

Morphologic review of 1000 soft tissue sarcomas from the Scandinavian Sarcoma Group (SSG) Register

The peer-review committee experience

Jeanne M MEIS-KINDBLOM¹, Bodil BJERKEHAGE², Tom BÖHLING³, Henryk DOMANSKI⁴, Tore B HALVORSEN⁵, Olle LARSSON⁶, Peer LILLEN⁷, Olaf MYHRE-JENSEN⁸, Elisabeth STENWIG², Martti VIROLAINEN³, Helena WILLÉN⁴, Måns ÅKERMAN⁴ and Lars-Gunnar KINDBLOM¹

¹Sahlgrenska University Hospital, Gothenburg, Sweden; ²The Norwegian Radium Hospital, Oslo, Norway; ³University of Helsinki, Helsinki, Finland; ⁴University Hospital in Lund, Lund, Sweden; ⁵The Region hospital in Trondheim, Trondheim, Norway; ⁶Karolinska Hospital, Stockholm, Sweden; ⁷Haukeland Hospital, Bergen Norway; and ⁸Aarhus Hospital, Aarhus, Denmark

Correspondence: Lars-Gunnar Kindblom, M.D., Ph.D., Sahlgrenska Hospital, Dept. of Pathology, SE-413 45 Göteborg, Sweden

Since the SSG began 20 years ago, Scandinavian pathologists with a particular interest in soft tissue and bone tumors have met on a regular basis to discuss scientific and diagnostic issues and to review cases reported to the SSG Register which have caused diagnostic problems. The morphologic review of cases has been the basis for analyses with the aim to define morphologic and clinical prognostic factors for specific sarcomas and to provide meaningful clinical and morphologic information with regard to grading. The morphology group within the SSG has also formulated practical guidelines for the handling of surgical specimens and for the morphologic diagnosis of soft tissue and bone tumors, has participated in the design of numerous treatment protocols and treatment evaluation programs, and has organized specialty and multidisciplinary scientific and practical diagnostic seminars. In 1995, a more formalized peer-review committee with 10–11 pathologists representing Sweden, Norway, Finland, and Denmark was created. Since then, the committee has met regularly in Gothenburg, Sweden four to five times per year. To date, the committee has reviewed more than 1000 sarcomas in detail from the SSG Register, representing approximately one fourth of all cases.

Purpose of the peer-review

The goals of the peer-review committee were to: 1) evaluate the accuracy of the morphologic data in the SSG Register files; 2) re-evaluate and reclassify the

cases within the Register according to updated sarcoma classification schemes including new entities which had not been previously recognized and in light of recent technical advances; 3) provide a sound morphologic basis for studies which attempted to identify clinical and morphologic factors of prognostic significance and for studies which evaluated the effects of various treatment protocols; 4) set forth uniform guidelines and principles for morphologic–diagnostic procedures, histologic typing, grading of tumors, assessment of surgical resection margins, etc. at various Scandinavian sarcoma centers to facilitate and optimize treatment as well as comparison of cases; 5) increase morphologic expertise among the committee members as well as train younger pathologists; and 6) to transmit this knowledge to other pathologists within Scandinavia and internationally.

Design of the peer-review

Based upon the information in the SSG Register files (1986–1998), the participating pathology laboratories were asked to submit copies of the relevant clinical histories, pathology reports, routinely stained histologic slides or paraffin blocks, and when available, immunostains of the primary tumor. In some cases, reports of electron microscopy, DNA–ploidy, or cytogenetic analyses were available for review. A standardized protocol was used for the review process and was designed to include pertinent information regarding: 1) patient age and sex; 2) tumor site and depth; 3)

tumor size; 4) primary diagnosis; 5) peer-review committee consensus diagnosis (or alternative diagnoses when no consensus was reached); and 6) grade of the primary tumor at the time of diagnosis and grade of the primary tumor assigned by the peer-review committee based on a IV-tiered grading scheme. The grading scheme included factors such as cellularity, pleomorphism and nuclear atypia, necrosis, mitotic activity (rated as low, moderate or high), and the histologic diagnosis in those sarcomas in which grade and prognosis is inherently influenced by the type of sarcoma (Markhede et al. 1982; Angervall et al. 1986; Myhre-Jensen 1991; Gustafson 1994); 7) type of tumor interface with normal tissues (predominantly pushing versus infiltrative margins); 8) presence or absence of vascular invasion; and 9) need of additional analysis, in particular, immunostains, in order to arrive at a definite diagnosis.

Results

Of the more than 1000 cases reviewed thus far, the overwhelming majority of cases consisted of those with submitted diagnoses of malignant fibrous histiocytoma (MFH) (613 cases), liposarcoma (216) and synovial sarcoma (148); relatively small groups of osteosarcoma in the elderly and clear cell sarcoma were also reviewed. The details of the peer-review analysis and results of correlative clinicopathologic and prognostic studies regarding these entities will be presented in several ongoing projects. The histologic appearances of various lesions encountered in this series of cases are illustrated in Figures 1–18 and commented on in the Legends to the Figures.

