Digital imaging in diagnostic hematopathology

André Tichelli
Hematology
Basel, Switzerland
iPath-network notification: pancytopenia (797656)

iPath

An: tichelli@datacomm.ch

Dear user tichelli

New Email Address: Please do not send cases to ipath@unibas.ch anymore. Send all cases to the news email address: ipathmail@ipath-network.com

There is a new case in the group "INCTR - Ethiopian Bone Marrow Study Project".

To review the case on-line, please click here.

<table>
<thead>
<tr>
<th>pancytopenia</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Title:</strong> pancytopenia</td>
</tr>
<tr>
<td><strong>Subtitle:</strong> AML, M5</td>
</tr>
<tr>
<td><strong>Type:</strong> bone marrow aspiration</td>
</tr>
<tr>
<td><strong>Sender:</strong> mahlet</td>
</tr>
</tbody>
</table>

- symptoms of anemia, productive cough
- pancytopenia, cell counts not stated.
- Peripheral smear - no pictures. no blasts seen.
Hemoglobin 56 g/L  
WBC 2.7 G/L  
Platelets 48 G/L  

Symptoms of anemia, productive cough  
Pancytopenia, cell counts not stated.  
Peripheral smear - no pictures, no blasts seen.
1. Digital imaging in diagnostic hematopathology - telehematopathology

2. Systems of telehematopathology
   ▫ Static image system
   ▫ Virtual slide system
   ▫ Real-time system
   ▫ Hybrid system

3. Pro and cons
   ▫ Telehematopathology
   ▫ Each individual system

4. Applications of telehematopathology
Digital imaging in hematopathology

- Telemedicine
  - Use of medical information exchanged from one site to another via electronic communication

- Telehematopathology
  - A branch of telemedicine
  - Uses telecommunication technology to facilitate transfer of image-rich hematopathology data between remote locations

Static image-based system or store-and-forward

**Principle**
- Image captured from a digital camera connected to the microscope
- Digital images are downloaded on a server
- Internet connection to an telehematopathology network
- Diagnostic exchange worldwide

**Technical needs**
- Light microscope
- Digital camera connected to the microscope
- PC work station
- Internet access
- Access to a telehematopathology network
Partners involved

- Case submitter (sender) hematologist / pathologist
  - Submission of a case
    - Formulation of the question
    - Clinical information
    - Blood values
    - Any diagnostic material to be reviewed

- Experts
  - Any expert in the field connected to the diagnostic network
  - Can ask additional questions
  - Provide a diagnosis or differential diagnosis
  - Advice about additional investigations & management

- Diagnostic material
  - Static images
  - Videos
  - Others (flow cytometry, molecular genetics)
Prerequisite for a correct diagnosis with telehematopathology

- Formulation of the question and needed information addressed to the expert
  - Not different from glass slide microscopy
- Technically adequate smears
  - Not different from glass slide microscopy
- Technically good quality images
  - High resolution
  - All used magnifications
  - Including oil immersion magnifications
- Selection of regions of interest
  - Demonstrate abnormalities needed by the expert to make a correct diagnosis
Selection of abnormalities - case of AML
Selection of abnormalities

1. Hyperplasia erythropoiesis, macroblastic
2. Strong dyserythropoiesis (>50%)
3. Increase of blast equivalents (erythroid blasts)

Final diagnosis:
AML, erythroleukemia, pure erythroid
Selection of abnormalities - megakaryocytes

The choice of abnormalities presented by the sender is determinant.
Diagnostic concordance between microscopy and static telehematopathology

**Good concordance**
- Acute leukemia with high proportion of blasts
  - Selection of the abnormalities does not make problems
  - Percentage of blasts (≥20%) not difficult

**Poor concordance**
- MDS with dysplastic changes
  - Borderline or heterogeneous blast increase
- Reactive changes
- Assessment of response to treatment
  - Residual blasts – counting the blasts

**Histology versus cytology**
- Histology shows topography – easier to demonstrate on static images
- Cytology shows single cell morphology

Histology from Attilio Orazio
Asynchronous working with the static image system

- No need to make appointments for discussion on diagnosis with static image system
- May be important in case of time differences
Advantages

- Simplest telehematopathology system
  - Low building-up costs
  - Easy to install and to use
  - High quality slides possible
  - Minimal internet requirements
- Asynchrony of working between sender and experts
- Multiple experts from different countries worldwide
- Application in education
- Storage of didactic slides
  - Low storage costs of slides

Limitations

- The sender has to know hematopathology
  - Choice of significant abnormalities
  - Quantitative information have to be provided by the case submitter
- Expert only see what is shown on the images
  - Risk of inconvenient slide selection
- Choice of relevant static slide images can be time consuming
- Expertise of the experts
  - Depending on the inclusion criteria for being an expert
- Time delay for the interchange between sender and expert
Virtual slide systems

