REVIEW

The Role of the Surgical Pathologist in Medical Practice

By B.T. French*

INTRODUCTION

Pathologists are variously thought of as slightly or even seriously eccentric people who sit for long periods in contemplation over their microscopes and books, only emerging to make profound observations on the cause of some disease or other, often after the patient has actually succumbed to its effects. Alternatively, the pathologist may be greeted at social gatherings by an inquiry as to how many corpses have been dissected that day, as the lay impression of a pathologist's activities does not seem to include any association with living people. The contribution of the autopsy to clinical medicine has already been described[1]. This paper reviews the role of the surgical pathologist in medical practice, and highlights recent developments in the field of histopathology.

THE DEVELOPMENT OF SURGICAL PATHOLOGY

Between the birth of the compound microscope, usually attributed to Galileo in the year 1610[2], and the birth of microscopic pathology, there is a gap of almost 250 years. Many of the doubts about light microscopic observations during that time were the result of the numerous artefacts due to the inability to correct lenses for chromatic and spherical aberrations, together with problems of specimen preparation. The turning point came in 1830, when the father of Lord Lister perfected the achromatic objective, thereby removing many of the artefacts that had plagued the early users of the instrument. Even so, there were still some sceptics: Dr. Kidd of Oxford University, "after examining some delicate morphological preparation, made answer first, that he did not believe in it, and, secondly, that if it were true he did not think God meant us to know it"[3].

Microscopic examination of tissue specimens was first utilized as a means of early clinical diagnosis around the middle of the 19th century[4]. This followed the development of the concept of cells as units of structure and function by Schwann (1837), and the theory of the cellular basis of disease by Virchow (1852). The majority of the early applications of surgical biopsy were related to the diagnosis of cancer, although the concept of the demonstration of a specific cell as a basis for cancer diagnosis was strongly opposed by a number of surgeons. Even Virchow in 1988 warned of the limited value of microscopic examination of biopsy material. Despite these arguments, the practical value of biopsy was increasingly recognized towards the end of the 19th century in Europe and the United States by both gynaecologists and surgeons. The acceptance of surgical biopsy was hastened by the invention of the freezing microtome in 1895, and

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the introduction of the frozen section for intraoperative diagnosis.

THE ELECTRON MICROSCOPE

A new phase began with the need to understand cellular and molecular structure and function, requiring examination of tissues at high levels of magnification. The limitation of the light microscope then became its ability to distinguish between two points, i.e. the resolving power. As early as 1873 it was realized that objects closer together than 1/3 the wavelength of the illuminating light (about 0.2mμ in the middle of the visible spectrum) cannot be seen as more than a blur no matter how much they are magnified[5]. Following research related to the development of the cathode ray oscilloscope, the technical problems of generating, controlling and visualizing electrons were all solved by the early 1920s. It required only the realization that the electron beam could form an image, and that this image could be magnified by magnetic fields.

The first electron microscope was produced in 1931, and although its magnification was only 17.4X, the instruments of today are only technical refinements of the first model. Resolving power now achievable is of the order of < 0.3nm, about 1000 times that of a light microscope. The first scanning electron microscope was actually produced in 1938, but did not come into general use until the transmission electron microscope was fully perfected, due to the need for further technical development.

Apart from research, the best known diagnostic applications include renal and muscle pathology, but it has been estimated that up to 5% of the total workload of a major pathology department may benefit by using electron microscopy[6]. In particular, this includes viral identification, storage diseases, and liver pathology. The electron microscope is of little assistance in distinguishing benign from malignant processes. The most useful application in tumour pathology is in the determination of histogenesis in cases where histological differentiation is incomplete, e.g. endocrine tumours, multiple myeloma, malignant lymphoma, epithelial tumours, and mesenchymal tumours. The use of electron microscopy, as with any other diagnostic procedure, should be discretionary, keeping in mind the cost of the test as against the prognostic or therapeutic implications for the patient. For example, inappropriate uses include the demonstration of secretory granules in a known functioning pituitary adenoma, or changing the diagnosis from poorly differentiated squamous carcinoma to poorly differentiated adenocarcinoma when the treatment protocol is the same.