Retained diagnoses

The peer-review committee consensus diagnosis was in agreement with the primary contributor's diagnosis regarding the diagnosis of sarcoma and the type of the sarcoma in 70% of reviewed cases. In 95% of these cases, there was also agreement in terms of grade of malignancy when low grade was equated with grade I and II tumors and high grade was equated with grade III and IV tumors. In 20% of the cases, the peer-review committee grading differed by one grade (either higher or lower) from that of the contributor; however, the tumor remained in the same low or high grade group as before.

The cases accepted within the MFH group (66%) revealed a wide morphologic spectrum, ranging from paucicellular myxofibrosarcomas with minimal atypia to highly cellular, large-cell, pleomorphic sarcomas. All cases demonstrating definite light micro-

scopic and/or immunohistochemical evidence of lipogenic, smooth muscle, striated muscle, nerve sheath, vascular or other type of differentiation were reclassified accordingly.

The cases accepted as liposarcoma (72%) could in most cases be subclassified as well differentiated (including sclerosing and lipoma-like types), myxoid or round-cell (or intermediate/mixed), pleomorphic, or dedifferentiated types. There were also examples of liposarcoma with unusual mixed or intermediate features as well as both low and high grade spindle cell variants.

The cases accepted as synovial sarcoma (85%) were subclassified as monophasic fibrous or biphasic type. Immunostains for EMA and/or cytokeratins were often required to confirm the diagnosis of monophasic synovial sarcoma. A subgroup of synovial sarcomas were additionally classified as poorly differentiated (i.e., they were highly cellular tumors with primitive cells showing prominent nuclear atypia, high mitotic activity and frequent necrosis) as previously described (Meis-Kindblom et al. 1996, Bergh et al. 1999).

Revised diagnoses

In 30% of the cases, the peer-review committee arrived at a different diagnosis than the original pathologist(s). In 20% of all cases, the committee *concurred with the diagnosis of sarcoma but reclassified the type of sarcoma*. In 20% of these, there was also a change in tumor grade but no change in high versus low grade sarcoma as defined previously. In 5% of cases in which the sarcoma diagnosis was reclassified, the committee revised the grade from low to high or high to low grade.

Most of the revised diagnoses involved cases which had originally been diagnosed as malignant fibrous histiocytoma (MFH); the majority of these were revised to diagnoses of fibrosarcoma, myofibroblastic sarcoma, spindle cell sarcoma not further classified, liposarcoma, and leiomyosarcoma. Rare examples of pleomorphic rhabdomyosarcoma, angiosarcoma, synovial sarcoma, malignant peripheral nerve sheath tumor, dermatofibrosarcoma protuberans, and osteosarcoma were also encountered. The reclassified sarcomas which had originally been diagnosed as liposarcoma were rediagnosed as myxofibrosarcoma, MFH, and extraskeletal myxoid chondrosarcoma. The reclassified "synovial sarcomas" were rediagnosed as fibrosarcoma, malignant peripheral nerve sheath tumor, myxofibrosarcoma, and spindle cell sarcoma not further classified.

In 2% of all cases, the committee arrived at an *al-*

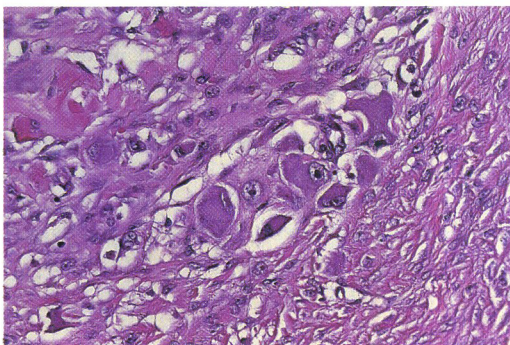


Figure 1. A case of proliferative fasciitis demonstrating pseudosarcomatous features such as vesicular nuclei, prominent nucleoli and cellular pleomorphism. Such cases are often mistaken for malignant fibrous histiocytoma.

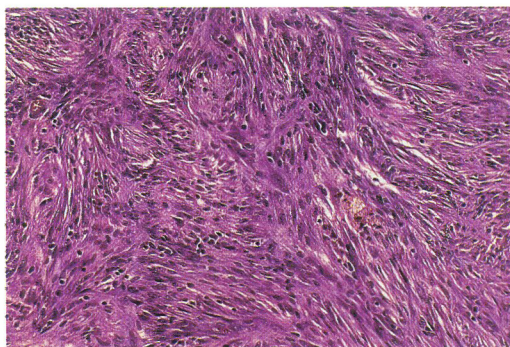
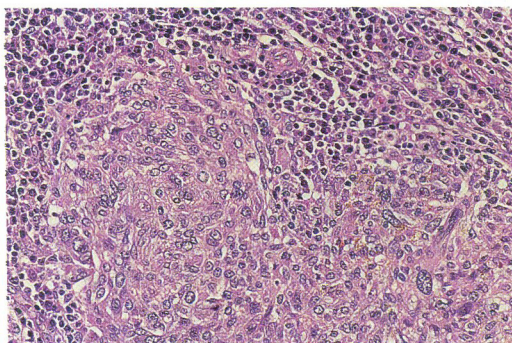


Figure 2. A cellular fibrous histiocytoma with a rather homogeneous proliferation of fibroblastic cells. Those cases of fibrous histiocytoma which lack a heterogeneous cell population (i.e., lack Touton-type giant cells, macrophages and hemosiderin deposition) are often mistaken for a fibrosarcoma or a malignant fibrous histiocytoma.



