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Reviews

The World Health Organization Histological Typing of Odontogenic Tumours. Introducing the Second Edition

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INTRODUCTION

THE FIRST WHO 'Histological Typing of Odontogenic Tumours, Jaw Cysts and Allied Lesions' was published 20 years ago, and in this 2nd edition [1] the basic framework of the Classification (see Table 1) remains essentially unchanged, with the same three main divisions: 'Neoplasms and Other Tumours Related to the Odontogenic Apparatus'; 'Neoplasms and Other Lesions Related to Bone', and 'Epithelial Cysts'. The last of these categories will not be discussed here; for a discussion of the whole revised Classification, together with key references, see Kramer *et al.* [2].

NEOPLASMS AND OTHER TUMOURS RELATED TO THE ODONTOGENIC APPARATUS

Recent advances in our understanding of the origins and the interactions of the odontogenic tissues have provided a sounder scientific basis for classification, but uncertainties remain. The classification used here is based firstly on behaviour, with a primary division into lesions generally regarded as 'benign' or 'malignant'.

The 'benign' category, which includes a number of entities that are probably or certainly non-neoplastic, is subdivided into three groups; lesions in which there is odontogenic epithelium without morphologically identifiable odontogenic ectomesenchyme; lesions in which both of these elements are identifiable (some with inductive changes leading to the formation of one or more of the dental hard tissues), and lesions in which odontogenic ectomesenchyme predominates although in some examples odontogenic epithelium may be 'included'. Here, the term 'included' is intended to indicate that if epithelium is present it appears to be included by chance rather than playing any essential role in the pathogenesis of the lesion.

In addition to a regrouping based on these subdivisions of the benign odontogenic tumours, there have been substantial changes in the section on ameloblastomas, some newly-recognised odontogenic tumours have been added, and some lesions designated in the first edition have been moved to another part of the classification or merged into different subgroups.

Amongst the ameloblastomas, there is now more detailed reference to the unicystic varieties, because both the surgical management and the prognosis of these lesions is often significantly different from that of other ameloblastomas. The desmoplastic ameloblastoma and the keratoameloblastoma are also discussed.

The squamous odontogenic tumour was first described after the publication of the first edition of the classification, and it has become accepted that this is a distinctive lesion rather than a variant of the ameloblastoma. Although it has an infiltrative pattern of growth, most examples respond to curettage, and recurrence is rare.

Another new addition is the clear cell odontogenic tumour, and few examples have been described so far. This too is a locally invasive neoplasm, but there is some evidence that it may be more aggressive than the ameloblastoma. Some examples may be frankly malignant (clear cell odontogenic carcinoma) and these are classified with the malignant variants of other odontogenic tumours.

Amongst the jaw lesions composed of proliferating odontogenic epithelium embedded in a cellular ectomesenchymal tissue that resembles the dental papilla, the compound and complex odontomas are clearly developmental anomalies: in their later stages they lay down increasing amounts of the dental hard tissues until the growth of the lesion is completed. However, if the lesion is excised before this final stage is reached, it may be difficult to distinguish the odontoma from other lesions that have the capacity for continued growth.

The ameloblastic fibroma is believed to be a true mixed tumour, in which both the epithelial and the ectomesenchymal elements are neoplastic. Lesions having a similar composition, but also showing inductive changes leading to the deposition of dentine alone, or dentine plus enamel, are termed ameloblastic fibrodentinoma (dentinoma in the previous classification) and ameloblastic fibro-odontoma, respectively. It is not clear whether the ameloblastic fibroma, ameloblastic fibrodentinoma and ameloblastic fibro-odontoma should be regarded as separate entities or as stages in the evolution of a single type of lesion, and there may be merit in continuing to separate them until more experience of their behaviour has been accumulated.

