Cajal cells. This marker is the best to define GISTs, as almost all of these tumors (leiomyomas and schwannomas excluded) are positive. In our experience, other CD34-positive tumors, such as solitary fibrous tumor, hemangiopericytoma and Kaposi's sarcoma, are negative but some primitive sarcomas have been positive. CD117-positive GISTs, especially the malignant ones, may also have c-kit gene mutations.

MyoDi is a transcriptional regulator present in developing skeletal muscle. It has been proven to be a sensitive and specific marker for rhabdomyosarcomas of children and adults, including poorly differentiated variants. This antigen is localized in the nucleus but cytoplasmic staining may be seen in non muscular tumors.

Cytoskeletal proteins of muscle cells, such as actin and myosin isoforms, have been shown to be useful in the evaluation of myofibroblastic, smooth muscle, pericytic and skeletal muscle differentiation; antibodies specific to smooth muscle, skeletal muscle, and cardiac isoforms of actin and myosin are available. Other cytoskeleton-associated proteins are also of interest and they include calmodulin, tropomyosin and isoforms of caldesmon and calponin.

Tyrosinase and melan-A (MART = melanoma antigen recognized by T-cells) are new markers for melanocytes. Both have been reported to be approximately equally sensitive as HMB-45 (80-90%) to detect amelanotic melanomas. Reactivity for both antigens is also seen in clear cell sarcoma of tendons and aponeuroses and melan-A is expressed in angiomyolipomas, lymphangiomyomas and related tumors. Melan-A may also react with adrenal cortical carcinomas.

Osteocalcin is a bone matrix protein, which appears specific for osteoid matrix, It has been employed in the analysis of skeletal and extraskeletal osteosarcomas, and found positive in both, while other tumor shave been negative. Osteonectin, another bone matrix protein, appears not specific and is present in many cell types including subsets of fibroblasts.

Fine needle aspiration in the diagnosis of soft tissue tumors in Sweden. A little goes a long way

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Fine needle aspiration (FNA) cytology has a long history and a strong tradition in Sweden. Pioneering work was done by well-known names such as S~derstr~m, Franzen, Zajicek, Esposti and Lowhagen.

In our hospital, FNA started in the beginning of the 1960s. Today, we analyze 6-7,000 FNA per year; about 70% of these are taken by the cytopathologist and the remainder is taken by clinicians and radiologists. Our files contain more than 150,000 cases and 4-5,000 of these are soft tissue lesions. All slides and reports are archived and since 1983, patient data and diagnosis have been registered in computer files. Currently, at the G6teborg Musculoskeletal Center at Sahlgrenska University Hospital in G6teborg, Sweden, FNA is considered to be a routine preoperative diagnostic procedure in the investigation of bone and soft tissue lesions. Biopsies for ENA are easily taken from almost any organ or lesion. The procedure causes little discomfort for the patient and can be performed without anesthesia on an outpatient basis. Complications are rare and, if any, almost always of minor significance. Soft tissue lesions in subcutaneous tissue are biopsied through the vertex of the lump. The aspiration site of more deeply located soft tissue and bone lesions, as well as the maximum depth of biopsy, are decided with the orthopedic surgeon. The FNA site is tattooed by the cytopathologist after biopsy. All biopsies are performed with needles with an 0.6-0.7 mm outer diameter. The number of passes varies according to the macroscopic yield but is usually 3-5 passes. After smearing, most slides are air-dried and stained according to May-GrQnewald-Giemsa. Slides are also fixed in alcohol and stained according to Papanicolaou or with hematoxilyn and eosin. Material is also usually collected in PBS for Cytospin preparation and immunocytochemistry.

In our hospital, the orthopedic tumor surgeons became interested early on in the development of FNA as a preoperative diagnostic procedure. Open surgical biopsy may be technically difficult to perform on bone and soft tissue tumors; it may also increase the risk of local recurrence after definitive surgery. In certain instances, surgical removal can be performed without a prior morphological diagnosis, provided clinical and radiographic findings indicate that the lesion is a primary tumor best treated by surgery and that the operative procedure does not lead to a significant functional loss. Usually, however, a preoperative diagnosis is mandatory to determine whether the lesion is reactive or neoplastic, benign or malignant, primary or metastatic, and to exclude lymphomas and other hematopoietic malignancies as well as those sarcomas that require therapy other than primary surgery. If the planned surgical procedure could lead to functional loss, a preoperative morphological diagnosis is mandatory. Based on our experiences with FNA in the preoperative diagnosis of soft tissue and bone tumors, we believe that:

i) FNA must always be interpreted in the context of the clinical findings and imaging studies. Accurate interpretation of FNA of bone and soft tissue lesions requires a high level of morphological expertise since these are relatively rare tumors with a wide cytologic-histologic spectrum, replete with diagnostic pitfalls. Therefore, FNA of primary bone and soft tissue lesions should be performed only at medical centers with expertise in the diagnosis and treatment of such tumors.