Figures 3 and 4. Angiomatoid malignant fibrous histiocytoma (also referred to as angiomatoid fibrous histiocytoma to underscore its low grade malignant behavior). The lymphoid cuff surrounding syncytial arrangements of fibroblastic-fibrohistiocytic cells in this tumor causes confusion with metastatic carcinoma and melanoma. The dilated, hemorrhagic pseudovascular spaces, plasma cells and bland nuclear features of the tumor cells are all clues to the correct diagnosis.

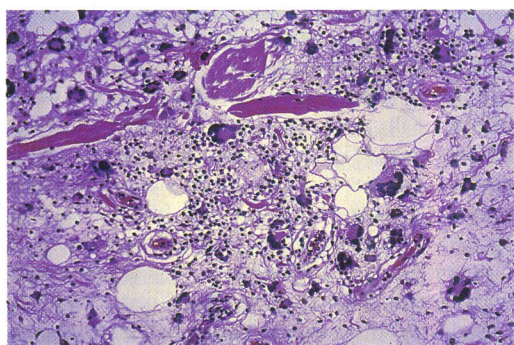


Figure 5. A pleomorphic lipoma simulating a well differentiated liposarcoma. Transitional forms containing bland spindle cells (i.e., mixed pleomorphic-spindle cell lipoma) attest to the close relationship between pleomorphic lipoma and spindle cell lipoma.

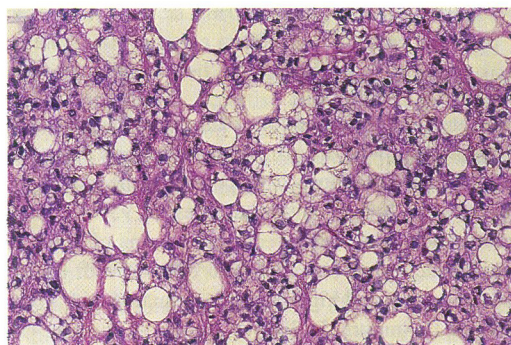
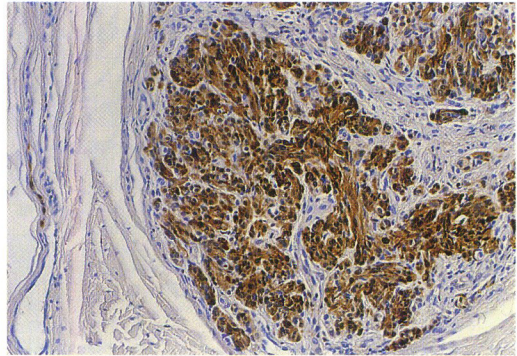
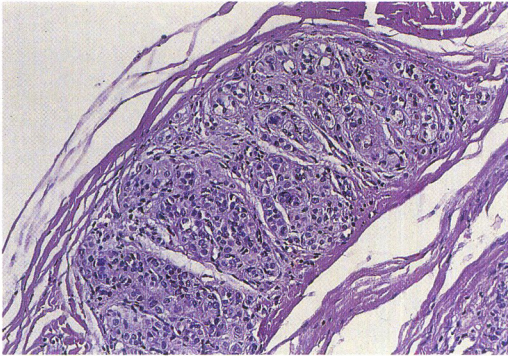


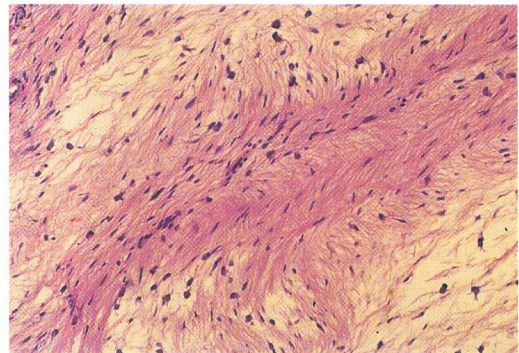
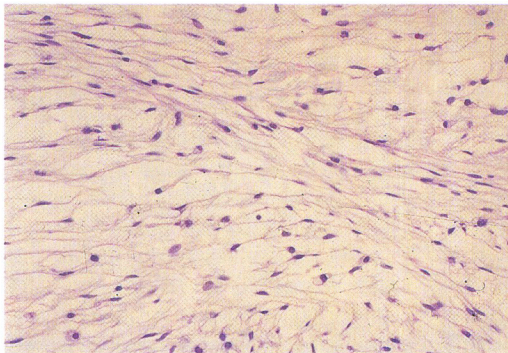
Figure 6. An example of a chondroid lipoma simulating a liposarcoma.

ternative non-sarcomatous malignant diagnosis that included primary or metastatic carcinoma and melanoma, malignant lymphoma, malignant mixed Müllerian tumor and mesothelioma. These revised diag-

noses were supported by additional immunostainings which were performed and then re-evaluated by the committee. In some cases, there was also follow-up information available which supported the revised di-



Figures 7 and 8. A benign epithelioid schwannoma demonstrating strong immunoreactivity for S100 protein.



