Investigating a Surrogate Marker to Distinguish Astrocytomas and Oligodendrogliomas

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Experiences and Benefits

It was a fascinating experience to observe and take part in brain autopsy in the cut-up room. I assisted with the slicing of brain sections, interpreting the macroscopic pathology, and investigating which regions required further microscopic examination. To go through the case history and then correlate the associated findings in order to try and reach a diagnosis was a satisfying process. Perhaps unsurprisingly, some diagnoses were common, and there were similar risk factors and exposures observed in many of the decedents who found themselves in the neuropathology department. I was impressed with how the clinical and laboratory staff approached this challenging and humbling work.

I visited the laboratory many times during my project, and it was nice to get to know other members of the team working in the department. Producing the immunohistochemical slides is a time-consuming, multistage process and it was interesting to see how each stage was carried out.

I also appreciated the time my supervisors gave up to show me interesting cases down the microscope. It was a great experience to learn about the different features of some nervous system tumours that would lead to certain diagnoses or grading. Directly relevant for my project too; it was interesting to learn about the molecular genetics that is becoming so prevalent across histopathology. Some of these molecular features appear to correlate with tumour prognosis more closely than conventional histological appearances.

Project Summary

The most recent guidelines for diagnosing tumours of the central nervous system include the use of molecular testing to distinguish different tumour entities. This can be particularly important for oligodendrogliomas and astrocytomas since these can look very similar down the microscope. Oligodendrogliomas tend to be distinguishable from astrocytomas by the presence of an Isocitrate Dehydrogenase (IDH) mutation and 1p/19q codeletion. It has previously been reported that trimethylation of lysine at codon 27 on the histone 3 gene (H3K27me3) correlates to the 1p/19q codeletion status in IDH mutant gliomas, and therefore could be a potential surrogate marker for aiding diagnosis. We wanted to investigate this further with our own cohort of gliomas.

A series of 78 glioma specimens, previously diagnosed by consultant neuropathologists within the host department, were stained with antibodies (AB6147 & C36B11) to detect the

presence of H3K27me3. Microscopic analysis determined the proportion of positively stained nuclei in each case.

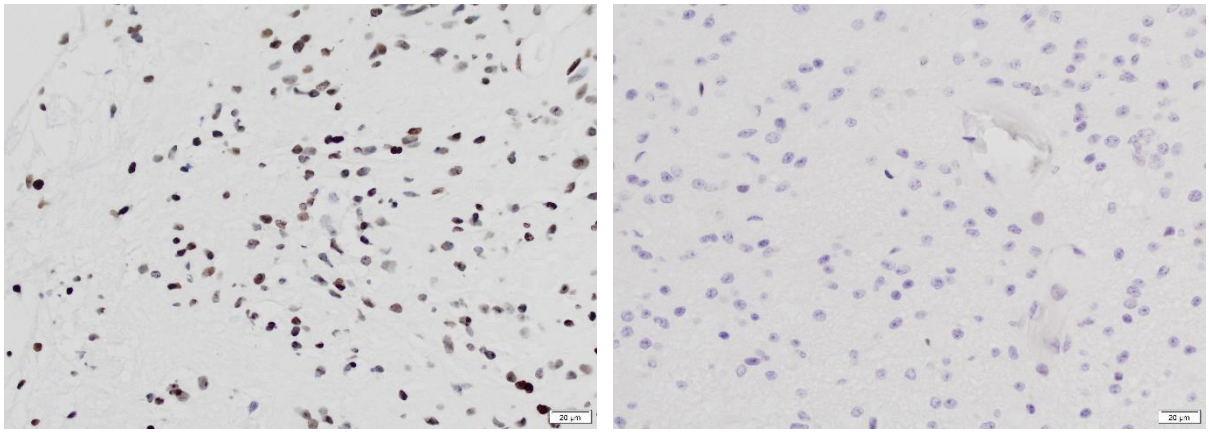

Figure 1 | Staining patterns using C36B11 antibody. The left image shows the positive staining in one of the glial tumour specimens using the C36B11 H3K27me3 antibody, whereas the glioma shown in the image on the right is negative using this stain.

Specimens were categorised into clearly positive (>90% nuclei stained), partially positive (10-90% nuclei stained), and negative (<10% nuclei stained). In consideration of whether a slide was positive overall, any sample that retained >10% nuclear staining was considered positive.

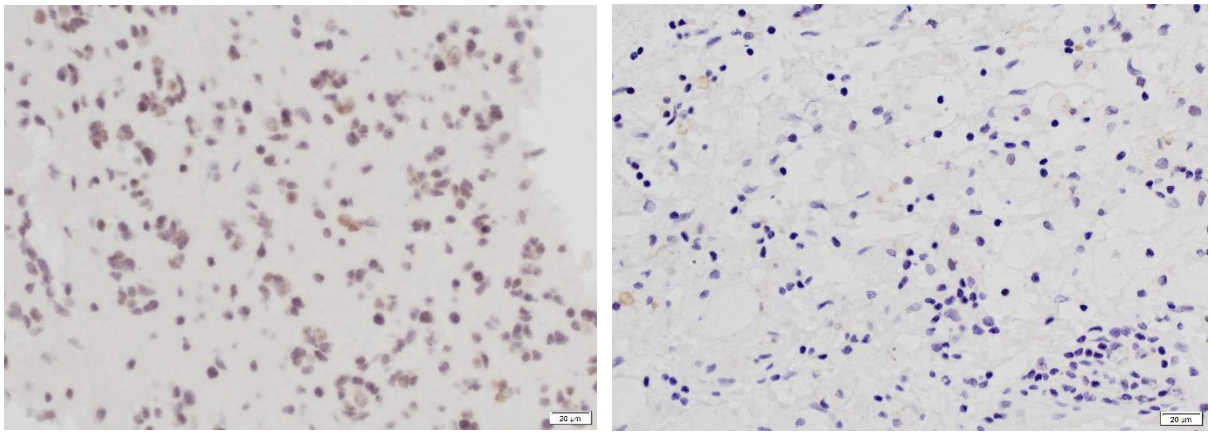

Figure 2 | Staining patterns using AB6147 antibody. The left image shows the positive staining in one of the glial tumour specimens using the AB6147 H3K27me3 antibody, whereas the glioma shown in the image on the right is negative using this stain.

In total, for the monoclonal antibody C36B11 (see fig 1), the nuclear staining was retained in very few cases in oligodendrogliomas (10/54, 19%), whereas around half of astrocytoma specimens retained their staining (11/24, 46%). For the monoclonal antibody AB6147 (see fig 2), the vast majority of oligodendrogliomas were found to be positive (44/54, 81%), whereas all astrocytomas (24/24, 100%) were found to be positive.

In conclusion, neither antibody was sensitive or specific enough for us to recommend its diagnostic use. The antibody AB6147 was shown to have a very poor ability to distinguish the different gliomas, and whilst antibody C36B11 was better at distinguishing oligodendrogliomas and astrocytomas, this was still not at a rate that could be considered useful.

Department of Neuropathology, North Bristol NHS Trust, August 2021.