Introduction to Pathology

Ali Khurram
Senior Clinical Lecturer and Consultant Pathologist
University of Sheffield/Sheffield Teaching Hospitals NHS Foundation Trust

@sakhurram

Overview

• What is Pathology?
• What happens behind the scenes
• Features that a pathologist looks for
• Challenges in Pathology
• Digital Pathology and Artificial Intelligence

What is Pathology?

• Study of disease
  – It is the bridge between science and medicine underpinning every aspect of patient care, from diagnostic testing and treatment advice to using cutting-edge genomic technologies and preventative healthcare.

• Causes
• Pathogenic mechanisms of disease
• Clinical manifestations
• Disease progression and sequelae

• Disease
  – A condition in which the presence of an abnormality of the body causes a loss of normal health.

What is Pathology

• Diverse - Anatomical Path (tissues), Clinical Path (body fluids)
  – Surgical pathology (Histopathology)
  – Cytology
  – Forensic
  – Haematology
  – Chemical Pathology
  – Microbiology
  – Clinical Immunology
  – Molecular Pathology and Genetics
  – Toxicology
  – Veterinary Pathology

Histopathology - Features in the tissue that can be observed microscopically

Specimen received in lab
Formalin preserves (life-like state)
Gross Examination & Cut up
Processing (Dehydration + clearing)
Embedding (in Paraffin Wax)
Sectioning
Staining (usually H&E as a start)
Slides to pathologist for reporting
Quality assurance checks

Journey of a histopathology specimen

When the pathology reveals itself... Follow it
Analyse the histological changes that take place in the tissues (including Inflammation, Immune reactions, Tumours)

Important to establish the diagnosis and to determine patient management

**Things we look for**

- Normal and Abnormal tissue
- Structure, Context
- Epithelial features (normal, reactive, hyperplastic, dysplastic/precancerous, cancer)
- Stromal/connective tissue features
- Immune cells
- Underlying tissue (muscle, fat etc.)
- Clinical and Radiological correlation
- Immunohistochemistry and Molecular features

**Things we look for - in Tumours**

- Benign v Malignant
- Size, colour, shape of cells and nuclei
- Mitoses (shape and number)
- Grading
- Margins
- Stromal/Microenvironment
- Invasion into surrounding structure
- Immune response (type of cells)
- Nerve, vessel, bone invasion
- Clinical and Radiological correlation
- Immunohistochemistry and Molecular features

**Types of tumours**

**Benign**
- Resemble the tissue of origin
- Remain localised & do not spread to other sites in the body
- Well circumscribed

**Malignant**
- Less likely to resemble tissue of origin
- Do not remain localised but spread to other sites in the body
- Infiltrate and invade surrounding tissues

**Types of malignant tumours/neoplasms**

- Arising from epithelium: Carcinoma (cancer)
- Arising from glandular tissue: Adenocarcinoma
- Arising from connective tissue: Sarcoma
- Arising from lymphocytes: Lymphoma
Grading of cancers

- Grading gives an indication of prognosis/behaviour and informs treatment
- Helps differentiate tumours that may do well from tumours that may not
- Common Grading systems
  - 3 tier (well, moderate, poorly differentiated) or Grade 1-3
  - 2 tier (high and low grade)
  - Subjective, complex and difficult to reproduce for some cancers

Example: Oral Squamous Cell Carcinoma
Mouth Cancer

Well differentiated
Resembles cell of origin
Expresses keratins (differentiation)

Moderately differentiated
Resembles cell of origin
May produce some keratin

Poorly differentiated
No keratin (does not differentiate)
May not resemble cell of origin (anaplastic)

Depth of invasion
> 5mm has a worse prognosis

Local spread
Spread into muscle
Superficial spread
**Perineural spread/invasion**

Involving nerves at the advancing edge

Related to poor prognosis and recurrence

**Tumour in vessels**

- **Lymphatics**
- **Blood vessels**

**Spread to bone**

Tumour enters the lymph node via the lymphatic drainage from the primary tumour site

**p16 status—HPV associated SCC**

**Immune cells**

- **Lymphocytes**
- **Plasma cells**
- **Neutrophils**
- **Macrophages**

**LEVEL III METASTATIC DEPOSIT**

- Metastatic SCC
- Level III
- Macrophagic
- Diameter: 65 mm
- ECS
- Tumour at anterior margin
- 0.5-1.5 mm from deep margin, 1.5 mm from superficial margin
- Perineural invasion + lymphovascular in metastasis
Pathological Staging