Figures 9 and 10. Juxta-articular myxomas demonstrating increased cellularity and relative avascularity. Similar changes may be seen in intramuscular myxoma, causing misdiagnosis as a myxofibrosarcoma or malignant fibrous histiocytoma.

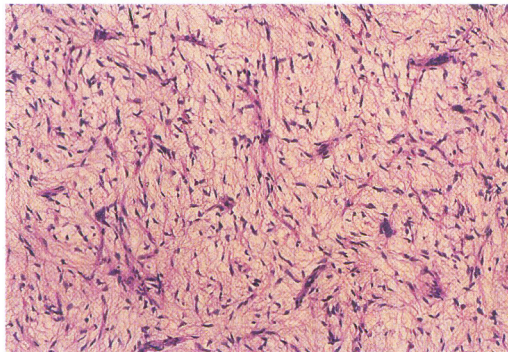


Figure 11. Myxofibrosarcoma demonstrating a uniform spindle cell proliferation similar to a myxoma. However, the degree of cellularity and vascularity are increased compared to myxoma (compare with Figures 9 and 10).

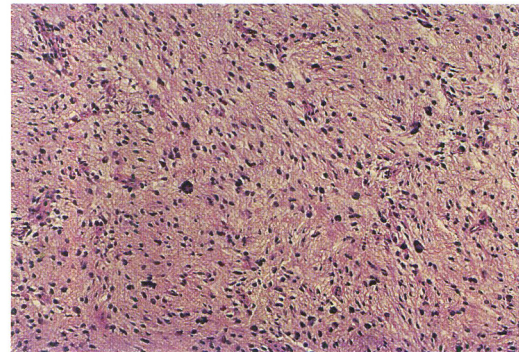


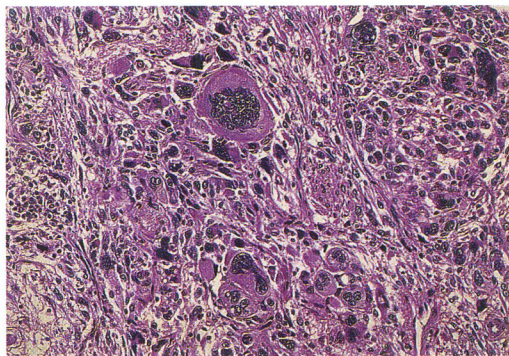
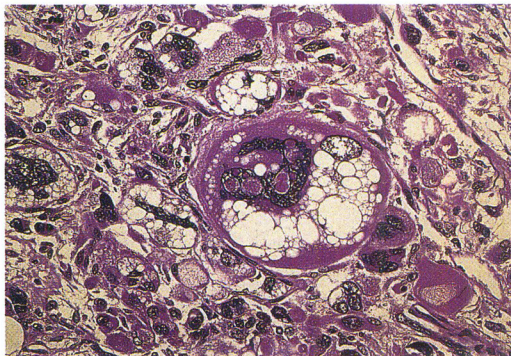
Figure 12. Malignant fibrous histiocytoma showing cellular pleomorphism and a focal storiform pattern.

agnosis of the committee.

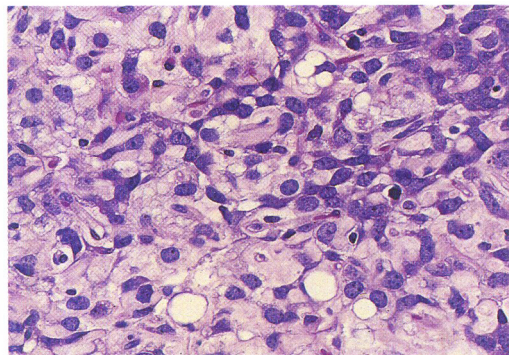
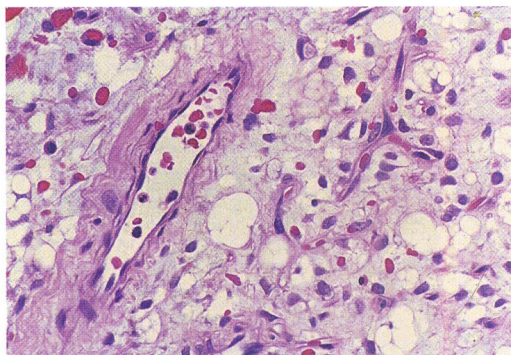
In 2% of all cases, the primary diagnosis was based upon material that was considered to be *insufficient, non-representative, artifactually distorted or otherwise unacceptable for diagnosis*. In some of these cases the tumors were inoperable and further attempts to obtain diagnostic material were not made.

Initially in 5% of all 1000 cases, the committee rendered a diagnosis of a *benign mesenchymal lesion* and in 1% a diagnosis of *uncertain malignant potential or a borderline malignant lesion*. All but one of these cases had originally been diagnosed as MFH or liposarcoma.

The benign diagnoses, in order of frequency in the



Figures 13 and 14. Pleomorphic liposarcoma with grotesquely enlarged lipoblasts. Other areas of the tumor (Figure 14) without lipoblastic differentiation are indistinguishable from MFH.



Figures 15 and 16. Myxoid liposarcoma and its cellular (round cell) variant. The delicate capillary-like vasculature and lipoblasts characteristically seen in the classical cases of myxoid liposarcoma are frequently obscured in the cellular-round cell examples of the tumor.

