Neuropathology Service Specification

Neuromuscular pathology (including muscle, peripheral nerve and skin biopsies)

The British Neuropathological Society (BNS)
Professional Affairs Committee

1 Aims

This document aims to develop a national framework on how neuromuscular pathology services should and could be organised so that all patients and service users have fair access to specialist services taking into account local service configurations. Therefore, this document focuses on principles for guidance as opposed to specifics, and has a more nation-wide focus rather than being a blueprint for individual departments.

2 Background

Specialist neuromuscular pathology services are essential to support specialist neuromuscular centres in providing a comprehensive service for patients with neuromuscular diseases. The setting requires a well-established multidisciplinary approach with pathologists working closely with clinicians and scientists. Furthermore, the setting benefits from a strong teaching and research ethic with routine access for patients to a wide range of high quality trials, some of which may require pathology input.

There is not a 'one-size-fits-all' model, nor should there be. A small number of neuroscience centres have access to the full range of specialist neuromuscular pathology services on site. Some centres are networked and provide cross-cover for aspects of their service. Others have arrangements in place for sending samples elsewhere for analysis. **Whatever the pathway, there should be equitable, good quality and timely access to the full range of neuromuscular pathology expertise for all neuromuscular clinics.**

3 Overarching Principles

3.1 Access to Multidisciplinary Team Input

Every patient in the UK requiring specialist neuromuscular input should have timely access to a specialist neuromuscular service, which has easy access to all specialist areas supporting the clinical service. These include neuromuscular pathology (the main focus of this service specification), neurophysiology, radiological imaging (e.g. muscle MRI), immunology (antibody serology to include standard myositis-specific, myositis-associated and neuroimmunology panels), genetics (including mitochondrial genetics), as well as physiotherapy, occupational therapy and any other relevant services. There should be a close relationship between neuromuscular pathologists and the clinical team with regular multidisciplinary meetings to form meaningful clinico-pathological correlations, e.g. muscle biopsy clinical review meetings. This is particularly important if a specialist neuromuscular pathology service is delivered remotely and there is less room for ad hoc contact and discussions. Alternatively, room for regular discussions should be created. It is important to recognise that many neuromuscular diseases don't exhibit specific findings on pathology and cannot be diagnosed on

pathology alone. Bearing that in mind, the pathology may contribute an important piece to the 'diagnostic puzzle' but it may not be the key piece. Compared to other areas of pathology (e.g. neuro-oncology) the conclusions are less 'black and white' and a balanced communication of findings is very important, albeit more challenging than 'black and white' situations.

3.2 Technical Laboratory Expertise

There are very few independent super specialist neuromuscular laboratories. Neuromuscular pathology services are typically embedded within diagnostic neuropathology services, many of which are part of larger Cellular Pathology departments. It can be challenging to maintain and future-proof specialist neuromuscular expertise amongst laboratory biomedical scientist staff. It is crucial that specialist neuromuscular pathology services receive the necessary support and funding to maintain the technical expertise required to process and stain muscle biopsies, peripheral nerve biopsies and skin biopsies for intra-epidermal nerve fibre density (IENFD) counts, where these services are offered. There should be a dedicated team of staff to support the service, who have been adequately trained and are able to maintain their competencies. Routine access to electron microscopy (EM) should also be available. It is recognised, that this may no longer be on-site for a number of departments, but there should be an established pathway. In order to provide evidence of a high quality service, laboratories are expected to operate within the context of a UKAS accreditation. It is understood, that not every single technique or stain may be within UKAS scope at any one time but overall UKAS accreditation should be achieved and maintained. Laboratories are also expected to sign up for relevant NEQAS modules (e.g. muscle).