IMMUNOHISTOLOGY

Although histopathological knowledge and technique have advanced considerably, the basic principles of diagnosis based upon examination of a tissue section have not changed since Virchow's publication of Cellular Pathology in 1856. However experienced the pathologist, the application and interpretation of morphological criteria remain subjective, even at the ultrastructural level. Recognition of these limitations provided the incentive for the development of special stains and histochemical techniques to validate the morphological criteria. Many of these however, are nonspecific. For example, the much used PAS technique shows positive staining for a large number of different substances and structures[7], including basement membranes, amoebae, fungi, corpora amylaceae, amyloid, thyroid colloid, glycogen, and Russell bodies, so that the results of such staining procedures have to be interpreted with regard to the histological features.

In 1941 Coons and associates introduced the use of the immunofluorescent staining technique[8]. This method utilizes specific antibodies labelled with a fluorescent dye, which are then allowed to react with a tissue section and examined with a fluorescence microscope. This allows specific recognition of a cell according to the antigenic properties of the cell or its products. Although useful in some areas of pathology, for example in demonstrating immune complex deposition in glomerulonephritis and immunoglobulin deposition in the pemphigus group of skin disorders, the technique has not received widespread application in other areas of histopathology. This is mainly because the method requires fresh tissue, and the fluorescent stained cryostat sections are difficult to interpret.

IMMUNOPEROXIDASE

The labelling of antibodies by enzymes, in particular horseradish peroxidase, was introduced in 1966[9]. The peroxidase label can be identified in

tissues by adding a suitable chromogen substrate to produce a coloured reaction product visible by light microscopy, and has the advantage of being able to be used to localise antigens in conventionally processed, formalin fixed, paraffin embedded tissues. Following the initial demonstration of immunoglobulin in routinely processed tissues in 1974, a wide range of antigens have been demonstrated. Additionally, the brown reaction product can be rendered electron opaque by osmium tetroxide, so that exact localization can be obtained using the electron microscope.

MONOCLONAL ANTIBODIES

The major restriction with these methods proved to be the specificity of the primary antibody. The methods for purification of antigen for immunization of animals, harvesting of sera, and affinity absorption were difficult and time consuming[10]. The antisera produced consisted of a multiplicity of different antibodies, including preexisting antibodies in the immunized animal. In 1975 a method for producing monoclonal antibodies was described, but its importance was not realized for some time[11]. These antibodies are produced from mouse hybridoma cell lines, and have specific activity for a single antigen. They can also be produced in unlimited amounts, and can be standardized for use in different laboratories.

One of the most important applications of these techniques is in the diagnosis of neoplasia in very small tissue biopsies, as are encountered from endoscopy procedures. Cells which may only appear suspicious using morphological criteria may show positive labelling with an appropriate monoclonal antibody. Much progress has also been made in the identification of cells or tissues from which tumours have arisen. Monoclonal antibodies have now been developed which recognize either epithelial or lymphoid tissue. This approach has led to revision of the initial histopathological diagnosis in a significant proportion of cases. It has been shown that the majority of anaplastic neoplasms over which there had been diagnostic disagreement proved to be lymphoma rather than carcinoma. Thus, when there is doubt as to the nature of an anaplastic tumour, it is likely to be of lymphoid origin, and immunohistological study will reveal its true nature. The cost-effectiveness of the immunohistological approach should be kept in mind. The cost of a panel of monoclonal antibodies may be more attractive than the cost of further intensive investigations when the diagnostic problem remains unsolved.

CONCLUSION

The surgical pathologist requires a wide knowledge of clinical medicine as well as detailed knowledge of his own subject. He must be able to advise his clinical colleagues about biopsy indications and procedures, and to be aware of their limitations. A surgical pathology report must indicate not only whether a lesion is malignant or not, but also the extent of the disease, adequacy of excision, prognosis and recommendations for further investigations or treatment. As stated by the American pathologist Richard Reed[12] "it is not enough to be able to recite by rote the microscopic findings once the clinical diagnosis has been established... the ability to integrate microscopic findings into a meaningful interpretation is the distinguishing characteristic of a pathologist and is the art of pathology."

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