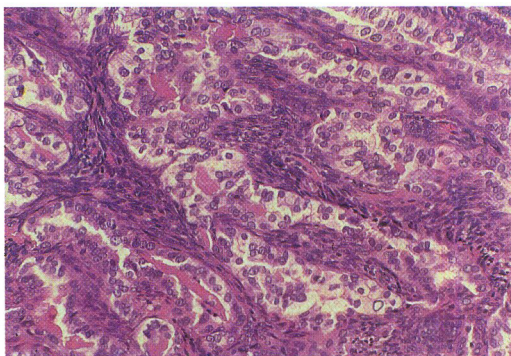


Figure 17. A typical example of biphasic synovial sarcoma.

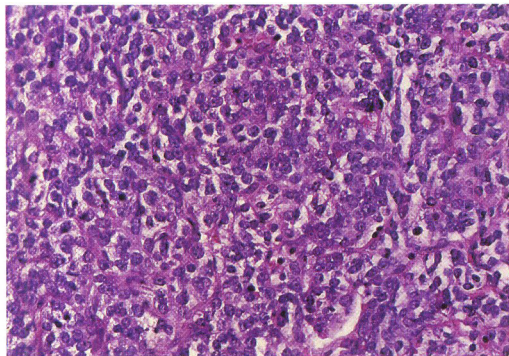


Figure 18. An example of a poorly differentiated synovial sarcoma simulating a small round cell malignant neoplasm such as Ewing's sarcoma—primitive neuroectodermal tumor. The poorly differentiated types of synovial sarcoma have a poor prognosis.

MFH group were: benign fibrous histiocytoma (particularly cellular and deep-seated variants) (Santa Cruz and Kyriakos 1981; Fletcher 1990); intramuscular and juxta-articular myxoma (Enzinger 1965; Kindblom et al. 1974; Meis and Enzinger 1992); spindle cell-pleomorphic lipoma (Angervall et al. 1976; Enzinger and Harvey 1975; Shmooker and Enzinger

1981); nodular and proliferative fasciitis (including a child) (Chung and Enzinger 1975; Dahl et al. 1972; Meis and Enzinger 1992); and xanthogranuloma. Tumors of uncertain malignant potential or borderline malignant tumors within the MFH group included: solitary fibrous tumor, dermatofibrosarcoma protuberans, Kaposi's sarcoma, angiomatoid (malignant)

fibrous histiocytoma (Enzinger 1979; Costa and Weiss 1990), mixed cutaneous tumor, and meningioma. The pseudosarcomatous lesions primarily diagnosed as liposarcoma included: intramuscular myxoma, spindle cell–pleomorphic lipoma, lipoma with regressive changes, and chondroid lipoma (Meis and Enzinger 1993; Kindblom and Meis–Kindblom 1995). The only “synovial sarcoma” reclassified as a “pseudosarcoma” was a recently described entity, benign epithelioid schwannoma (Kindblom et al. 1998). Of all the benign, pseudosarcomatous lesions, 75% had been misdiagnosed as a low grade (grade I or II) sarcoma and 25% as a high grade (grade III or IV) sarcoma.

Comments

The experience of the SSG peer review committee is in keeping with the general view that soft tissue tumor pathology is a particularly demanding and difficult diagnostic area. There are many reasons for this: the relative rarity of soft tissue lesions, the plethora of clinically and morphologically distinct entities that occur within soft tissues, their extremely wide clinical and morphologic spectrum, the difficulties in finding morphologic features that are prognostically significant for all types of sarcomas, and not least, the treacherous pitfalls of pseudosarcomas and malignant sarcomatoid lesions. Thus, more than one third of the sarcoma diagnoses in the SSG files were revised by the committee. It is noteworthy, however, that two thirds of these were reclassifications to a different type of sarcoma and in 95% of these cases, the grade of malignancy (low or high) was retained. Since most adult soft tissue sarcoma treatment protocols are not based on the specific type of sarcoma, the reclassification of the types of sarcomas in our study had little impact with regard to treatment.

It is clinically significant, however, that 5% of the reviewed cases were reclassified as benign lesions and that 1% were either borderline malignant or of uncertain malignant potential. The overwhelming majority of these cases (75%) had been misdiagnosed as a low grade sarcoma. Subsequently the patients either received no further treatment or they had extended local re-excisions of their primary tumors. In our review of over 1000 soft tissue sarcomas, there were only 3 cases in which adjunctive radiotherapy and/or chemotherapy was given after the misdiagnosis of a high grade sarcoma.

Other clinically significant misdiagnoses included those few cases of primary and metastatic carcinoma, melanoma, and less commonly lymphoma and mesothelioma which were called sarcomas. The treat-

ment in these cases would probably have differed significantly from a primary sarcoma.

Equally important were those cases in which the committee deemed that there was insufficient material for a histologic diagnosis. The reasons for this inadequacy included minimal tissue, artifactual damage or non-representative tissue. The pathologist should not be compelled to render a diagnosis under these circumstances, but rather should be encouraged to discuss the case further with the responsible clinician in order to understand the clinical picture better and to determine the feasibility of rebiopsy or other alternative diagnostic techniques such as fine needle aspiration. The committee also bore in mind that the primary pathologists in these cases may well have had access to additional clinical information and the benefit of ancillary diagnostic techniques which influenced their diagnoses and that the peer review committee may not have been aware of these other factors.