3.3 Molecular / Genetics / Genomics Access and Interface with Research and Trials

Given the advances made in uncovering more and more genetic causes of neuromuscular diseases, easy access to molecular testing, which may allow targeted genetic testing (e.g. immunoblotting in muscle biopsies), genetics and genomics as part of the diagnostic work-up is important. Whilst the overall genetic / genomic testing strategy is typically overseen by the specialist clinical team, neuromuscular pathology can provide very important and sometimes crucial information to direct such testing or increasingly to validate results (e.g. variants of uncertain significance). Furthermore, frozen tissue may be required for such genetic testing. This is particularly important for mitochondrial genetic testing. Given that there are many very rare neuromuscular diseases, which are not all covered by standard gene testing panels, there is a need to work closely with the research interface, which may represent a patient's sole chance of arriving at a genetic diagnosis. Again, this is typically orchestrated by the clinical team but oftentimes requires support by pathology and any findings may require validation and, thus, close collaboration is required. Finally, there should be a low threshold to support neuromuscular disease trials, which require pathology input. There are an increasing number of trials in the field and, importantly, these include an increasing number of treatment trials. Pathology input is required for some of them. It is highly desirable that there should be mechanisms in place for routine feedback of relevant genetic investigation results to pathologists so they can be recorded if or when a final integrated diagnosis is achieved.

3.4 Access to Digital Pathology (Whole Slide Scanning)

In reality, many specialist neuromuscular services require a limited number of dedicated neuromuscular pathology diagnostic hours and these may be in the hands of a small number of pathologists with the appropriate expertise across the country. Given that access to digital pathology

technology (whole slide scanning) is now well established it should be routinely available for all neuromuscular pathology work in order to support remote reporting (temporary or long term), sharing of challenging cases, super-specialist reviews, teaching, training and research. However, it is acknowledged that muscle pathologists would still need routine access to glass slides as subtle findings may be tricky to explore via digital means alone and this would be case dependent. With the exception of skin biopsies for IENFD, the routine scanning of neuromuscular biopsies is straightforward from a technical point of view. It is hoped that with appropriate refinements digital pathology may play an important role in the analysis of skin biopsies for IENFD, where there is the perceived opportunity for at least some automation of counts at some point in the future.

3.5 Networking

Given the above considerations, the need for networking to fulfil local service requirements is self-evident. Importantly, there is no 'one-size-fits-all' model and, therefore, the emphasis should be on empowering local services to work together in order to establish their best possible network solution for a particular point in time. As far as neuromuscular pathology is concerned, secure and timely transport of samples and slides is an important consideration if there is no local access to specialist laboratory support or scanning. Equally, secure and timely transport of slides for review by another centre if requested for clinical management purposes is important. Timeliness of results and communication with the clinical team (if pathologists work remotely) is another consideration. In the context of the current COVID pandemic, many centres have had to plan for remote working more routinely and important lessons have been learnt for successful implementation including the need for dedicated IT support. Specifically, there is no requirement for a neuromuscular clinical service to have on-site muscle pathology services. Muscle pathology services can be provided by remote laboratories, providing there are robust lines of communication between the clinical teams and the laboratory as well as agreements regarding service standards.

3.5 Nationally Commissioned Specialist Services

It is recognised that in the UK there are several nationally commissioned specialist services focusing on particular disease categories (e.g. mitochondrial, congenital myopathies and muscular dystrophies, limb girdle muscular dystrophies etc.). Local centres are encouraged to make use of such services and include them in their diagnostic pathways. It is recognised that with the current reconfiguration of genetic / genomic services at a national level, there may be changes over the next few years.

4 Specifics for Muscle, Nerve and Skin biopsies

4.1 Muscle biopsies

The Royal College of Pathologists (RCPath) 'Tissue pathways for non-neoplastic neuropathology specimens' (August 2020)[1] provide specific guidance for skeletal muscle biopsies. Of note, they provide more detailed information on the nationally commissioned specialist services. It cannot be emphasised enough how important timely access to basic clinical information and investigation findings remains when reporting muscle biopsies (e.g. basic characterisation and distribution of weakness, CK measurements, muscle MRI imaging and autoantibody results if indicated). Such access has an immediate impact on the level of clinicopathological correlation, which can be provided in the report.