- Peripheral blood or bone marrow smears are scanned to high resolution digital images
  - Whole slide is scanned
  - Possibility to view at different magnification (with/without oil immersion)
Example of a scanned case

- 57-year old male patients, without previous medical history
- Sent for suspicion of acute leukemia
- Peripheral blood counts

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Results</th>
<th>Reference values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemoglobin</td>
<td>125</td>
<td>130 – 150 g/L</td>
</tr>
<tr>
<td>MCV</td>
<td>82</td>
<td>680-95 fL</td>
</tr>
<tr>
<td>WBC</td>
<td>54</td>
<td>3.5-10 G/L</td>
</tr>
<tr>
<td>Platelets</td>
<td>86</td>
<td>150-400 G/L</td>
</tr>
</tbody>
</table>

Peripheral blood smear
http://histodb2.usz.ch/VSlideDB_HAD?conffHash=dcd87b8d9b154a61194411a5724884d31480969c_HAD

Bone marrow MGG
http://histodb2.usz.ch/VSlideDB_HAD?conffHash=1cbbea515ddcd4a8f317514df59416cd97b9f5a3_HAD

Bone marrow Peroxydase
http://histodb2.usz.ch/VSlideDB_HAD?conffHash=5d3424750f8a62c69e324cdf298aba25efd738af_HAD
Partners involved

- Same partners as for the static image system
  - Case submitter and experts

- Case submitter (sender)
  - do not need to be a specialist
  - has not to select the images of interest
  - still needs to provide additional clinical and diagnostic information

- Experts
  - Can make the diagnosis as he does on the microscope
  - He is not dependent on the selection done by the sender
  - However, good material and adequate magnifications for diagnosis

- No synchronization between sender and expert needed
  - Sender and expert can make their job independently
  - Different experts located anywhere in the world can participate
Prerequisite for a correct diagnosis

- Formulation of the order and information addressed to the experts
  - Not different from standard procedure

- Technically adequate smears
  - Not different from traditional microscopy

- Technically good quality of scanning
  - Scanned for different magnification
  - For hematology, including magnification with oil immersion
Advantages and limitations

Advantages

- The expert can review the whole case and search for abnormality
  - Like real daily work
  - Not dependent on the case submitter
- The sender does not need to be a specialist
- Asynchronize capture of image files between case submitter and experts for subsequent viewing
- Storage of hemato-pathology material
- Use for educational purpose

Limitations

- Slide scanning
  - Infrastructure needed
  - Time and technicians
  - Electronic space to store scanned files
- Large storage size
  - 60 Mb to 5.2 GB
- Need of good internet connections
- Security issues concerns
- In case of an educational event, demonstration of rare abnormalities may be unsuccessful (no time to seek)
  - Static image is more secure
Real time systems
Procedure

- A case submitter demonstrates a case by commenting it
- One or several users follow directly the demonstration and have the possibility to make interventions
- Applications
  - mainly for educational purpose
  - rather than for direct diagnosis
- Synchronization
  - between case submitter and users/experts absolute necessary
  - rather used for recurrent timely fixed events
  - participants have to be reliable (be in time)
- Optimal internet connection is an absolute prerequisite
Hybrid telehematopathology systems

- Multi-modality telehematopathology

- Simultaneous utilization of more than one system
  - Static image and virtual slide systems
  - Static image and real time system
  - Virtual slide and real time system
  - All the together
Applications of telehematopathology

- Primary consultation for diagnosis of hematological diseases
  - Fasten the diagnostic process
  - Involving expert in the field worldwide
  - Involving subspecialties

- Second opinion from experts

- Education and training
  - International exchanges of knowledge and experience
  - Standardization of diagnosis

- Quality assessment of diagnosis

- Storage of cases
Organization of a hematopathology network

- **Diagnostic Network**
  - Internationally connected and supported by an independent provider
  - Involved enough experts to provide fast and good comments
  - Flexible interchange between case submitter and experts
  - It is not a facebook/twitter

- **Experts**
  - Good experts in the field
    - Not open access, where anybody can give his opinion
    - The case submitter has to rely on the quality of the comments
  - Fast answer on a submitted case

- **Case submitter**
  - Has to provide all needed information
  - Blood counts at least Hemoglobin, MCV, WBC and platelets
  - Depending on the system used, also differential counts

- **Quality assurance of the provided diagnosis**
  - An expert is not free of errors
  - Procedure to control the performance of the system
Conclusions

- Telehematopathology is an important diagnostic tool particularly for regions who have no experts in the field.
- Advantages and limitations of each system have to be known.
- As more information the case submitter provides, as higher is the possibility of a good interpretation of a case.
- Over-interpretation is a risk from the expert’s point of view.
- In future, virtual slide bank could replace the storage of smears.