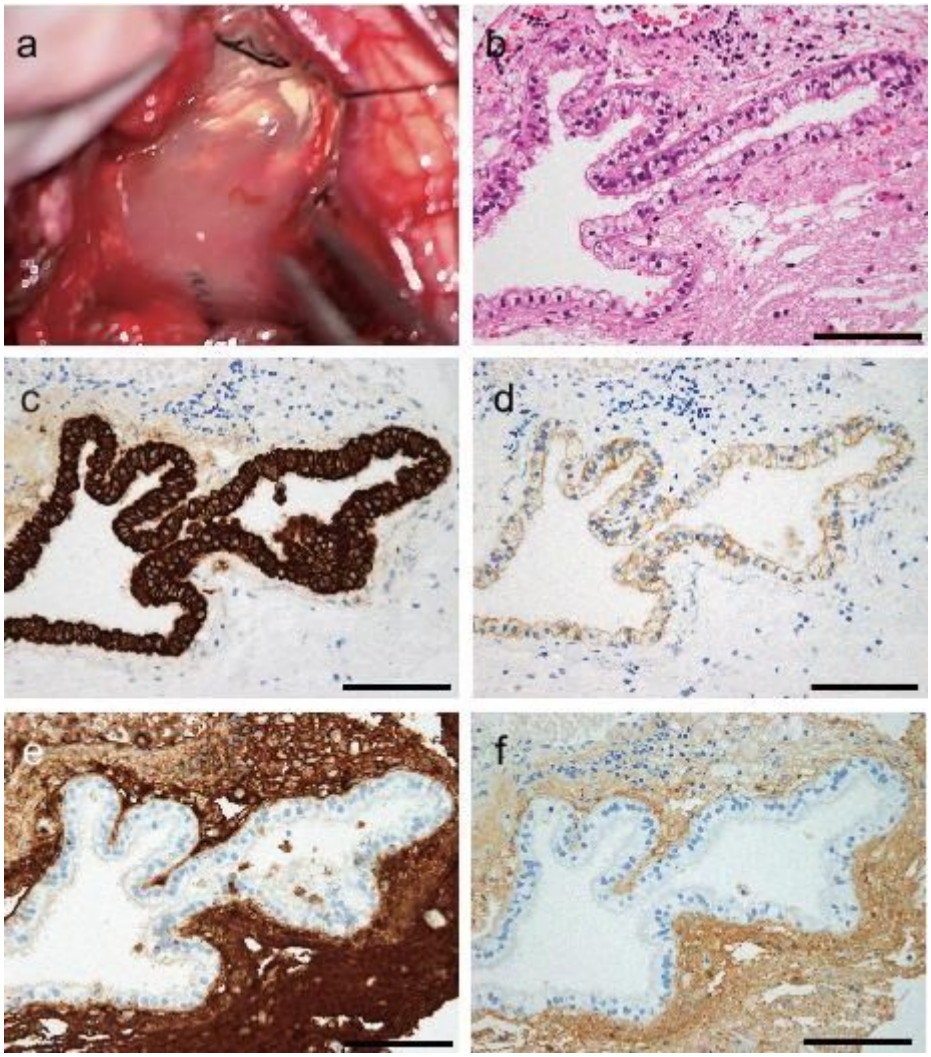

Figure 2

Intraoperative view (a) , its microscopic examination (b) and immunohistochemical findings (c-f). The ciliated columnar cells lining the cystic lesion were positive for cytokeratin 7 (c) and 20 (d) but negative for glial fibrillary acidic protein (e) and S-100 (f). Scale bar = 100 μm (a–d).

