Acta Neuropathol (2012) 123:293–294
DOI 10.1007/s00401-012-0955-y

EDITORIAL

Peripheral nerve sheath tumors: the elegant chapter in surgical neuropathology

Fausto J. Rodriguez

Published online: 5 February 2012

> "The highest goal that man can achieve is amazement."
>
> Goethe

Peripheral nerve sheath tumors encompass a dynamic, evolving, exciting field of surgical neuropathology. It currently lies at a unique intersection between the students of the nervous system and those of soft tissue, and benefits greatly from their complementary interaction. Now, I have to admit it is with mixed emotions that I approach this cluster of articles on peripheral nerve sheath tumors appearing in this issue of *Acta Neuropathologica*.

On September of this past year, Bernd W. Scheithauer, my teacher, always so enthusiastic about the pathology of peripheral nerve tumors, passed away. Some of his former trainees and close collaborators teamed up to create a well illustrated, practical manuscript to approach some of the difficult problems many neuropathologists struggle with in the day to day diagnosis of peripheral nerve tumors. This subject was very close to Bernd's heart and to him I would like to dedicate this paper and this cluster.

In this practical review of the pathology of peripheral nerve sheath tumors, we discuss diagnostic criteria and unusual variants of schwannoma, neurofibroma, perineurioma, and malignant peripheral nerve sheath tumor (MPNST). We also review the increasing literature on hybrid tumors that do not conform to standard classification schemes, as well as some unusual pseudoneoplastic lesions that unexpectedly arrive to the neuropathologist microscope from time to time. We also discuss the difficult, confusing area of MPNST grading, and make an attempt to propose preliminary recommendations to upcoming WHO classifications, based on a growing literature and our combined practical experience.

Numerous advances have been brought forward in our understanding of the biology of peripheral nerve sheath tumors, particularly those with a Schwann cell phenotype. This field has benefited from numerous advances in high throughput technologies, and knowledge of genetics resulting in ingenious model systems to study Schwann cell neoplasia and the contribution of the tumor microenvironment. Steven Carroll has done an outstanding job in reviewing current concepts in our molecular understanding of Schwann cell neoplasms, specifically neurofibromas, schwannomas and MPNST. The importance of *NF1* mutations in the development of neurofibromas and MPNSTs, RAS signaling, and the contribution of non-neoplastic cells to Schwann cell tumorigenesis are covered in detail. Current evidence which provides a model for different cells of origin for plexiform and dermal neurofibromas, among the most remarkable recent discoveries in the field, is presented in insightful form and summarized with colorful, practical diagrams. Key insights into current efforts toward molecularly guided therapeutics are also discussed as appropriate.

In a separate article, resulting from a rewarding collaboration with Gareth Evans and Constantine Stratakis, we provide an update on the diagnostic criteria for the different syndromes associated with peripheral nerve neoplasia, as well as a summary of pathogenesis. Clinical criteria for the different neurofibromatoses, and classification schemes that incorporate molecular data, such as the recently proposed Baser criteria for NF2 are presented. Evolving knowledge of the clinical presentation and genetic features of the "youngest" syndrome (i.e. schwannomatosis) are likely to impact grading schemes, forming the basis of a timely discussion. Coverage of the Carney Complex, a unique syndrome associated with the enigmatic and

F. J. Rodriguez (✉)
Division of Neuropathology, Department of Pathology,
Johns Hopkins University, 720 Rutland Avenue,
Ross Building, 512B, Baltimore, MD 21205, USA
e-mail: frodrig4@jhmi.edu

diagnostically challenging melanotic schwannoma is a hallmark of this review, given its frequent omission in reviews of genetic syndromes of peripheral nerve tumors. We hope that this serves as a useful, accessible resource for those interested in the spectrum of syndromes associated with peripheral nerve tumors.

I was also personally excited to see *Acta Neuropathologica*, as a neuropathology journal, to be chosen for publication of the meeting report of the 2011 annual Children's Tumor Foundation meeting (also known as "the neurofibromatosis" meeting). This is a truly multidisciplinary meeting that yearly brings clinicians from a plurality of specialties and basic scientists together, and as a neuropathologist it has been one of the most personal educational experiences in the past years. In this report Michel Kalamarides, Nancy Ratner and the organizers synthesize the remarkable efforts that are ocurring in neurofibromatosis research, ranging from progressive refinement of model systems to rationally designed clinical trials, a model of true multidisciplinary collaboration. We hope this report continues to entice and attract some of our readers, as well as some of the brightest pathology minds out there, to this fruitful, evolving, medical field.

In reviewing this cluster in final form my mind goes back to my fellowship days, when we were reviewing a plexiform neurofibroma at around 8 pm in the multiheaded scope (formal signouts with Scheithauer often did not start before 6 pm), and I naively asked Bernd, "why are you so excited about this tumor?" He looked at me and smiled "because it is elegant"; his same signature smile can be recognized in the picture Caterina Giannini chose for his obituary, a timely component of the current issue. Even in his late years, Bernd never lost the refreshing capacity for excitement and amazement in his daily work. I am sure he would have been excited to see this cluster in final form. So readers, we have tried to share this opportunity for amazement in the beauty of the peripheral nervous system, and the complexity of its tumors, in memory of one of its most prolific scholars and advocates.