The odontoameloblastoma, another rare tumour, has a structure and behaviour like that of the ameloblastoma, but it also includes an odontoma-like element. It is important,

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Table 1. *WHO Histological Typing of Odontogenic Tumours. Second Edition*, 1992

1. Neoplasms and other tumours related to the odontogenic apparatus	
1.1. Benign	
1.1.1. Odontogenic epithelium without odontogenic ectomesenchyme	
1.1.1.1. Ameloblastoma	9310/0*
1.1.1.2. Squamous odontogenic tumour	9312/0
1.1.1.3. Calcifying epithelial odontogenic tumour (Pindborg tumour)	9340/0
1.1.1.4. Clear cell odontogenic tumour	9270/9
1.1.2. Odontogenic epithelium with odontogenic ectomesenchyme, with or without dental hard tissue formation	
1.1.2.1. Ameloblastic fibroma	9330/0
1.1.2.2. Ameloblastic fibrodentinoma (dentinoma) and ameloblastic fibro-odontoma	9290/0
1.1.2.3. Odontoameloblastoma	9311/0
1.1.2.4. Adenomatoid odontogenic tumour	9300/0
1.1.2.5. Calcifying odontogenic cyst	9301/0
1.1.2.6. Complex odontoma	9282/0
1.1.2.7. Compound odontoma	9281/0
1.1.3. Odontogenic ectomesenchyme with or without included odontogenic epithelium	
1.1.3.1. Odontogenic fibroma	†
1.1.3.2. Myxoma (odontogenic myxoma, myxofibroma)	9320/0
1.1.3.3. Benign cementoblastoma (cementoblastoma, true cementoma)	9273/0
1.2. Malignant	
1.2.1. Odontogenic carcinomas	
1.2.1.1. Malignant ameloblastoma	9310/3
1.2.1.2. Primary intraosseous carcinoma	9270/3
1.2.1.3. Malignant variants of other odontogenic epithelial tumours	‡
1.2.1.4. Malignant changes in odontogenic cysts	9270/3
1.2.2. Odontogenic sarcomas	
1.2.2.1. Ameloblastic fibrosarcoma (ameloblastic sarcoma)	9330/3
1.2.2.2. Ameloblastic fibrodentinosarcoma and ameloblastic fibro-odontosarcoma	9290/3
1.2.3. Odontogenic carcinosarcoma	8980/3
2. Neoplasms and other lesions related to bone	
2.1. Osteogenic neoplasms	
2.1.1. Cemento-ossifying fibroma (cementifying fibroma, ossifying fibroma)	§
2.2. Non-neoplastic bone lesions	
2.2.1. Fibrous dysplasia of the jaws	74910
2.2.2. Cemento-osseous dysplasias	
2.2.2.1. Periapical cemental dysplasia (periapical fibrous dysplasia)	9272/0
2.2.2.2. Florid cemento-osseous dysplasia (gigantiform cementoma, familial multiple cementomas)	9275/0
2.2.2.3. Other cemento-osseous dysplasias	
2.2.3. Cherubism (familial multilocular cystic disease of the jaws)	70980
2.2.4. Central giant cell granuloma	44130
2.2.5. Aneurysmal bone cyst	33640
2.2.6. Solitary bone cyst (traumatic, simple, haemorrhagic bone cyst)	33404
2.3. Other tumours	
2.3.1. Melanotic neuroectodermal tumour of infancy (melanotic progonoma)	9363/0
3. Epithelial cysts	
3.1. Developmental	
3.1.1. Odontogenic	
3.1.1.1. "Gingival cyst" of infants (Epstein pearls)	26540
3.1.1.2. Odontogenic keratocyst (primordial cyst)	26530
3.1.1.3. Dentigerous (follicular) cyst	26560
3.1.1.4. Eruption cyst	26550
3.1.1.5. Lateral periodontal cyst	26520
3.1.1.6. Gingival cyst in adults	26540
3.1.1.7. Glandular odontogenic cyst; sialo-odontogenic cyst	26520
3.1.2. Nonodontogenic	
3.1.2.1. Nasopalatine duct (incisive canal) cyst	26600
3.1.2.2. Nasolabial (nasoalveolar) cyst	26500
3.2. Inflammatory	
3.2.1. Radicular cyst	43800
3.2.1.1. Apical and lateral radicular cyst	
3.2.1.2. Residual radicular cyst	
3.2.2. Paradental (inflammatory collateral, mandibular infected buccal) cyst	26520