Considering all the problems in the morphologic diagnosis of soft tissue tumors, the quality and accuracy of the information in the SSG files is surprisingly good. The 90% concurrence rate between the SSG peer review committee diagnoses and the primary pathologists' diagnoses of sarcoma, 70% concurrence rate regarding tumor classification and the 95% rate of agreement with regard to tumor grade as well as the 5% rate of misdiagnosis of pseudosarcomas compares favorably to most consultation practices dealing with sarcomas. This is not surprising when one considers that the majority of the cases in the SSG files had been primarily diagnosed at a soft tissue sarcoma center somewhere in Scandinavia or were sent to a recognized soft tissue tumor expert. In fact, in a large percentage of the 1000+ cases reviewed in this study, one or more members of the committee had been involved in the primary diagnosis. The composition and size of the peer review committee is such that biases involved in reviewing ones' own diagnoses would be minimized by the review of several other pathologists as well as time (i.e., a pathologist does not remember all cases they have seen so he or she are probably objective when reviewing the case, the ideas and experience of a pathologist and the diagnostic criteria may change with time, and the clinical course of a patient may well indicate if there has been a serious misdiagnosis).

The percentage of misdiagnosed pseudosarcomas in the SSG files from 1986–1998 was significantly lower when compared to an older series of reviewed soft tissue sarcomas reported to the Swedish Cancer Register from 1958–1964 (Dahl and Angervall 1977). The reasons for the differences between the two series may be related to lack of expert consultation, lack of

centralization of sarcoma diagnosis and treatment, and lack of diagnostic ancillary techniques such as immunohistochemistry that are readily available today. Other reasons include an increased awareness of the more common pseudosarcomas among general surgical pathologists, such as nodular fasciitis and spindle cell lipoma, and the fact that some recently described entities, such as chondroid lipoma (Meis and Enzinger 1993), benign epithelioid schwannoma (Kindblom et al. 1998) and proliferative fasciitis in children (Meis and Enzinger 1992), were not recognized at that time; consequently they were misdiagnosed as malignant.

Most of the revised diagnoses of sarcoma occurred within the MFH and the liposarcoma groups. This is not surprising when one considers the problems involved in defining MFH and true lipogenic differentiation as well as controversies regarding the distinction between atypical lipoma, pleomorphic lipoma, and well differentiated liposarcoma. Myxofibrosarcoma (Angervall et al. 1977; Merck et al. 1983) is a relatively well-defined sarcoma in the fibroblastic–myofibroblastic–fibrohistiocytic spectrum that is commonly referred to as the myxoid variant of MFH (Weiss and Enzinger 1977; Weiss and Enzinger 1978; Kearney et al. 1980; Fletcher 1992). For the purposes of this review, we included all cases of myxofibrosarcoma within the category of MFH. We generally reserve the term high grade MFH for those grade sarcomas which have spindled, bizarre, pleomorphic but otherwise nondescript cells (Merck 1983). Many other sarcomas, such as leiomyosarcoma, liposarcoma, angiosarcoma, dermatofibrosarcoma protuberans and malignant peripheral nerve sheath tumor, may display high grade MFH-like areas. Such foci have generally been viewed as a form of tumor progression and in special instances referred to as “dedifferentiation” (Brooks 1986; Meis 1991; Fletcher 1992). Distinction of these tumors from MFH requires identification of better differentiated or more histologically characteristic areas within the tumor. Carcinomas, lymphomas, and melanomas (Lodding et al. 1990) may also simulate MFH. Consequently, the diagnosis of MFH is one of exclusion, often requiring extensive sampling of the tumor and application of ancillary diagnostic techniques such as immunohistochemistry or electron microscopy. It is therefore understandable that one third of cases in our review which were originally diagnosed as MFH were reclassified as another type of sarcoma with MFH-like features, or less frequently, as carcinoma, malignant melanoma, lymphoma, malignant mixed Müllerian tumor or mesothelioma. We suspect that even more cases could have been reclassified had there been fewer inadequate biopsies, more

extensive sampling of resected tumors and more immunostains performed at the time of the original diagnosis.

The review of liposarcomas within the SSG files illustrates many problems that frequently arise in the diagnosis of lipomatous tumors, including: 1) the distinction of cells with true lipogenic differentiation from other cells with vacuolated, clear cytoplasm; 2) the definition of lipoblasts and their significance; 3) the distinction of benign and reactive fatty lesions from true liposarcomas; 4) recognition of liposarcomas which do not fit into currently recommended classification schemes; and 5) distinction of liposarcoma from other malignancies invading fat.

The lowest incidence of revised diagnoses occurred among synovial sarcomas, which is not surprising in view of the characteristic histologic features of both the biphasic and monophasic fibrous types. Moreover, immunohistochemical and cytogenetic features further distinguish it from other spindled and epithelioid sarcomas. Only one benign lesion had been misdiagnosed as a synovial sarcoma in this series of cases; it was a benign epithelioid schwannoma, a recently described entity which is frequently mistaken for a sarcoma (Kindblom et al. 1998). These results are in stark contrast to an older Swedish series of synovial sarcomas in which 10% of the cases were reclassified as benign lesions, particularly pigmented villonodular tenosynovitis (Moberger et al. 1968).

