

PII: S0959-8049(96)00527-8

Contra:

W.J. Mooi

Department of Pathology, Erasmus University, P.O. Box 1738, 3000 DR Rotterdam, The Netherlands

WHAT IS the likelihood of local tumour recurrence and metastatic spread? Where are metastases most likely to occur? What is the time interval in which most recurrences become clinically evident? What beneficial effect can be expected from adjuvant non-surgical therapies? These are some of the key questions which the histopathology report of a resected soft tissue sarcoma should provide answers to.

Unfortunately, there is no easy road to success, since the first step in the evaluation is, and remains, identification of the histological tumour type. This requires a detailed knowledge of the plethora of specific entities which have been recognised in soft tissue tumour pathology. Since many of these are rare, pathologists not working in specialised centres will not know most of them from personal experience. Moreover, many entities closely resemble each other histologically, so that their differential diagnosis requires a detailed knowledge of each, including age distributions, preferred sites, presenting symptoms, macroscopic and microscopic appearances as well as, in several instances, distinguishing features obtained by histochemistry, immunohistochemistry, electron microscopy and cytogenetics.

Since, as a group, soft tissue sarcomas are uncommon and are subdivided into so many different entities, there is an understandable desire to view (diagnose, treat) these tumours as a single group rather than as a heterogeneous collection of different entities. Accrual in clinical trials benefits from inclusion criteria allowing for various different sarcoma subtypes. This line of approach would appear to be supported by studies reporting prognostic significance of histological soft tissue grading, bypassing tumour type [1, 2]. Indeed, there is no doubt that, if grouped together, sarcomas can be subdivided into different groups with different prognosis, based on simple histological grading criteria [1–5], such as the mitotic count [2, 6, 7] and the presence or absence of necrosis [8, 9].

However, when applied to the individual case, such an approach has serious disadvantages and may easily lead to an inappropriate assessment of the key questions listed above. Some soft tissue sarcomas show few mitoses and lack necrosis, yet carry a guarded or even poor prognosis: examples include clear cell sarcoma of soft parts and alveolar soft part sarcoma. Others, such as infantile fibrosarcoma, have many mitoses, but a higher cure rate. Indeed, even within one type of differentiation, mitotic counts may have different meanings according to site, the best known example being smooth muscle tumours of the uterus versus those of the gastro-intestinal tract or soft tissues. Some tumours tend to recur locally, others at a distance, requiring different follow-up strategies.

Five-year disease-free survival equals cure in some sarcoma types, but only a 50% chance of cure in others.

If lung carcinomas, gastric carcinomas, colonic carcinomas and endometrial carcinomas were grouped together into one group of “visceral carcinoma”, such a heterogeneous group could probably be subdivided into subgroups with different grades, and it seems reasonable to assume that the group of visceral carcinomas with many mitoses would, as a group, carry a worse prognosis than those with few mitoses. However, no one would advocate grouping these tumours together. If fact, a similar grouping together of different types of sarcoma, from different sites of the body, can only be understood because of the relative rarity of these tumours and the difficulty that exists in the diagnosis of some of the individual histological types.

As stated above, there can be no doubt that the determination of the tumour type is the first and most important task of the diagnostic pathologist investigating a soft tissue tumour. A report of “spindle cell sarcoma, ‘x’ mitoses, no necrosis, therefore of intermediate grade”, would lack this information. Lack of precision in tumour typing cannot be compensated for by apparent precision in tumour grading.

At this juncture, it should be pointed out that apparently detailed and precise information on tumour grade tends to instill trust and confidence. A pathology report stating that a spindle cell tumour has two mitotic figures per 2 mm² and lacks necrosis and that as a consequence of these findings, the patient has a 90% chance of 5-year survival, would at first glance appear to be superior to a report merely stating that the tumour is a clear cell sarcoma. However, the latter statement may well be the more accurate one. Certainly, a clear cell sarcoma, a rare tumour which often exhibits few mitoses and in which necrosis is a rare finding, leads to the death of the patient in the majority of cases, sometimes after a disease-free period of many years. So, even if the figure of 90% 5-year survival may be correct for the *total* group of sarcomas lacking necrosis and showing few mitoses, this does not apply to the subgroup of clear cell sarcomas. A similar argument applies to alveolar soft part sarcomas, malignant granular cell tumours and a number of other sarcoma types.

Postoperative survival is not the only clinically relevant parameter. Chance of local recurrence (e.g. high tendency in fibromatosis and dermatofibrosarcoma protuberans), type of spread (e.g. lymph node metastases in epitheloid sarcoma, rhabdomyosarcoma, but not, or very rarely, in liposarcoma, fibrosarcoma) are also very important and are related to tumour type rather than grade. In addition, as-

sociations between a single entity and other associated disease and risk factors are less likely to be noticed, when the entity is not studied as a separate tumour type. Clinical relevance is not limited to tumour prognosis.