ii) With FNA, sufficient material is obtained in 85-90% of cases to ascertain whether a lesion is primary or metastatic, benign or malignant and low- or high-grade malignant. In many cases, a specific diagnosis can be rendered or suggested. FNA of bone and soft tissue tumors also provides useful information about which tumors should be targeted for further investigation (such as morphological, cytogenetic, molecular biological studies) at the time of surgical resection.

iii) FNA is an easy, fast and cost-effective method for morphologic diagnosis that does not, with the exception of small children, require any anesthesia.

iv) FNA entails many of the same diagnostic problems and pitfalls that open biopsies of bone and soft tissue lesions have. However, FNA allows more extensive, representative sampling than an open biopsy and can be guided by imaging procedures such as CT and ultrasound.

v) When FNA is used as the primary diagnostic procedure, a less

radical or mutilating surgery can be performed in many instances.

vi) May-GrQnewald-Giemsa staining and a staining based on alcohol fixation (hematoxylin-eosin or Papanicolaou) often supplement each other and both should be used.

vii) Embedding of FNA is useful for preservation of architecture (light microscopy) and for ultrastructural and immunohistochemical analysis.

viii) FNA are well suited for DNA ploidy studies, cytogenetics, fluorescence *in situ* hybridization (FISH) and polymerase chain reaction (PCR) analyses.

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Fine needle aspiration of soft tissue tumors: The Mayo Clinic perspective

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Fine needle aspiration (FNA) biopsy of bone and soft tissue tumors has been in use at the Mayo Clinic since 1993. It was introduced in our routine practice due to the need for a fast diagnosis of bone and soft tissue sarcomas which would allow appropriate therapeutic management of the patients with high-grade sarcomas undergoing preoperative chemotherapy or radiotherapy in order to facilitate conservative surgical resections.

At the Mayo Clinic, the procedure for FNA is done at two different locations: at the outpatient building and at St. Mary's Hospital. The procedure is performed more frequently by a radiologist and less frequently by a surgeon. The pathologist does not perform the aspiration at the Mayo Clinic.

In approximately 80% of the cases, at least two passes are done. The first pass is done with a 23- or 24-gauge needle to obtain fluid that is smeared and immediately fixed in alcohol. After the smears are obtained, a second pass is performed with a Tru-cut needle to obtain a fragment of tissue that is immediately put in saline. In several cases, more than two passes are performed and numerous smears and fragments of tissue are obtained. The smears and the tissue fragments are sent to the frozen section laboratory of each hospital where the smears are stained using a modified, fast Papanicolaou method; no Duff-Quick is performed. If the immediate examination of the smears yields a negative result, the biopsy fragment, or fragments, are frozen and examined until we obtain a positive diagnosis or confirm the negative result found with the examination of the smears. If the immediate examination of the Papanicolaou-stained smears yields a positive result, the tissue fragment, or fragments, are immediately placed in 10% formalin and routinely processed to permit the appropriate classification of the tumor,as well as to permit the use of ancillary techniques. The negative or positive result is immediately reported to the performing physician and the FNA procedure is repeated if the result does not correlate with the clinical findings. The next day, the final result is communicated to the patient's physician.

Since we have tissue available for examination in the vast majority of the cases, no cell block is necessary in our practice. In only a few cases, about 20% of the total number, only smears are sent with no tissue available. These cases correspond to cases in which a benign diagnosis, such as infection, is strongly suspected and in such cases, no tissue is available. Despite the fact that we have tissue fragments in almost every case, we report a nonbiased cytologic diagnosis in every case before the tissue fragment is examined.

From January 1,1993 to December 31, 1996, we examined 222 FNA biopsies at the Mayo Clinic with 124 of them (56%) yielding positive results. Considering only the diagnosis of the Papanicolaou-stained smears, we had 52 false-negative (23.4%) cases. However, after the examination of the tissue, this figure dropped to 13 false-negative (5.9%) cases. The tumors that yielded false-negative cytologic results were 25 benign tumors and 27 sarcomas and the most common histopathological types associated with false-negative cytology were osteosarcoma, desmoid tumor and well-differentiated liposarcoma.

Considering only the recorded diagnosis of the Papanicolaou-stained smears, we had seven false-positive (3.2%) cases. These seven cases are the following: a hemangioma called suspicious for sarcoma; an aneurysmal bone cyst interpreted as giant cell tumor; a cellular schwannoma diagnosed as spindle cell sarcoma; a synovial chondromatosis in which the smears were considered consistent with chondrosarcoma; a glomus tumor that was erroneously interpreted as small round cell sarcoma; and two cases of abscesses with organization that were mistaken for possible spindle cell sarcomas. However, after the histopathological examination of the tissue fragments, just one of the seven cases was erroneously diagnosed. It was a cellular schwannoma showing mitotic activity and degenerative cellular atypia in which the examining pathologist failed to observe the misleading features and did not ask for an SiQO protein stain. The patient was operated on after receiving preoperative radiotherapy and the diagnosis of cellular schwannoma was rendered after the examination of the surgical specimen.

At the Mayo Clinic, we feel comfortable with the possibility of having tissue fragment(s) to corroborate the cytologic diagnosis and we strongly recommend its use since, in our hands, it is providing efficient results associated with no clinical complications.