An Elective at Memorial Sloan Kettering Cancer Center, New York

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Planning my Elective

During my time studying medicine, I have become interested in understanding the mechanisms of disease, particularly at the cellular and molecular level. As a result, I did my intercalated degree in molecular biology and am now considering pathology as a career option. To make up for the limited exposure as part of the undergraduate medical curriculum, I planned to organise my final-year elective in pathology.

Whilst presenting at the Joint BDIAP and Pathological Society summer conference in Maastricht, I was talking to one of the professors at the University of Leeds who suggested doing an elective at Memorial Sloan Kettering Cancer Center (MSK) in New York, linking me up with the Chief Attending in Colorectal Surgery there. I have previously undertaken done student selected components relating to cancer medicine and pathology, and this is an ongoing interest of mine, so to spend time at one of the most reputable specialist cancer hospitals in the world is truly an immense privilege.

Corresponding with the team at MSK, I organised to spend some time working in diagnostic pathology to explore my interest further as well as spending some time in clinical surgery to consolidate my knowledge from surgical rotations in Edinburgh and provide a wider context for the role of the pathologist.

Living in New York City

Although MSK now has many campuses across the New York state, I was based at the main campus in Manhattan, right in the heart of New York City. Accommodation is notoriously expensive and can be difficult to find. Instead, I chose to stay with family in the suburbs of Long Island. This meant that I could save a considerable amount of money on accommodation but also meant that I had a long commute of up to two hours door-to-door in each direction, which meant getting up very early for days when I had to be there for seven in the morning! Peak time bus and subway services could get very busy and crowded and navigating this extensive public transport network certainly did take some getting used to! However, within a few days, I had become more confident and was able to find my way in the morning without having to defer to Google maps.

Anatomic Pathology

During my time at Edinburgh, I have not had any significant exposure to pathology as clinical specialty and was therefore excited to come to the anatomic pathology department at MSK. The department is split into several subspecialist teams and I was working with the gastrointestinal pathology team.

In the mornings we had a daily 'sign out' session where an attending pathologist would sit with fellows to review the slides and finalise reports for gastrointestinal cases that had come in over the past day. This ranged from biopsies to large resection specimens from MSK itself, as well as reviewing slides from other hospitals where patients are seeking an opinion from or are transferring their care to MSK. In many ways I found this analogous to ward rounds in other branches of medicine with the juniors having reviewed the cases previously and now presenting them for senior review. The sheer volume of cases coming to sign out meant that initially I found it very fast-paced and difficult to keep up. With time, however, I slowly became better at identifying the common pathologies seen and could identify and distinguish between things like adenomas, hyperplastic polyps, sessile serrated polyps and invasive adenocarcinoma.

In these sessions, I was particularly fascinated by the logical stepwise approach taken in the work up of a biopsy where the underlying diagnosis is not immediately apparent. For example, a common scenario is a biopsy of a malignant liver lesion which could either be a primary tumour (e.g. hepatocellular carcinoma, intrahepatic cholangiocarcinoma) or a metastasis with unknown primary. In some cases, a diagnosis with reasonable confidence could be made based on the clinical history and morphology on haematoxylin & eosin (H&E)-stained sections. If there is a previous cancer diagnosis, then it can be useful to compare H&E morphology of the new lesion with that of the potential primary. With the high volume of cases at MSK, a lot of the old glass slides are not stored in the Manhattan campus itself, meaning that it can take time to retrieve previous slides for a patient. However, adoption of routine whole-slide scanning has made this much easier as pathologists can now easily bring up old material on the computer. 'Digital pathology' is rapidly developing and could one day replace microscopes all together, analogous to digitisation of radiology [1,2].

Whilst a detailed clinical history and review of morphology can help narrow down the diagnosis, in many cases there are still several plausible diagnoses and further work-up is required. The main ancillary technique used is immunohistochemistry, allowing visualisation of tumour protein expression. It was interesting to learn about the rationale for which immuostains to include when considering different differential diagnoses, and how this depended on the patient's clinical history and tumour morphology. Interestingly, at MSK, all invasive carcinomas of the gastrointestinal tract are stained for mismatch repair proteins (namely: MSH2, MLH1, PMS2 and MLH6) as a screen for microsatellite instability (MSI). Despite being recommended by NICE [3], this is not yet routine in UK pathology practice (based on personal experience and discussion with pathologists), where only select cases are screened for mismatch repair deficiency. Primarily, this is important for screening of Lynch syndrome, but detecting MSI may also have a role in predicting prognosis and influencing management. MSI can be considered a biomarker for response to therapy with immunotherapy [4,5], with clinical trials looking at the use of immune-checkpoint inhibitors in colorectal cancer with MSI [6,7].