4.2 Peripheral nerve biopsies

The RCPath 'Tissue pathways for non-neoplastic neuropathology specimens (August 2020)[1] provide specific guidance for peripheral nerve biopsies. Most specialist neuromuscular centres would still only see small numbers, typically ~10-20 a year. To investigate for vasculitis or other inflammatory processes, amyloid or neoplasia (lymphoma) is relatively straightforward and covers the main indications for such biopsies. However, a more nuanced assessment in order to characterise axonal loss and / or demyelination requires more detailed characterisation and access to semithin preparations and electron microscopy. Access to good quality clinical information is important and close collaboration with the clinical team is required.

4.3 Skin biopsies for intraepidermal nerve fibre density (IENFD)

The RCPath 'Tissue pathways for non-neoplastic neuropathology specimens (August 2020)[1] provide specific guidance for skin biopsy intraepidermal nerve fibre density (IENFD) counts. This is a relatively new but now well-established technique. It is available at several but not all neuromuscular centres. There is a high demand for this technique as it is essential in the work-up and diagnosis of suspected small fibre neuropathies. All small fibre neuropathy clinics should have access to this technique, either remotely or on site. Given that the technique itself requires specialist skills it takes time to introduce it into the diagnostic repertoire of a laboratory, particularly, if dedicated neuromuscular laboratory support is limited.

5. Turnaround times

The RCPath 'Key assurance indicators for pathology services' (November 2019)[2] states: *'Local patient pathways, agreed with requesters, shall include anticipated turnaround times for all relevant laboratory investigations.'* This provides in-built flexibility for neuromuscular pathology services to agree turnaround time targets for muscle, peripheral nerve and skin biopsies for IENFD with their service users. This should be audited at least annually. Importantly, turnaround targets are no substitute for clinical judgement tailored to individual cases. As indicated by the clinical information, muscle and peripheral nerve biopsies should be screened for conditions, such as vasculitis early in the process (within a day or two), so the clinical team can be provided with timely information critical to patient management. Following the initial screen, biopsies can be assigned to routine or priority reporting. Skin biopsies for IENFD tend not to be urgent. The symptomatology is typically chronic and so agreed turnaround time targets may be substantially longer when compared to muscle and peripheral nerve biopsies. As ever, if a biopsy (whatever its nature) is marked as urgent by the clinical team it should be treated as such.

Keeping Up-To-Date and Future-Proofing Services

There are a number of specialist societies and meetings, which support the neuromuscular community. Of note, there is the British Myology Society (BMS) and the British Peripheral Nerve Society (BPNS). There are larger international societies such as the World Muscle Society (WMS) and there is the British Neuropathological Society (BNS), which also covers neuromuscular pathology. These organisations and others organise regular meetings, which provide ideal opportunities for specialists from multidisciplinary fields to keep up with new developments and networking. The Royal College of Pathologists (RCPath) produces regular updates to reporting guidance and tissue pathways including neuromuscular pathology. However, neuromuscular pathology remains a small and specialised field and, therefore, succession planning and future-proofing of services is of particular

importance both at the laboratory technical as well as the diagnostic level. This should be actively pursued by creating appropriate opportunities for individuals (e.g. to attend and present at meetings, to apply for neuromuscular fellowships and placements and to get involved with research).

Conclusion

It is hoped that this service specification can be used as a guide to services, service users, funders and other interested parties in order to set up, maintain and improve specialist neuromuscular pathology services to suit local needs, which may change over time. This document is not designed to be comprehensive or prescriptive. A few key points have been summarised below.

Key Points

- No 'one-size-fits-all' model – empowerment of local stakeholders to configure best possible service configuration according to their needs
- Equitable access to all components of a specialist neuromuscular service (on-site or remotely via networking) to include autoantibody serology, specialist neuromuscular imaging, genetics / genomics (including mitochondrial) and others
- Routine trial support and close interface with research to benefit neuromuscular patients
- Routine pathways to include referrals to nationally commissioned services as clinically indicated
- Routine access to whole slide digital scanning to facilitate remote working, super-specialist reviews, teaching, training etc.
- Keeping up-to-date and future proofing of neuromuscular pathology services (technical as well as diagnostic)

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