Ultimately, the tumour was diagnosed as localised biphasic mesothelioma with prominent myxoid stroma.

Because of the unusual histology of pleural tumours which are composed of a large proportion of myxoid components and a small portion of epithelioid components, and also the rarity of LMM with prominent myxoid stroma, the differential diagnoses from other types of sarcomas, especially myxofibrosarcoma, are required for the diagnosis. The current 2021 World Health Organization classification has included myxoid stroma in the typing, indicating favourable prognosis;⁸ however, the present tumour was found at autopsy, and it is impossible to argue the prognosis in this case.

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Progression of mesothelioma *in situ* to invasive disease 4 years and 10 months after initial diagnosis

Sir,

In 2017¹ we reported the first case of mesothelioma *in situ* (MIS) that was diagnosed using the now accepted diagnostic criteria. MIS is a preinvasive mesothelial lesion which was recognised as a concept as early as 1992² but has only now been incorporated as a diagnostic entity into the current World Health Organization (WHO) classification of thoracic tumours.³ The patient at the time presented with recurrent pleural effusions over the space of several months, and a biopsy at the time showed non-invasive focally papillary mesothelial proliferation with minimal mesothelial atypia and loss of BAP1. At that time, MTAP labelling was not available, and CDKN2A by fluorescence *in situ* hybridisation was not readily available; also, it is important to remember that neither were recognised as a diagnostic tool at that time. The diagnosis of MIS at that time was not recognised in this context, but because of the molecular significance of the unequivocal loss of BAP1, we flagged the finding to the clinicians and a decision for close clinical follow up was made.

Since we reported this case there has been renewed interest in the concept of MIS,^{4,5} but only a handful of cases that have reported progression of MIS to invasive tumour.^{6,7} In a recent publication we noted that over 4 years later, there had been no progression in this case.⁸ This patient had originally presented with recurrent pleural effusions, which were not overly cellular but showed mild cytological atypia and deletion of BAP1, and some papillary proliferations in a later sample. Radiology at the time showed pleural effusion, with no plaques and no nodularity (Fig. 1A), and no nodularity was visualised at thoracoscopy. The patient underwent talc pleurodesis, and the effusion resolved. Monitoring was by 6-monthly computed tomography (CT) scans and the patient remained free of detectable tumour and asymptomatic. However, 4 years and 10 months after the initial presentation with mesothelioma *in situ*/BAP1 deleted atypical mesothelial proliferation on cytology, the patient presented again acutely with pleural effusion and radiologically rapid progression to invasive disease. The CT at this time showed multifocal nodular pleural thickening with the largest area of thickening being located in the right lateral costophrenic angle, indenting the surface of the right liver lobe (Fig. 1B).

Effusion cytology now showed highly cellular pleural effusion with morular and papillary proliferations, typical of mesothelioma with an epithelioid component (Fig. 2). A biopsy of the new tumour showed invasive epithelioid mesothelioma, with the typical immunohistochemical profile of an epithelioid mesothelioma, showing positive labelling for calretinin, WT1, HBME1, and D2-40, with BAP1 loss and

Fig. 1 (A) Chest CT at the time of presentation reveals a small residual loculated right posterior pleural effusion. Fluid is also noted scattered within the right lung interlobar fissures. There is minor patchy ground opacity at the posterior right lung base, however no mass lesion is identified. There is no consolidation. (B) Current CT shows multiple contrast-enhancing pleural mass lesions and no parenchymal lung lesion.

Fig. 2 (A) The current pleural effusion shows highly cellular pleural effusion with morule formation and (B) complex clusters with some papillae.

Fig. 3 (A) H&E stained section of current pleural biopsy shows invasive epithelioid tumour (left) adjacent to foreign-body type giant cell reaction associated with pleurodesis (right). (B) Immunohistochemistry for BAP1 shows loss of nuclear labelling in the invasive tumour.

retained MTAP (**Fig. 3**). Pleurodesis-related changes of foreign-body type giant cell reaction were present directly adjacent to the invasive tumour.

The follow-up on this case highlights the need for extended follow-up in patients with BAP1 (or MTAP/CDKN2A) deleted mesothelial proliferations, and emphasises the current understanding embodied in the WHO definition of MIS as preinvasive disease; MIS is truly a precursor to mesothelioma with an epithelioid component. Our observations suggest that there may be a need to include MIS in the staging of mesothelioma. Consideration may also be given to further therapy options at the time of diagnosis in order to improve the clinical outcome.