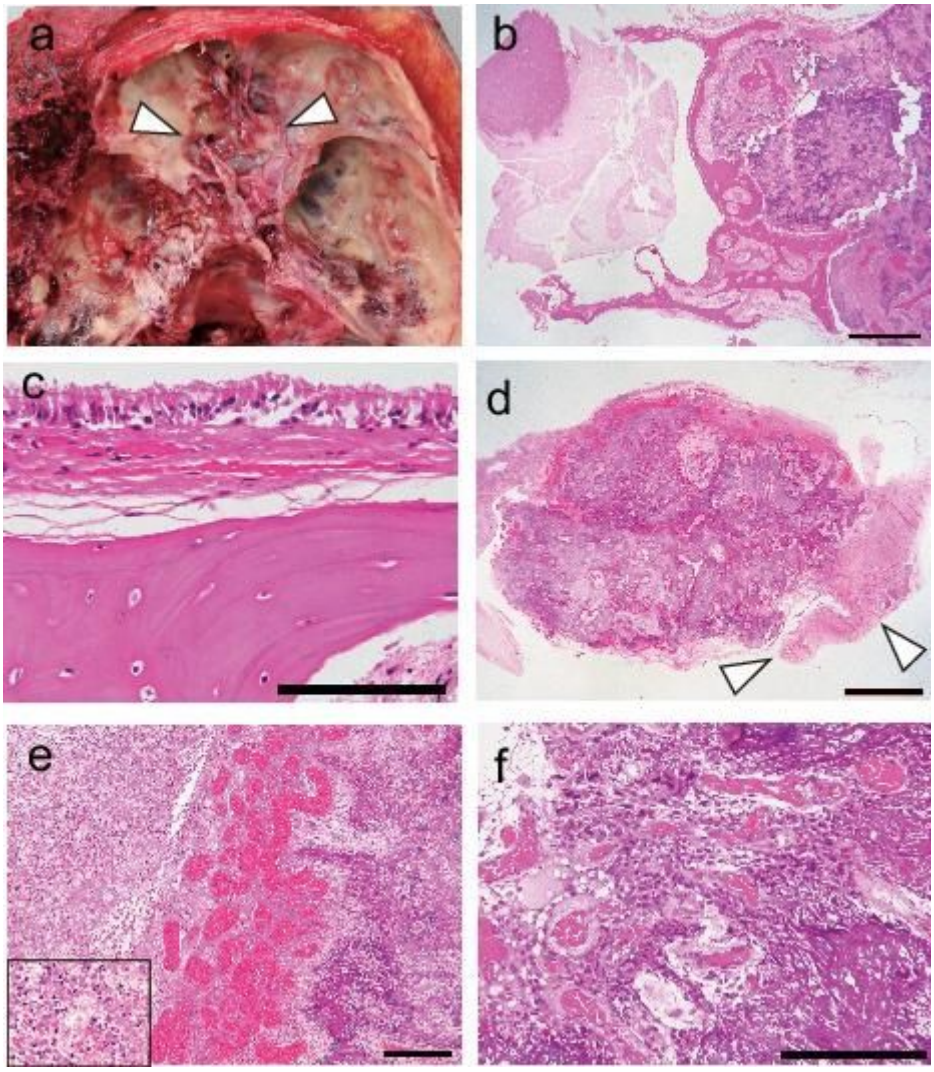

Figure 3

Pathological findings of the autopsy specimen. (a) A large bone defect in the midline of the anterior cranial base (arrowhead). (b) A hard mass composed of fibrous cartilage-like matrix with massive linear calcification and partial minimal ossification. (c) A cystic lesion lined by a single-layered ciliated columnar cell adjacent to the calcified mass lesion. (d) A hard mass containing collagen fibres and hyaline cartilage-like stroma with dural attachment (arrowheads). (e) Adjacent to the calcified lesion (right side), granulation tissue containing many capillaries (centre) and necrotic tissue containing inflammatory cells, including neutrophils and macrophages (left side), were observed (inset: higher magnification of infiltrating inflammatory cells). (f) Round-to-oval epithelioid cells and giant cells surrounding the calcified lesion. Scale bar = 2 mm (b, d), 200 μm (e, f), 100 μm (c)