Extent of disease
• varies according to site
  – Size
  – Depth of invasion
  – Bone involvement
  – Metastasis (regional and distant)
  – HPV status (head and neck)

Diagnosis and Prognosis

• Intuition/Gut feeling
• Clinicopathological correlation
• Context is critical
• Guidelines and datasets
• Pattern recognition

Roman Bridge Pattern
Intraductal Carcinoma

Swiss Cheese/Cribriform Pattern
Adenoid Cystic Carcinoma

Herringbone Pattern
Fibrosarcoma

Staghorn Vessels
Haemangiopericytoma, Solitary Fibrous Tumour
Challenges in Pathology

- Workforce numbers
- Increase demand related to increased population and ageing
- Sub-specialty specificity / availability
- Continually changing landscape of understanding (e.g. WHO books)
- Lack of clinical information
- Diagnostic and Prognostic tests
  - Molecular Testing (FISH, PCR, RNA Seq, WGS)
  - Availability of tests and expertise to interpret
- Cost and time implications
- Need for quick, accurate testing, Efficiency and TAT improvement, cost reduction, wider availability (developing countries), New biomarkers, Quantitative analysis
Digital Pathology
• Digitised version of glass slides
• Slide scanner to obtain Whole Slide Images (WSI)
• Excellent teaching and sharing tool
• ‘Immortalisation’ of glass slides
• Now becoming popular for use in diagnostic reporting (remote reporting, case discussion, efficiency, audit trail, error reduction)
• Large information rich images ideal for machine learning and AI algorithms

Traditional histopathology (Conventional Light Microscopy)
• Microscope required
• Remote viewing not possible
• Multiple microscopes needed for teaching, training
• One slide at a time
• Manual analysis
• Archival/retrieval – lots of glass!
• Cannot integrate into data systems

Digital pathology
• Needs a scanner and a computer
• Can view multiple slides
• Objective/Quantitative analysis
• Remote access
• Digital storage
• Integration with Lab systems
• Provides multigigapixel information rich images ideal for image analysis, development of AI based tools

AI
• H&E examination is key
• Additional investigations (IHC, molecular etc.)
  • Availability, cost, interpretation, reactivity etc.
  • Objective quantification, reproducibility
• Role for digital pathology and AI
• Some features not always clinically correlated
  • Scoring for adverse parameters (pH, LVI, TILs, HER2)
  • Hidden features, unknown correlations
  • Quality relationship of different cell type within tissues?
• Are pathologists considering everything possible?
• Machine/Deep Learning/AI – potential aid to routine histopathology to maximise and quantify information gained from H&E sections + improve detection and consistency

Digital Pathology Market Worth
756.1 Million USD by 2022 - Exclusive Report by MarketsandMarkets™

DIAGNOSIS
Phenotypic vs genotypic
• Genotype: Structural disorder
• Phenotype: Clinical disorders

Big Data
• Digitalisation of pathology
• AI in research and diagnostic healthcare

Digital Pathology strategy 2019

Digital Pathology Resource Guide

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**CAMELYON16 CHALLENGE**

- Detection of breast cancer metastasis using AI
- N=270 (110 with mets and 160 without)
- IHC used to confirm diagnosis + for training algorithms
- Accuracy tested on an unseen cohort (n=129 WSI)
- Same set also evaluated by 11 experienced pathologists
- Best algorithms performed significantly better than pathologists

**Annotations**

- Detailed annotations required to tackle novel clinical problems and handcrafted features
  - Tedious
  - Time consuming
  - Physically demanding
- Can AI help?
  - Algorithms for automatic/semi-automatic annotations
  - Reduce time and variability

**Can AI help pathologists?**

**Will AI replace pathologists? Unlikely!**
Summary

- Pathology - Study of Disease
- Takes into account a large number of features including clinical radiological as well as pathological features (requires extensive and meticulous analysis)
- Context and Pattern Recognition - Important
- Numerous elements of Pathology are subjective. Not always "scientific." Not every single feature is considered!
- Digital Pathology and AI can aid diagnosis (efficient, consistent, quantitative) and provide prognostic information.

Thank You

s.khurram@sheffield.ac.uk

@skhurrarm