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Keratoameloblastomatous transformation of a recurrent unicystic ameloblastoma: a novel case raising diagnostic and classification difficulties

Sir,

The origin and nature of keratoameloblastoma (KAM) and/or solid odontogenic keratocyst (SOKC) have never been studied comprehensively. In a recent issue of *Pathology*, Zhang *et al.*¹ presented a series of KAM/SOKC cases and discussed their pathological profile and mutational status with an extensive review of the literature. The authors suggested that although the degree of transformation may vary, KAM should be classified as SOKC with ameloblastomatous changes.¹ Their conclusion supported our own view that KAM and SOKC may share a histogenetic relationship.^{2,3} There is currently an overall agreement on the existence of the clinicopathological spectrum of KAM and SOKC.¹ Here we present the first known reported case of unicystic AM (UAM) showing late recurrence as a mixture of follicular AM and KAM/SOKC. This rare curiosity invites two alternative interpretations: (1) UAM may be a novel histogenetic source of KAM/SOKC, and (2) KAM/SOKC ex UAM may represent part of the morphological spectrum of AMs.

A 32-year-old man was referred for treatment of a 2 cm radiolucent area in the premolar region of the left mandible. Radiographs revealed a well corticated, rounded unilocular cystic lesion extending from the incisor to the second premolar (Fig. 1A,B). It had caused thinning of the buccal cortex and resorbed the roots of the canine and premolars (Fig. 1B). The cyst aspirate contained dark liquid with no keratin debris (Fig. 1C). The cyst was treated by enucleation and curettage, and grossly was found to have a single cavity lined with a very thin wall of uniform thickness. Microscopically, it exhibited a simple lining of non-keratinised epithelium with focal areas of ameloblastic changes (a peripheral basal layer of columnar to cuboidal cells with hyperchromatic nuclei arranged in a palisading pattern with reverse polarity) and, despite a careful search, neither papillary projections into the lumen nor solid islands within

the wall were evident, thus fulfilling the criteria for UAM of the luminal type (Fig. 1D–F). Approximately 5 years after surgery, radiographic examination yielded a multilocular lesion suggestive of recurrence (Fig. 2A). The tumour was managed by marginal resection. The surgical specimen lacked the UAM configuration and was diagnosed histologically as solid/multicystic AM of the follicular type, infiltrating deep into the bone (Fig. 2B,C). The AM epithelium also exhibited the classic growth pattern of KAM/SOKC, consisting of multiple keratinising cysts of various sizes with mural nests of acanthomatous AM (Fig. 2B,D,E). Notably, some of the lining epithelium showed ameloblastomatous transformation (Fig. 2F). At the invasive front, small follicles of KAM permeated widely between medullary bone trabeculae (Fig. 2G). Collectively, the recurrent lesion showed features of both acanthomatous change in a classic follicular AM with other areas of more classical KAM/SOKC. The patient has been followed for 7 years, and no sign of recurrence has been observed.

The term 'KAM' was coined by Pindborg⁴ in 1970 to describe a specific type of acanthomatous AM with microscopic features of keratinising cyst. Since then, many examples have appeared in the literature under a variety of names.^{1–3,5} Although there are well defined criteria for the histopathological diagnosis of KAM,⁵ this tumour was not recognised as a separate type of AM in the latest World Health Organization (WHO) classification,⁶ and the term 'KAM' itself has not been adopted. As evident in a review of SOKC by Zhang *et al.*,¹ many descriptive terms have been used,^{5,7} but in 2003 our group initially reported a recurrent OKC with invasive foci of KAM in the surrounding bone, applying the prefix 'solid-cystic tumour variant'.² With the accumulation of published cases, in 2012 we also provided evidence that SOKC and KAM are likely related entities, representing a continuous spectrum of a single tumour type.³ In the OKC section of the 2017 WHO classification, there is only a brief comment on SOKC as an evolving entity,⁶ and unlike KAM, no formal publication has yet defined SOKC on the basis of reproducible diagnostic criteria.¹ However, it is generally accepted that some OKCs are neoplastic in nature, and capable of transformation into AM, ameloblastic carcinoma or cystic squamous cell carcinoma reminiscent of carcinoma cuniculatum.^{8–10}

In the present case, the primary lesion fitted the category of UAM clinically, radiologically and pathologically.⁶ This UAM recurred 5 years after conservative surgery and showed an unexpected shift in morphology. The recurrent tumour was of the follicular type characterised by the absence of UAM architecture and the presence of dominant and distinctive areas of KAM/SOKC. There has been only a single reported case of recurrent UAM, expressing an unusual histological transformation.¹¹ The original UAM lesion recurred 23 years later in the form of granular/acanthomatous AM of the follicular type with invasive foci of squamous cell carcinoma, but with an absolute lack of KAM/SOKC features. There are two possible explanations for the natural history of the present lesion. The first is that, in addition to OKC, UAM may be another histogenetic source of KAM/SOKC. The second is that any change from UAM to KAM/SOKC may simply span a broad histological spectrum seen in AMs.

Considering that the histological subtypes of AM (including acanthomatous, granular and basaloid) are interchangeable in some circumstances and not permanent