With recent advances in genomic technology, tumour mutation profiling has become an important in the diagnosis and management of cancer. For example, *EGFR* mutation testing in lung cancer may allow

the use of 'personalised' medicine in the form of tyrosine kinase inhibitors. At MSK, I was impressed to learn that they have developed their own assay (MSK-IMPACT: 'Integrated Mutation Profiling of Actionable Cancer Targets') where targeted sequencing of 468 cancer genes is performed on tumour and a matched germline sample (e.g. blood) [8]. This is performed at MSK on most advanced cancers allowing the oncologist to see if a particular patient would benefit from targeted chemotherapy or be a candidate for any ongoing clinical trials. Interestingly, in this approach, therapy can be targeted to mutational profile rather than anatomical site of tumour [9]. This goes well above and beyond what I have seen in UK practice, where selective use of single gene panels is the norm.

Another part of the pathologist's job is macroscopic ('gross') examination and dissection of resection specimens. In contrast to what I have seen in the UK, most of the 'grossing' at MSK was done by pathologist assistants (PAs) rather than medically-qualified pathologists. Spending some time with the PAs, I observed gross examination of a variety of specimens. This provided the opportunity to study the anatomy in greater detail and additionally, it was interesting to see the rationale for which tissue blocks to take.

Colorectal Surgery

MSK is a high-volume tertiary/quaternary cancer hospital and I had plentiful opportunities to observe operations for the resection of both colonic and rectal cancer. This nicely complemented my experience in GI pathology. In my surgical placements in Edinburgh, I have seen such operations performed open or sometimes laparoscopically. Interestingly, at MSK, pretty much all colorectal resections are performed robot-assisted using the Da Vinci Xi® surgical system (Intuitive Surgical). Robotic surgery allows minimally-invasive procedures to be performed with greater precision compared to 'free hand' laparoscopy, and has the potential for improved surgical outcomes [10]. From a student-perspective, observing robotic surgery had the additional benefit of getting to see the relevant anatomy in much greater detail. Observing from the spare control console gave a good 'close up' 3D view of the operating field. For example, whilst watching a total mesorectal excision, I could easily visualise anatomy of the rectum and the plane of dissection.

One of the interesting cases I saw involved a patient who was initially scheduled for a robotic abdominoperineal resection (APR) for low rectal cancer. However, on initial laparoscopy, suspicious-looking peritoneal nodules were noted. Proceeding with a full APR in such a patient with disseminated peritoneal metastases would be fruitless, and so a biopsy was taken and sent to pathology for frozen section. Around twenty minutes later, a pathologist was put on loudspeaker telling the whole operating room that these nodules were indeed metastatic adenocarcinoma, and the operation was changed to a formation of diversion colostomy. I was impressed by this ability to provide a quick intraoperative diagnosis which changed the course of the operation and saved the patient a pointless major resection.

I have an interest in research and academia and was particularly interested by the many ongoing studies and clinical trials at MSK. One of the cases I observed involved a patient who had a previous right

hemicolectomy for caecal adenocarcinoma presenting a few years later with peritoneal carcinomatosis. Traditionally, such patients would be treated palliatively, but now debulking surgery followed by intraperitoneal chemotherapy has emerged as a therapeutic option for potential long-term survival [11]. This patient was under the ICARuS (Intraperitoneal Chemotherapy After cytoReductive Surgery) trial where patients are randomised to either (i) early post-operative intraperitoneal chemotherapy (EPIC; three days of folinic acid and 5-fluorouracil) or (ii) heated intraperitoneal chemotherapy (HIPEC; heated mitomycin C for 100 minutes immediately after the operation) [11]. During the operation itself, the team did not know which the patient would be getting. As the operation concluded, it was exciting to watch the nurse phone the research manager for this study who told us that patient would be getting HIPEC. This is something I had not even heard about, never mind seen in practice, before coming in that day.

Overall Reflections

Throughout my elective at MSK I have had the opportunity to observe care at different time points in a cancer patient's journey. For example, I have gone over the initial biopsy slides with the pathologists, then been in the surgical clinic where these results are discussed with the patient and management is planned. Then I have had the chance to watch the resection in the operating room and see the PA dissecting the specimen and selecting tissue sections. Finally, I have gone over the resection histology with pathologists. By attending disease management team meetings, I was also able to see discussion of radiology for cancer staging and neoadjuvant/adjuvant chemotherapy and radiotherapy.

Overall, I have enjoyed working in such a 'super-specialist' institution and this elective has reinforced my desire to pursue a career in pathology – a specialty that is central to the care of a cancer patient.

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