REX HEALTHCARE

Laboratory Bulletin...

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Fine Needle Aspiration of the Breast: Is There a Role for This Diagnostic Tool?

Prostatic fine needle aspiration was developed to provide a less aggressive, but reliable method of diagnosing prostate adenocarcinoma in lieu of large core biopsies. With the advent of ultrasound directed smaller core devices, the interest in prostate fine needle aspiration has remarkably waned with time. The same situation has developed in the area of breast pathology. Now, there are multiple diagnostic tools available to diagnose breast carcinoma. These include the ultrasound directed biopsy devices, stereotactic biopsies and the ABBI procedure. Each of these devices provide the pathologist with a tissue rather than a purely cellular specimen. The morphologic advantage of these devices over fine needle aspiration is the capability of providing tissue architectural integrity to differentiate intraductal from invasive ductal carcinoma.

Fine needle aspiration, however, is a cost-effective method of sampling and evaluating recurrent breast cysts with or without a residual mass. In addition, benign fibroadenomata usually display a characteristic cytologic pattern.

A correlation study involving 118 paired cases between fine needle aspiration of the breast and follow-up surgical biopsy confirmation has been completed at Rex for 1996 and 1997. The sensitivity of the aspiration test was 65% for the two years and was low, considering acceptable sensitivity is greater than 90-95%. A review of all the false negatives confirmed the absence of malignant cells in 7 of 8 false negative cases. This finding implies that sampling error is an important factor in the aspiration procedure and ideal specimen preparation is crucial in attempting to reduce the preanalytic error rate.

For breast cysts, we recommend placing the fluid contents of the cyst in their entirety in a transport fluid media (i.e., Cytolyte solution) and sending the transport material to the laboratory directly with the appropriate label and paperwork. For solid lesions or masses, we recommend at least 3-4 passes be made. The first two passes are dedicated to direct smear preparation, and are prepared in a similar fashion to a peripheral blood smear. From the first two passes, one slide from each pair of slides is allowed to air dry and the other is fixed in 95% alcohol. The remaining one or two passes should be expelled into Cytolyte solution. Both the smears and Cytolyte solution must be appropriately labeled and sent together with the corresponding paperwork. Instructional material for physician office staff for specimen preparation is available upon request. Please contact either Dr. Nance at 784-3286 or Dr. Sorge at 784-3062 for additional information concerning this topic.

John P. Sorge, MD

The PT Ratio Says Goodbye

The Prothrombin time (PT) ratio and the International Normalized Ratio (INR) are currently included on the laboratory reports when a PT is requested. However, the PT ratio is no longer considered useful in monitoring patients on anticoagulant therapy. Its inclusion on the report is no longer necessary and may lead to confusion. Therefore, as of June 1 the PT ratio will no longer be reported.

The INR was introduced about 10 years ago as a means of normalizing PT values between laboratories. For the majority of patients, an INR between 2.0 and 3.0 is therapeutic for venous thrombosis. Numerous studies have documented that use of the INR improves the overall control of oral anticoagulation and lessens potential complications. A recent study of Canadian physicians has documented an increased desire for INR reporting, either as INR only or as INR plus PT in seconds.

The INR adjusts for the difference in sensitivity of individual thromboplastin reagents to a universal standard with a known relationship to the antithrombotic effects of oral anticoagulants. The American College of Chest Physicians recommends that all laboratories use thromboplastins with increased sensitivity rather than the less sensitive ones currently in use in many laboratories. As the reagents used in laboratories become more sensitive, the normal (baseline) PT and the therapeutic range in seconds for oral anticoagulants will increase. The INR will still have the same therapeutic range, i.e. 2.0 to 3.0, but the normal range of the PT in seconds may be longer compared to current values.

Reference:
Brigden, M., Johnson, M, INR reporting in Canadian Medical Laboratories, An update. Am. Journal of Clinical Pathology, 1998;103:589-594.

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Tick-Borne Disease in North Carolina

Rocky Mountain Spotted Fever

The most commonly reported tick-borne disease across the state is Rocky Mountain spotted fever (RMSF), with anywhere from 30-300 cases per year. The vector of this disease is the American dog tick *Dermacentor variabilis*, which transmits the microorganism *Rickettsia rickettsii*, the causative agent of RMSF. This gram negative microbe is an obligate intracellular bacterium that grows inside human endothelial cells. The disease can be quite severe, even fatal, especially if not promptly treated with appropriate antibiotics. The most commonly reported symptoms include fever, severe headache, rash, malaise, myalgia, nausea, vomiting, abdominal pain, and cough. Occasionally, altered mental status, seizures, coma, neurologic signs, and abnormal CSF may occur. Treatment with tetracycline or chloramphenicol antibiotics are effective in treating RMSF. Serologic confirmation of the illness is done at the North Carolina State Laboratory of Public Health (NCSLPH) by indirect immunofluorescence assay (IFA).

Human Monocytic Ehrlichiosis

An emerging tick-borne disease that can present clinical symptoms similar to RMSF is known as Human Monocytic Ehrlichiosis (HME). Ehrlichiosis has been added to the list of reportable diseases in North Carolina. The putative vector is the lone star tick *Amblyomma americanum*, and possibly *D. variabilis*, which transmits the microorganism *Ehrlichia chaffeensis*. This microbe is an obligate intracellular bacterium that grows inside monocytes. The disease can range from mild to severe, presumably due to underlying host factors. Reported clinical symptoms include fever, headache, pharyngitis, nausea, vomiting, mild hepatitis, and encephalopathy. The occurrence of rash is much less frequent than with RMSF. Ehrlichiosis should be considered in the differential diagnosis whenever elevated SGOT/SGPT, leukopenia and thrombocytopenia accompany a fever of unknown origin. The antibiotic treatment

of choice is oxytetracycline or doxycycline, as chloramphenicol is not effective. Serologic confirmation of HME is done at the NCSLPH by IFA.