Finally, the main issue of clinical importance is the distinction between reactive or benign mesenchymal lesions on the one hand, and sarcomas on the other. Overdiagnosis and underdiagnosis of soft tissue sarcomas are both very serious problems, which result from the rarity and "worrisome" appearance of some sarcoma simulators, and from the deceptively "indolent" appearance of some sarcomas. It is the avoidance of such misinterpretations of soft tissue lesions which calls for a detailed knowledge of the many soft tissue entities that have been identified and documented.

Is there not place for sarcoma grading at all? There is. The points raised above are only intended to argue that proper tumour typing should be the basis of the evaluation. When this has been achieved, grading can, and should, be used as an *adjunct* in the assessment of several sarcoma types [10–13], based on various parameters. Some sarcoma types are always high grade. Since it is now clear that the biological behaviour of sarcomas varies according to histological tumour type, and that the significance of mitotic activity and (absence of) necrosis varies in different types of sarcoma [13], there is no place for grading systems which bypass tumour type. Sarcoma grading can never replace sarcoma typing, and in my opinion, any move in that direction should, therefore, be actively discouraged.

1. van Unnik JAM, Coindre JM, Contesso C, *et al.* Grading of

soft tissue sarcomas: experience of the EORTC Soft Tissue and Bone Sarcoma Group. *Eur J Cancer* 1993, **29A**, 2089–2093.

2. van Unnik JAM. Classification of soft-tissue sarcomas. *Hematol Oncol Clin North Am* 1995, **9**, 677–700.
3. Coindre JM, Trojani M, Contesso G, *et al.* Reproducibility of a histopathologic grading system for adult soft tissue sarcoma. *Cancer* 1986, **58**, 306–309.
4. Jensen OM, Hogh J, Ostgaard SE, Nordentoft AN, Sneppen O. Histopathological grading of soft tissue tumours. Prognostic significance in a prospective study of 278 consecutive cases. *J Pathol* 1991, **163**, 19–24.
5. Tomita Y, Kuratsu S, Naka N, *et al.* A staging system for soft-tissue sarcoma and its evaluation in relation to treatment. *Int J Cancer* 1994, **58**, 168–173.
6. Tsujimoto M, Aozasa K, Ueda T, Morimura Y, Komatsubara Y, Doi T. Multivariate analysis for histologic prognostic factors in soft tissue sarcomas. *Cancer* 1988, **62**, 994–998.
7. Singer S, Corson JM, Gonin R, Labow B, Eberlein TJ. Prognostic factors predictive of survival and local recurrence for extremity soft tissue sarcoma. *Ann Surg* 1995, **219**, 165–173.
8. Costa J, Wesley RA, Glatstein E, Rosenberg SA. The grading of soft tissue sarcomas. Results of a clinicohistopathologic correlation in a series of 163 cases. *Cancer* 1984, **53**, 530–534.
9. Kulander BG, Polissar L, Yang CY, Woods JS. Grading of soft tissue sarcomas: necrosis as a determinant of survival. *Mod Pathol* 1989, **2**, 205–208.
10. Leyvraz S, Costa J. Histological diagnosis and grading of soft-tissue sarcomas. *Semin Surg Oncol* 1988, **4**, 3–6.
11. Mandard AM, Petiot JF, Marnay J, *et al.* Prognostic factors in soft tissue sarcomas. A multivariate analysis of 109 cases. *Cancer* 1989, **63**, 1437–1451.
12. Hashimoto H, Daimaru Y, Takeshita S, Tsuneyoshi M, Enjoji M. Prognostic significance of histological parameters of soft tissue sarcomas. *Cancer* 1992, **70**, 2816–2822.
13. Enzinger FM, Weiss SW. *Soft Tissue Tumors*. St. Louis, MO, Mosby, 1995, 4–15.

PII: S0959-8049(96)00526-6

Arbiter:

M. Harris

Department of Pathology, Christie Hospital, Manchester M20 4BX, U.K.

I FIND myself in the difficult position of being the arbiter between two authors who do not disagree! Daugaard argues for the broad-based value of grading in assessing the prognosis of soft tissue sarcomas, whilst Mooi points out the primary importance of histological typing, arguing that in some cases the type is a good indicator of likely behaviour whereas grade can be misleading. However, both authors acknowledge that each parameter has its place in clinical prognostication and in trial analysis, and that there is an interplay between the two, a view with which I agree.

As an aside, it is remarkable that these traditional approaches remain the most useful tools and that they have not been supplanted by newer techniques such as ploidy measurements, proliferation indices, oncogene expression,

etc. Of course, such methods may eventually supplant classical histology, but in the meantime we should attempt to refine and adapt existing traditional grading systems and to define more precisely how they relate to histological type.

Difficulties exist because of the rarity of soft tissue sarcomas coupled with the wide range of histological subtypes. Thus, clinical studies tend to report on, at most, 200–300 cases and usually these are made up of many histological subtypes and sometimes even include visceral sarcomas along with soft tissue tumours. In these circumstances, the impact of a particular grading system on individual histological subtypes is impossible to determine statistically—only the overall picture can be assessed. There is a need to examine systematically the effectiveness of current grading