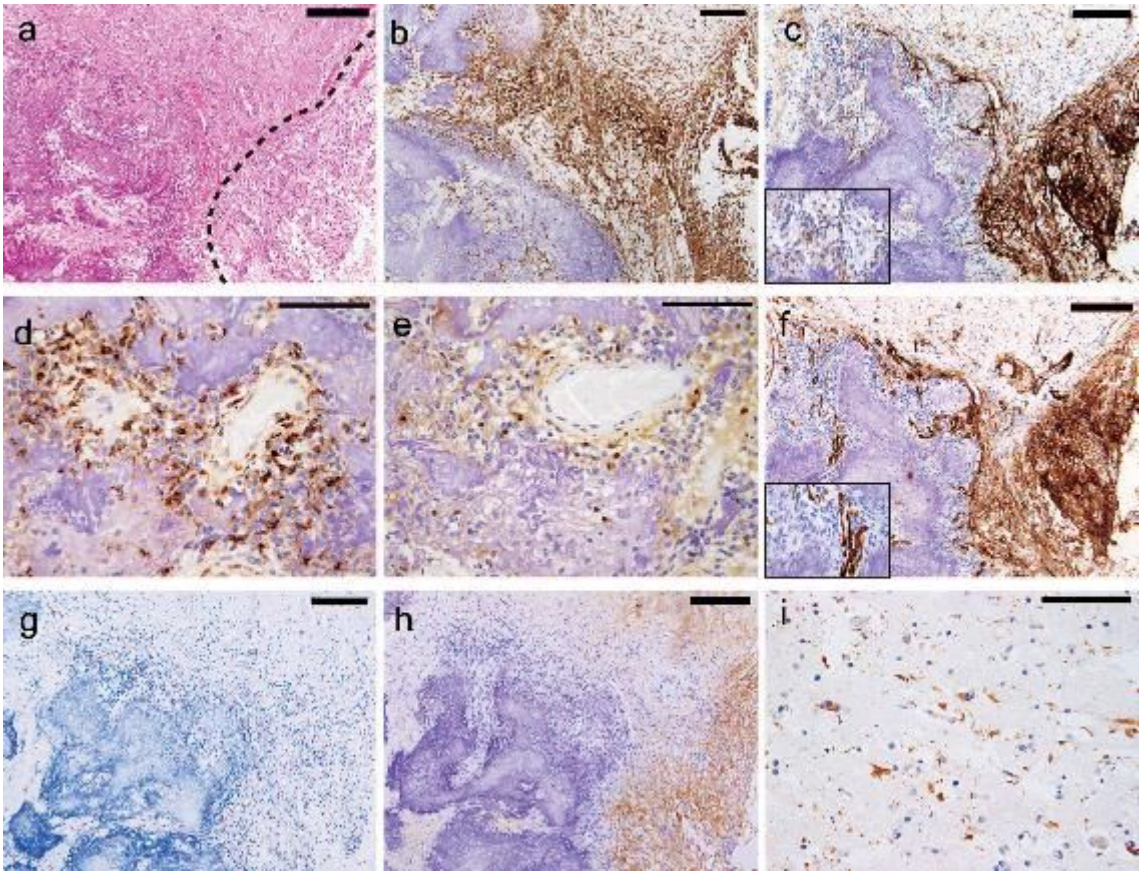

Figure 4

Immunohistochemical findings of the autopsy specimen. (a) HE staining, (b–i) immunostaining. Insets are hyper magnification view of the round-to-oval epithelioid cells and giant cells surrounding the calcified lesion. (a) Adjacent to the dural attachment area of the calcified lesion (left side of the dashed line), focal meningothelial hyperplasia up to 1 mm in diameter was identified (right side of the dashed line). The former lesion was diffusely positive for vimentin (c), focally positive for EMA (c), CD68 (d) and S-100 (e) but negative for SSTR2 (f), pan-cytokeratin [cytokeratin AE1/AE3 + CAM5.2] (g), GFAP (h). In contrast, the latter lesion was diffusely positive for vimentin (b), EMA (c), SSTR2 (f) but negative for pan-cytokeratin (g) and GFAP (h). Also, CD68 and S-100 were negative in the latter lesion (results not shown). (i) In the background brain tissues, many amyloid precursor protein-positive cells indicating the presence of cyto-injurious damage were observed. Scale bar = 200 μm (a–c, f–h), 100 μm (d, e, i).

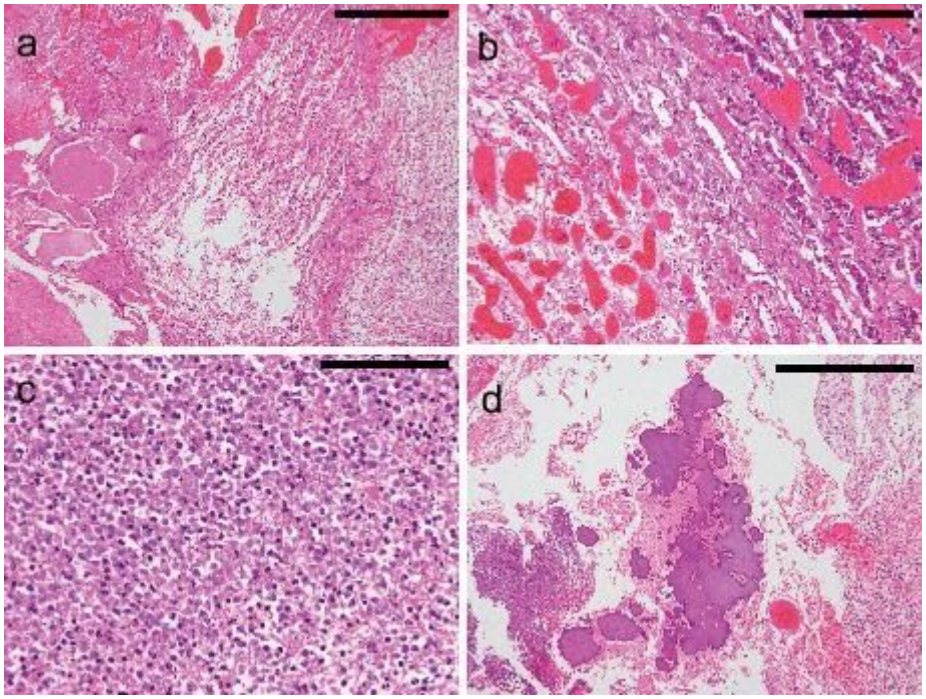

Figure 5

Histopathological findings in the pituitary gland. (a–d) Hematoxylin and eosin staining. (a) Marked necrosis was observed in the pituitary gland. (b) Adjacent to the background pituitary tissue (right), granulation tissue formation indicating the presence of chronic tissue damage was identified (left). (c) In the necrotic area, marked neutrophil infiltration was observed. (d) In the necrotic tissue, a calcified lesion indicating the involvement of the CAPNON into the pituitary gland was identified. Scale bar = 1 mm (a, d), 200 μm (b), 100 μm (c)

Supplementary Files

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- CAREchecklistEnglish2013.pdf