The review committee attempted to reevaluate all cases according to a standardized protocol. This work was somewhat hampered by the highly variable degree of tissue sampling. In particular, tumor necrosis, vascular invasion and type of tumor interface with the surrounding tissues were often impossible to evaluate due to poor sampling of the specimen. This experience has led to the development of detailed guidelines for the handling of soft tissue tumor specimens and standardized protocols for reporting the histopathologic findings; these guidelines have been forwarded to all pathology departments in Scandinavia. These guidelines include, among other things, a recommendation of one block per cm. of tumor, using the largest tumor dimension (e.g., a minimum of 5 blocks from a 5 x 4 x 3 cm tumor). Sections from the tumor interface with surrounding normal tissues (i.e., the periphery of the tumor) are highly recommended to evaluate whether the tumor interface is predominantly pushing or infiltrative and to better assess vascular invasion. We believe that the standardized reporting protocol we developed will improve the quality and clinical utility of the pathology report as well as facilitate future review of cases.

Ethical issues involved in revision of histologic

misdiagnoses of clinical significance have arisen in the course of our review, indicating the need for adequate planning before embarking upon such a project. Our review was not blind (i.e., the patient identity was known in all cases). Moreover, the cases were relatively recent and many of the patients still alive. Several are being followed regularly for their originally diagnosed tumors. These misdiagnoses affect not only the patients and the pathologists involved in the case, but other clinical specialties within the SSG as well. A decision has now been made to provide the heads of all contributing pathology departments with the peer review committees protocol in all reviewed cases, including those with a revised diagnosis. How to proceed with the information in the latter group is currently under discussion with medical–legal experts.

The size and composition of the peer review committee was designed to be representative of all participating Scandinavian countries, to represent all major sarcoma centers, and to include the most experienced soft tissue pathologists as well as to provide younger pathologists with the opportunity to see a large number of cases in a relatively short period of time. The peer review process has been a pleasant, enlightening, and profitable experience for all of its members, regardless of their prior level of expertise. It has fostered greater collegiality among its members, and it has provided a sound basis for future clinicopathologic studies and evaluation of treatment protocols. Hopefully the feedback of the peer reviewed protocols received by the contributing pathology departments and the suggested guidelines of the committee regarding specimen handling and standardized pathology reports will improve the quality of morphologic diagnosis of soft tissue tumors.

Conclusions

1. Morphologic re-evaluation of the diagnosis and assignment of malignancy grade in all sarcomas within the SSG Register is essential for studies which attempt to correlate the clinical and morphologic factors with prognosis.
2. The rarity and extremely wide morphologic spectrum of soft tissue sarcomas as well as its simulators (including melanoma, lymphoma and carcinoma as well as pseudosarcomatous benign neoplastic and reactive lesions) make the morphologic diagnosis of soft tissue tumors particularly demanding. A multidisciplinary, center-based approach to their diagnosis involving integration of clinical, radiographic, molecular biologic and genetic information with the histologic findings is therefore

essential not only for diagnostic accuracy in the individual case but also to obtain and maintain diagnostic expertise in the area. In difficult and rare cases, a second opinion or diagnosis by two independent experts is highly encouraged.

3. The application of guidelines for the handling of surgical specimens and the use of standardized forms or protocols for reporting the diagnosis improve the quality and utility of the pathologic diagnosis.
4. Before a systematic pathologic review of cases by a committee is undertaken, there should be a plan which addresses how to handle those cases in which there is a major diagnostic revision which affects treatment and prognosis.
5. The creation of a SSG peer review committee has helped to standardize sarcoma diagnoses in Scandinavia, provided the opportunity to review a large series of rare tumors in a short period of time, provided young pathologists on the committee with a unique opportunity to gain diagnostic expertise in soft tissue sarcomas, and has facilitated the development of a system whereby contributing pathologists receive feedback and instructive or educational information regarding their cases.

Acknowledgement

Financial support was granted by the Nordic Cancer Union.

- Angervall L, Dahl I, Kindblom L–G, Säve–Söderbergh J. Spindle cell lipoma. *Acta Path Microbiol Scand* [A] 1976; 84: 477–7.
- Angervall L, Kindblom L–G, Merck C. Myxofibrosarcoma, a study of 30 cases. *Acta Pathol Microbiol Scand* 1977; 85:[A]: 127–40.
- Angervall L, Kindblom L–G, Rydholm A, Stener B. The diagnosis and prognosis of soft tissue tumors. *Sem Diagn Pathol* 1986; 3: 240–58.
- Bergh P, Meis–Kindblom J M, Gherlinzoni F, Berlin Ö, Bacchini P, Bertoni F, Gunterberg B, Kindblom L–G. Synovial sarcoma: Identification of high and low risk groups. *Cancer* 1999; (in press).
- Brooks J J. The significance of double phenotypic pattern markers in human sarcomas. A new model of mesenchymal differentiation. *Am J Pathol* 1986; 125: 113–23.
- Chung E B, Enzinger F M. Proliferative fasciitis. *Cancer* 1975; 36: 1450–8.
- Costa M J, Weiss S W. Angiomatoid malignant fibrous histiocytoma. A follow–up study of 108 cases with evaluation of possible histologic predictors of outcome. *Am J Surg Pathol* 1990; 14: 1126–32.
- Dahl I, Angervall L, Magnusson S, Stener B. Classical and cystic nodular fasciitis. *Pathol Eur* 1972; 7: 211–21.

