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Mutational analysis of c-KIT and PDGFRA in GIST cases diagnosed locally

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Introduction: The pathogenesis of most gastrointestinal stromal tumours (GISTs) is associated with activating mutations of the proto-oncogene tyrosine kinase KIT (c-KIT). Activating mutations are also found in the homologous tyrosine kinase platelet-derived growth factor receptor α (PDGFRA). Accurate diagnosis of GIST is essential due to the availability of targeted therapy. Immunohistochemistry (IHC) for CD117 (c-KIT receptor) is routinely performed in the diagnostic workup, however, it does not provide complete sensitivity, as there are nearly 5% of GISTs that are CD117 negative. The aim of this study was to identify cKIT and PDGFRA mutations present in GIST cases diagnosed locally.

Methods: Fifty-two formalin-fixed, paraffin-embedded sections from 47 GIST patients diagnosed in the last 14 years were retrieved from the archives of the Histology Section, Pathology Department, Mater Dei Hospital. Haematoxylin and eosin staining and CD117 IHC were performed to guide laser microdissection of tumoural tissue. DNA was isolated following standard protocols. Polymerase chain reaction (PCR) was used to amplify exons 9, 11, 13, and 17 of the c-KIT gene and exons 12 and 18 of the PDFRA gene followed by sequencing analysis.

Results: Positive CD117 immunostaining was present in 95.7% of the cases. All of the c-KIT mutations identified (76.0%) were found in exon 11 while the PDGFRA mutation identified (2.2%) was present in exon 12. The c-KIT missense mutation Val560Asp was atypically present at a very high frequency (54.3%).

Conclusion: Mutational analysis can confirm diagnosis of GIST especially in CD117-negative suspect cases, can provide prognostic information and has the ability to predict therapy outcomes.