Human Granulocytic Ehrlichiosis

Another emerging tick-borne disease in North Carolina is Human Granulocytic Ehrlichiosis (HGE). Unlike HME, the vector is the black legged tick *Ixodes scapularis*. In addition, the bacterium grows inside granulocytes instead of monocytes. This disease is caused by an obligate intracellular gram negative bacterium closely related to *Ehrlichia equi* and *Ehrlichia phagocytophila*. The clinical presentation is similar to HME, which includes fever, headache, malaise and myalgia. Less frequent in occurrence, but helpful in diagnosis are the symptoms of anorexia, nausea, vomiting, diarrhea, cough, and sometimes confusion. Rash is very uncommon with HGE. The treatment of patients with doxycycline usually resolves the illness quickly. Currently, sera must be sent to the CDC via the NCSLPH for confirmation of a recent infection by IFA.

Lyme Disease

Lyme disease is caused by the bacterium *Borrelia burgdorferi*, a spirochete, and is transmitted by the black legged tick *I. scapularis*. This tick is found only infrequently in North Carolina, so while it is the most frequently reported tick-borne disease in the United States, less than 100 cases a year are reported in our state. This disease has several stages, the latter of which can usually be circumvented by antibiotic treatment. One to four weeks after the tick bite occurs the first stage, a “bullseye” type rash with central clearing (erythema migrans), appears that may measure up to 12 inches in diameter. In addition, flu-like symptoms such as headache, fever, myalgia, and malaise occur. One to three months after the tick bite, second stage problems with the nervous and/or cardiac systems may occur. In stage three, arthritis may develop in one or more large joints, such as the knees and shoulders. Prompt treatment with various antibiotics usually resolves the illness. Direct observation of the spirochetes in skin biopsies, culture of the organism, and serology are the current laboratory methods of diagnosis. Early stage serologic confirmation of disease is problematic, due to false results and the wide variability in interpretation of test results between laboratories. Enzyme-linked immunosorbent assays (EIA) followed by western immunoblotting is the recommendation, but no standardized tests are currently available. Currently, sera are screened at Rex and positives forwarded to Mayo Medical Labs for confirmation.

Babesiosis

This tick-borne disease is caused primarily by the protozoan *Babesia microti*, and is transmitted by the tick *I. scapularis*. This microbe grows within human red blood cells. Babesiosis is most common in the northeastern United States, similar to the distribution seen with Lyme disease. Symptoms include fever, chills, headache, myalgia, and hemolytic anemia. The disease is usually more severe in the elderly population and in splenectomized patients. The recommended antibiotic treatment is clindamycin with oral quinine. Laboratory diagnosis is done by direct observation of the organism in a blood smear (at Rex, order a peripheral smear review by a pathologist and indicate a clinical suspicion of babesiosis). Alternatively, serologic testing for antibodies can be ordered as a reference test. Sera are forwarded to the CDC by the NCSLPH for detection of a four-fold rise in titer between acute and convalescent sera reactive to *B. microti* or *Babesia* WA1.

Tularemia

This disease is caused by the bacterium *Francisella tularensis*, and in the south

central United States is transmitted by tick bites. Cases reported in the rest of the United States usually are caused by direct contact with infected rabbit tissue. Less than 5 cases per year are reported in North Carolina. A number of ticks have been reported to be vectors, including *D. variabilis*, *A. americanum* and *I. scapularis*. The symptoms include sudden spikes of fever, local skin ulcers, lymphadenopathy, conjunctivitis, and pneumonia. The antibiotic treatment of choice is streptomycin. At the NCSLPH, a bacterial precipitation test is performed to detect antibodies reactive to *F. tularensis*.

Other Tick-Borne Diseases/Disorders

Certain diseases occur primarily in the western half of the United States and are not of immediate concern to residents of North Carolina who lack a travel history to endemic areas. These include tick-borne relapsing fever and Colorado tick fever. Tick paralysis is a severe reaction to a paralyzing toxin secreted in the saliva of feeding ticks, mainly adult females in the *Dermacentor* and *Ixodes* genera. Cases of tick paralysis are observed infrequently in North Carolina.

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Addendum

For serologic confirmation of vector-borne disease (excluding Lyme), submit sera for the State Lab Rickettsia/Ehrlichia Panel which includes

- *Rickettsia rickettsii* (RMSF)
- Typhus group
- *Ehrlichia chaffeensis* (Ehrlichiosis)
- Q Fever (to be replaced by Human Granulocytic Ehrlichiosis testing later in 1998).

Single sera collected at patient presentation will be tested and a second serum collected two weeks later is recommended for final diagnosis.

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For further information, call the Laboratory (784-3040). Telephone extensions are: Pathologists' Direct Line (3201), Dr. Kleeman (3063), Sharon Logue (Lab Director 3055), Robin Ivosic (Core Lab Manager 3053), Linda Lompa (Blood Services Manager 785-4770), Kimberly Skelding (Customer Services Manager 3318), Rex Outreach (784-3040), Karen Sanderson (Lab Compliance Specialist 3396).