*Morphology code of the International Classification of Diseases for Oncology (ICD-O) and the Systematized Nomenclature of Medicine (SNOMED). †Central odontogenic fibroma 9321/0, peripheral odontogenic fibroma 9322/0. ‡Use appropriate tumour coding from 1.1 above, with behaviour code /3. §Ossifying fibroma 9262/0, cementifying fibroma 9274/0. 9262/0 is recommended for cemento-ossifying fibroma.

though sometimes difficult, to distinguish this neoplasm from an odontoma that has been excised whilst active but non-neoplastic odontogenic epithelium is still relatively abundant.

The calcifying odontogenic cyst was first described in 1962. Since then, studies on large numbers of cases have shown that the lesions of this group exhibit considerable diversity of structure and behaviour. Lesions corresponding most closely to the original description appear to be non-neoplastic; these are primarily cystic lesions, with the characteristic changes in their walls. Others (sometimes termed dentinogenic, or odontogenic, ghost cell tumour) are thought to be primarily neoplasms, with secondary changes similar to those in the calcifying odontogenic cyst. These may have an infiltrative pattern of growth. Although in the new classification they are still placed under the heading of calcifying odontogenic cyst, further experience may well provide reliable criteria for their separation.

Both the normal cementum that covers the root of the tooth, and the bundle bone that lines the socket, are formed by cells of, or derived from, the dental follicle. Apart from their different locations, on opposite sides of the periodontal ligament, the extent to which cementum and the adjacent bundle bone are different tissues is debatable. Also apparently composed of cementum are the "cementicles"—basophilic rounded masses found within the normal periodontal ligament and often partly fused with the cementum covering the root of the tooth.

A number of different jaw lesions also include a hard tissue resembling cementum, often in the form of rounded masses like "cementicles", and often accompanied by varying

amounts of tissue resembling either ordinary woven bone or metaplastic bone similar to that found in fibrous dysplasia. Some of these jaw lesions are clearly neoplastic, some are clearly non-neoplastic, and some are of uncertain status. However, typically cementum-like tissue is sometimes found in lesions of other parts of the skeleton, where it could not possibly be derived from the odontogenic apparatus. Therefore, it may be difficult to decide what is "cemental," what is "osseous," and how valid is the distinction.

Against this background, it is understandable that over the years there has been much wrestling with the classification of lesions that contain a cementum-like tissue, and it would be wrong to imply that the problems have been resolved. However, the picture does seem to be becoming clearer, and the new classification reflects the substantial changes in views of the cementum-containing lesions.

It is generally accepted that the benign cementoblastoma is a neoplasm, it almost always has a close relationship to the root of a tooth, and in the new classification it remains under the main heading of "Tumours and Other Lesions Related to the Odontogenic Apparatus." However, periapical cemental dysplasia, florid cemento-osseous dysplasia or gigantiform cementoma, and certain other less well-defined entities that formerly were grouped with the benign cementoblastoma under the heading "Cementomas" have now been transferred to the category of "Non-neoplastic Bone Lesions."

Myxoma of the jaws (odontogenic myxoma) is a benign but often ill-defined neoplasm that appears to have no counterpart elsewhere in the skeleton, and it is thought that this tumour is derived from the odontogenic mesoderm (ectomesenchyme). Generally the histological appearances are characteristic, but in the new edition attention is drawn to a common diagnostic trap. When a tooth fails to erupt, or if eruption is delayed, it may be found that the crown is surrounded by an area of radiolucency wider than that shown by the normal dental follicle; an appearance suggestive of a developing dentigerous cyst. Surgical exploration may reveal a soft and slightly mucinous tissue that histologically resembles the myxoma. Almost always, however, tissue with these features and in this particular location represents thickened dental follicle that has undergone a myxoid (but not a neoplastic) change.

