

SPECIAL ARTICLE

Historical development of the renal histopathology services in Malaysia

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Abstract

Western-style medicine was introduced to Malaya by the Portuguese, Dutch and British between the 1500s and 1800s. Although the earliest pathology laboratories were developed within hospitals towards the end of the 19th Century, histopathology emerged much later than the biochemistry and bacteriology services. The University Departments of Pathology were the pioneers of the renal histopathology diagnostic services. The Department of Pathology, University of Malaya (UM) received its first renal biopsy on 19 May 1968. Hospital Universiti Kebangsaan Malaysia (HUKM) and Hospital Universiti Sains Malaysia (HUSM) started their services in 1979 and 1987 respectively. It is notable that the early services in these University centres catered for both the university hospitals and the Ministry of Health (MOH) until the mid-1990s when MOH began to develop its own services, pivoted on renal pathologists trained through Fellowship programmes. Currently, key centres in the MOH are Kuala Lumpur Hospital, Sultanah Aminah Hospital Johor Bahru and Malacca Hospital. With the inclusion of renal biopsy interpretation in the Master of Pathology programmes, basic renal histopathology services became widely available throughout the country from 2000. This subsequently filtered out to the private sector as more histopathologists embraced private practice. There is now active continuing professional development in renal histopathology through clinicopathological discussions, seminars and workshops. Renal research on amyloid nephropathy, minimal change disease, IgA nephropathy, fibrillary glomerulonephritis, lupus nephritis and microwave technology have provided an insight into the patterns of renal pathology and changing criteria for biopsy. More recently, there has been increasing involvement of renal teams in clinical trials, particularly for lupus nephritis and renal transplant modulation.

Keywords: renal biopsy, renal pathology, history of pathology

INTRODUCTION

Ancient Greek and Roman civilisations have long recognised the existence of diseases which affected effluvia from the body. With the influx of science into the art of medical practice from the 8th to 12th Century AD, Arabic practitioners began to introduce examination of the urine for colour, sediment, smell and taste to guide diagnosis and prognostication of disease. However, it was not until the 1800s, that the pioneering work of Rokitsansky and Virchow drove home the concept of organ-based structural and cellular pathology. The classic reports by Richard Bright (1789-1855) from Guy's Hospital, London, linking the clinical manifestations of renal disease to morphological changes in the

kidneys can be regarded as one of the most important landmarks in the development of renal pathology.¹ Bright's observations were based on autopsy material, and thus suffered limitations in appreciating renal changes during life and serial changes during disease progression. The advent of the percutaneous renal biopsy in the 1950s,² together with developments in immunology and invention of the electron microscope, changed the scope and practice of renal histopathology entirely. From then, classification schemes, management, monitoring and therapeutic options for renal disease took on a clinicopathological basis. Modern-day renal histopathology service is strongly based on recognising histomorphological, immunohistopathological

and electron microscopical changes in renal biopsies.

EVOLUTION OF THE RENAL HISTOPATHOLOGY SERVICES IN MALAYSIA

Pioneers - The University Centres

Western-style medicine was introduced to Malaya by the Portuguese, Dutch and British between the 1500s and 1800s. Although the earliest pathology laboratories were developed within hospitals towards the end of the 19th Century, histopathology emerged much later than the biochemistry and bacteriology services. The Department of Pathology, University of Malaya (UM) received its first renal biopsy on 19 May 1968. This was performed by Dr. A.P. Mukherjee on a patient with anasarca and persistent microscopic haematuria and reported by Dr. KY Tang as part of the routine histopathology service.³ Much of the early renal histopathology service was focussed on the Paediatric nephrology practice of Professor Lam Khuan Leng and was provided largely by the late Professor K Prathap (Fig. 1). Lam had previously worked in Singapore, while Prathap received training in Australia. The adult clinical nephrology services were consolidated in the 1970s by Dr. Florence Wang and Dr. Chua Chin Teong of the Department of Medicine. In 1979 Dr. Looi Lai Meng joined the Department of Pathology, UM and teamed up with Prof Prathap to provide the renal histopathology services. From those early days, clinicopathological discussions at the microscope were normal phenomena. The



FIG. 1: Professor K Prathap—a pioneer in renal pathology

team worked well together and set about to systemically classify their observations, inclusive of immunofluorescence and electron microscopy findings, resulting in several landmark papers on the pathological patterns of renal disease in Malaysia.^{4,5,6} After Professor Prathap's untimely death in 1983, Professor Looi sustained the renal histopathology service until she was joined by Dr. Cheah Phaik Leng in 1987. Today, the renal histopathology service in UMMC is shared with other histopathologists in the Department who had either received in-service training from Prof. Looi or as part of their pathology specialist training (i.e. Master of Pathology programme).