- Dahl I, Angervall L. Pseudosarcomatous lesions of the soft tissues reported as sarcoma during a 6-year period (1958–1963). *Acta Path Microbiol Scand Sect A* 1977; 85: 917–30.
- Enzinger F M. Intramuscular myxoma. A review and follow-up study of 34 cases. *Am J Clin Pathol* 1965; 43: 104–13.
- Enzinger FM, Harvey DA. Spindle cell lipoma. *Cancer* 1975; 36: 1852–9.
- Enzinger F M. Angiomatoid malignant fibrous histiocytoma. A distinct fibrohistiocytic tumor of children and young adults simulating a vascular neoplasm. *Cancer* 1979; 44: 2147–57.
- Fletcher C D M. Benign fibrous histiocytoma of subcutaneous and deep soft tissue: A clinicopathologic analysis of 21 cases. *Am J Surg Pathol* 1990; 14: 801–9.
- Fletcher C D M. Pleomorphic malignant fibrous histiocytoma: Fact or fiction? A critical reappraisal based on 159 tumors diagnosed as pleomorphic sarcomas. *Am J Surg Pathol* 1992; 16: 213–28.
- Gustafson P. Soft tissue sarcoma. Epidemiology and prognosis in 508 patients. *Acta Orthop Scand (suppl 259)* 1994; 65: 1–31.
- Kearney M D, Soule E H, Ivins J C. Malignant fibrous histiocytoma. A retrospective study of 167 cases. *Cancer* 1980; 45: 167–78.
- Kindblom L–G, Stener B, Angervall L. Intramuscular myxoma. *Cancer* 1974; 34: 1737–44.
- Kindblom L–G, Meis–Kindblom J M. Chondroid lipoma: A detailed ultrastructural and immunohistochemical study with further observations regarding its differentiation. *Hum Pathol* 1995; 26: 706–15.
- Kindblom L–G, Meis–Kindblom J M, Havel G, Busch C. Benign epithelioid schwannoma. *Am J Surg Pathol* 1998; 22: 762–70.
- Lodding P, Kindblom L–G, Angervall L. Metastases of malignant melanoma simulating soft tissue sarcoma: a clinicopathologic, light and electron microscopic and immunohistochemical study of 21 cases. *Virchows Arch A* 1990; 417: 377–88.
- Markhede G, Angervall L, Stener B. A multivariate analysis of the prognosis after surgical treatment of malignant soft tissue tumors. *Cancer* 1982; 49: 1721–33.
- Meis J M. “Dedifferentiation” in bone and soft tissue tumors: A histological indicator of tumor progression. *Pathol Annu* 1991, Part I, edited by P.P. Rosen and R.E. Fechner; Appleton & Lange, Norwalk, pp. 37–62.
- Meis J M, Enzinger F M. Proliferative fasciitis and myositis of childhood. *Am J Surg Pathol* 1992; 16: 364–72.
- Meis J M, Enzinger F M. Juxta-articular myxoma: A clinical and pathologic study of 65 cases. *Hum Pathol* 1992; 23: 639–46.
- Meis J M, Enzinger F M. Chondroid lipoma: A unique tumor simulating liposarcoma and myxoid chondrosarcoma. *Am J Surg Pathol* 1993; 17: 1103–12.
- Meis–Kindblom J M, Stenman G, Kindblom L–G. Differential diagnosis of small round cell tumors. *Seminars in Diagn Pathol* 1996; 13: 213–41.
- Merck C, Angervall L, Kindblom L–G, Oden A. Myxofibrosarcoma—a malignant soft tissue tumor of fibroblastic–histiocytic origin; a clinicopathologic and prognostic study of 110 cases using multivariate analysis. *Acta Pathol Microbiol Scand* 1983; [A, Suppl 282].
- Moberger G, Nilsson U, Friberg S Jr. Synovial sarcoma. Histologic features and prognosis. *Acta Orthop Scand* 1968; Suppl 111.
- Myhre–Jensen O, Högh J, Östgaard S E, Nordentoft A M, Sneppen O. Histopathological grading of soft tissue tumors: prognostic significance in a prospective study of 278 consecutive cases. *J Pathol* 1991; 163: 19–24.
- Santa Cruz DJ, Kyriakos M. Aneurysmal (“angiomatoid”) fibrous histiocytoma of the skin. *Cancer* 1981; 47: 2053–61.
- Shmookler B M, Enzinger F M. Pleomorphic lipoma: A benign tumor simulating liposarcoma. A clinicopathologic analysis of 48 cases. *Cancer* 1981; 47: 126–133.
- Weiss S W, Enzinger F M. Myxoid variant of malignant fibrous histiocytoma. *Cancer* 1977; 39: 1672–89.
- Weiss S W, Enzinger F M. Malignant fibrous histiocytoma. An analysis of 200 cases. *Cancer* 1978; 41: 2250–66.