In the part of the classification relating to odontogenic carcinomas and sarcomas, a separate category has been introduced for malignant variants of "other" odontogenic epithelial tumours ("other" than malignant ameloblastoma and primary intraosseous carcinoma), and a new category has been introduced for the very rare odontogenic carcinosarcoma.

NEOPLASMS AND OTHER LESIONS RELATED TO BONE

In the jaws there are rare encapsulated (or at least well-demarcated) fibroblastic tumours that contain cementum-like material, metaplastic bone, or any mixture of the two. These tumours continue to grow until they are removed, at operation they can often be shelled out, and in these respects they are unlike the lesions of fibrous dysplasia. Thus, they appear to be benign neoplasms of bone, and they have been placed in this category. It is now generally accepted that the examples in which the mineralised component is predominantly cementum-like (the "cementifying fibromas") and those in which the main mineralised component is bone (the "ossifying fibromas") simply represent the ends of a continuous spectrum. The differences in the hard tissue pattern do not seem to be reflected in differences in behaviour, and these tumours are now placed together under the title "Cemento-ossifying fibroma".

It is important to recognise that these are distinctive jaw lesions; they should not be confused (though they often are) with lesions also termed ossifying fibroma and occuring in other parts of the skeleton.

It has already been noted that, unlike the cemento-ossifying fibroma, fibrous dysplasia of the jaws is a non-demarcated lesion and it is self-limiting. However, after the active phase of the lesion has passed, the affected bone may never return to normal either radiographically or histologically. If such an area of old fibrous dysplasia is explored surgically the tissue shows a rather characteristic appearance, sometimes referred to as "osseous keloid." In this old fibrous dysplasia lesion the metaplastic bone of the active lesion has been replaced by lamellar bone, but the trabeculae tend to run parallel to one another and to be placed quite close together in a fibrous tissue that is still moderately cellular. This distinctive appearance is now described and illustrated.

Lastly, in the group of non-neoplastic bone lesions, a number of the cementum-containing lesions that previously were classified elsewhere have now been reclassified and join fibrous dysplasia of the jaws, cherubism, central giant cell granuloma, aneurysmal bone cyst and solitary bone cyst. Also, reflecting the growing belief that periapical fibrous dysplasia, florid cemento-osseous dysplasia (gigantiform cementoma) and some other cemental lesions may represent parts of a single spectrum rather than separate entities, they are now grouped together as "cemento-osseous dysplasias" although the named clinicopathological presentations mentioned are still listed.

The authors of the WHO Histological Typing of Odontogenic Tumours believe that the new classification provides a workable basis, and one that reflects current opinion and current uncertainty. The revised format of the classification represents an attempt to group the lesions (and especially those of the odontogenic apparatus) on a more logical basis. It should also be emphasised that, whilst immunohistochemical and other techniques have enhanced our understanding of the pathogenesis of odontogenic tumours, the emphasis throughout this text is upon features that are of diagnostic value and observable by routine, and widely available, conventional histological techniques.

It is current WHO policy that the volumes in this series should contain only a limited number of colour illustrations, in order to maintain a reasonable sales price. However, for this new edition of "Histological Typing of Odontogenic Tumours," generous financial support from a number of donors has made it possible for all of the photomicrographs to be in colour. Also, as in the previous edition, the illustrations include reproductions of clinical radiographs where these show distinctive features.

1. Kramer IRH, Pindborg JJ, Shear M. Histological Typing of Odontogenic Tumours. *WHO International Classification of Tumours*. Hamburg, Springer, 1992.
2. Kramer IRH, Pindborg JJ, Shear M. The WHO Histological Typing of Odontogenic Tumours. A commentary on the second edition. *Cancer* 1992, 70, 2988–2994.