When the clinical nephrology services were established in the Ministry of Health (MOH) in the early 1970s, there was no renal histopathology service available in MOH. MOH renal biopsies were read by Professor Kannan Kutty of Universiti Kebangsaan Malaysia (UKM) as part of the histopathology service. From 1979, Dr Chong Siew Meng (UKM) provided the renal histopathology service for both the Nephrology Units of UKM and the Kuala Lumpur General Hospital. He was joined by Dr. Phang Koon Seng in 1981. When Dr. Chong left for Singapore in 1988, Dr. Phang shouldered the service until 1997 when the UKM Department of Pathology shifted to new premises at Hospital UKM (HUKM) in Cheras. Thereafter he catered mainly for HUKM and serviced only transplant biopsies from MOH. Dr. Wan Muhaizan joined the renal pathology team in the early 2000s after training in Australia. In 2008, Dr. Wan Muhaizan moved to the private sector. Dr. Phang retired from UKM in 2007 but continues to provide the service on a part-time basis.

Dr. P.K. Das, who was with the Medical School, Universiti Sains Malaysia (USM), started a renal histopathology service to cater for Penang General Hospital's needs in 1987/88. The service was brought over to Hospital Universiti Sains Malaysia (HUSM) when he shifted with the Medical School to Kubang Kerian, Kelantan in 1990. When he left for the private sector in 1995, the service was continued by other HUSM histopathologists. Currently Dr. S.S. Mutum reads the renal biopsies.

The Ministry of Health service

The renal histopathology service in the MOH really only took off in 1994/1995 in Johor Bahru after Dr. Khoo Joon Joon returned from training at the University of Edinburgh. Three

other MOH pathologists expanded the service after Fellowship training in renal pathology. In 1998, Dr. Chia Kam Pik, who trained at the Royal Free Hospital and Great Ormond Street Children's Hospital, London started the service in Hospital Penang, while Dr. Zakaria Jusoh, who trained in Newcastle-upon-Tyne, UK provided a service in Kuala Trengganu. When Dr. Nik Hashimah Yahya returned from training at the Radcliff Hospital, Oxford (UK) in 2005, she pivoted the service at Hospital Kuala Lumpur (HKL).

The MOH renal histopathology services is currently being strategised on a zone basis. It is planned that renal biopsies from the East Coast (Kelantan, Trengganu, Pahang and East Malaysia) will be serviced by Dr. Zakaria Jusoh at Kuala Trengganu, the South (Johor) by Associate Professor Khoo at Johor Bahru and the Central region (Perak, Wilayah Persekutuan and Selangor) by Dr. Nik Hashimah at HKL. Dr. Chia (who has moved to Malacca) will cover Malacca and Negri Sembilan, and also back-up the Central region. A fourth MOH pathologist, identified for Fellowship training in Canada, will provide for the Northern Zone (Penang, Kedah and Perlis).

Distribution of renal histopathology services

By 2000, basic renal histopathology services can be regarded as widely available throughout Malaysia. This is because the Master of Pathology (MPath) programme conducted by UM, UKM and USM, had revised its curriculum in 1987 to include basic competence

in renal biopsy interpretation. MPath-trained histopathologists, who formed the bulk of the diagnostic histopathology workforce from 1990 were able to put together a basic renal pathology service, together with immunofluorescence examinations. This also subsequently filtered out to the private sector as more histopathologists embraced private practice. Dr. R Pathmanathan services biopsies at Sime Darby Medical Centre (previously known as Subang Jaya Medical Centre), Dr. P.K. Das serves from Lam Wah Ee Hospital in Penang and services most of the private hospitals in Penang, Associate Professor J.J. Khoo (now in Monash University Malaysia) runs a service from the Sultanah Aminah Hospital Johor Bahru, while Dr. Wan Muhaizan and Dr. Phang provide service through LabLink (M) Sdn. Bhd. However, the services at both the Ministry of Health and private sector are limited by the lack of electron microscopy, which is only available in the University centres.

In 2008, the renal biopsy workload at HKL (covering MOH hospitals in Klang valley, Alor Setar, Kuantan, Penang and Kota Kinabalu) was 804 cases, compared to 570 at UMMC (Table 1). The latter figure included 176 from patients of UMMC itself. In addition, Prof. Looi and Prof. Cheah of UMMC have been providing renal histopathology services, including immunofluorescence examinations and electron microscopy if necessary, for various private sector and MOH hospitals since 1988. In 2008, this additional load amounted to 394 cases, and included biopsies received from Gribbles Pathology, Pathology and Clinical

TABLE 1: Distribution of renal biopses reported in main Malaysian centres, 2008

Centre	Number of renal biopsies reported
Hospital Kuala Lumpur	804
University Malaya Medical Centre, KL	570
Hospital Sultanah Aminah, Johor Bahru	197
Lam Wah Yee Hospital, Penang	150
Hospital Universiti Kebangsaan Malaysia	104
Sime Darby Medical Centre, Petaling Jaya	65
Hospital Universiti Sains Malaysia	25
Malacca Hospital	25
Hospital Trengganu	17

Laboratory, Clinipath (M) Sdn Bhd, Pantai Premier Pathology, Assunta Hospital (Petaling Jaya), Sunway Medical Centre (Petaling Jaya), Hospital Pakar Ampang Puteri (KL), Gleneagles Medical Centre (Penang), Loh Guan Lye Specialist Hospital (Penang), Hospital Pantai Ayer Keroh (Malacca), Puteri Specialist Hospital (Johor Bahru), Ipoh Specialist Centre, Timberland Medical Centre (Sarawak), Sarawak General Hospital and Hospital Tuanku Jaafar (Seremban). Occasionally transplant biopsies were also received from HKL.

TRAINING AND CONTINUING PROFESSIONAL DEVELOPMENT

Unlike the Fellowship training system of the MOH, most “renal pathologists” at the University Centres updated their skills through self-initiated apprenticeships, attachments and sabbatical programmes. Dr. P.K. Das trained with Professor R Sinniah at the University of Singapore before he began the service in Penang. Professor Looi trained under Professor Prathap, and later spent sabbatical and research time with Professor Helmut Rennke at the Brigham and Women’s Hospital, Harvard Medical School, USA. Professor Cheah received in-service training

from Professor Looi and subsequent instruction from Professor Stewart Fleming while pursuing molecular pathology research at the University of Edinburgh.

Recognising the importance of team work and clinico-pathological correlation in the renal services, most pathology departments have provisions for nephrologists to sit at multiviewing microscopes to discuss biopsies with pathologists. Over the years, there have been attempts at more formal, regular clinicopathological sessions, but heavy service commitments made this less regular than ideal. Notwithstanding, the involvement of pathologists in Nephrology Seminars and Conferences have become more visible over the years.^{7,8} Professors Looi and Cheah organised the first “Basic Workshop on Interpretation of the Renal Biopsy” under the aegis of the University of Malaya, Malaysian Society of Pathologists and Academy of Medicine Malaysia in Kuala Lumpur in August 1992. This hands-on workshop proved to be very popular with both nephrologists and pathologists and led the way to other similar workshops and seminars (Table 2) (Fig.2). Whenever the opportunity arose, talks from visiting renal pathologists were also arranged. Notable visitors were Professor

TABLE 2: Hands-on clinicopathological workshops and seminars on renal pathology (1992-2005)

Event	Organiser	Venue and Dates
1. Basic workshop on interpretation of the renal biopsy	Department of Pathology UM, Malaysian Society of Pathologists and Academy of Medicine Malaysia (AMM)	Faculty of Medicine, UM. 28-29 August 1992
2. Workshop on classification of glomerulonephritis and histopathology quiz	Penang International Teaching Course in Nephrology	Penang, 28 April - 1 May 1995.
3. Workshop on Interpretation of the Renal Biopsy	Malaysian Society of Nephrology, Malaysian Society of Pathologists and the Department of Pathology UM.	Faculty of Medicine, UM. 9-10 April 1999.
4. Primary Glomerulonephritis Workshop, Kuala Lumpur	Hospital UKM	Hospital UKM. 27-28 February 2004.
5. Teaching Seminars on Nephropathy by Professor Arthur Cohen, RCPA Visiting Professor.	Royal College of Pathologists of Australasia, Department of Pathology UM, Malaysian Society of Nephrology, and College of Pathologists AMM.	Faculty of Medicine, UM. 22-24 January 2005.



FIG. 2: At a renal workshop in UM, 2005. From left: Prof. L.M. Looi, Prof. Arthur Cohen, Prof. S.Y. Tan and Prof. P.L. Cheah.

R Sinniah (National University of Singapore), Professor Michael Dunnill (John Radcliffe Hospital, UK), and Professor Arthur Cohen (University of California, USA). Prof. Looi is also a member of the Renal Pathology Society (International) and was involved in the 2004 Revised Classification of Lupus Nephritis.⁹

RESEARCH

Research addressing renal pathophysiology and new technology are largely conducted at the academic (university) centres, where facilities for fundamental research such as immunohistochemistry, molecular techniques and electron microscopy are more readily available. Subjects of research have included amyloid nephropathy,¹⁰ minimal change disease,¹¹ IgA nephropathy,¹² fibrillary glomerulonephritis,^{13,14} lupus nephritis^{15,16} and microwave technology.¹⁷ Studies into the patterns of renal pathology have given an insight into the changing criteria for biopsy.^{4, 6,18,19,20} When it was established that childhood nephrotic syndrome was predominantly due to minimal change disease, childhood nephrotics were usually not biopsied unless they were steroid-resistant, steroid dependent or had recurrent disease. In adults, most centres have shown that lupus nephritis constitute the largest biopsied group, followed by minimal change disease and IgA nephropathy.^{6,18} More recently, there has been increasing involvement of the renal teams in clinical trials, particularly for lupus nephritis and renal transplant modulation.²¹

THE FUTURE

The historical development of the renal histopathology services has shown very laudable collaboration between pathologists and nephrologists that has gone beyond departmental and institutional boundaries. There has been good cooperation between the Universities and the Ministry of Health, that has now extended to the private sector. Teamwork and close consultation in the management of renal patients have been a unique and valuable hallmark of the renal services. We have no doubt that this will be further strengthened as goodwill has always prevailed on both sides. Much more can be done in terms of collaborative research. The advent of genomic and proteomic technologies has expanded the scope of fundamental research on renal pathogenesis and invites the possibilities of personalised and targetted renal therapy to be explored.

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