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Review of *Neoplastic Mimics in Dermatopathology,* by Mark R. Wick and James W. Patterson

Reviews by Puja K. Puri and Mark A. Hurt

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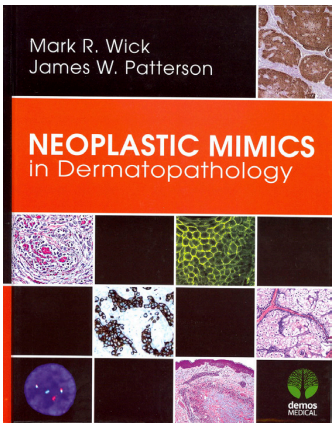

Figure 1. Wick MR, Patterson JW. Neoplastic Mimics in Dermatopathology. New York: Demos Medical, 2013. ISBN 978-1-62070-012-9; UPC 9781620700129; $160.

Review by Puja K. Puri, M.D.

Neoplastic Mimics in Dermatopathology is part of the Pathology of Neoplastic Mimics Series, which includes Thoracic and Cardiovascular Pathology and Genitourinary Pathology. Forthcoming volumes include Breast Pathology, Gastrointestinal and Liver, Gynecologic Pathology, Head and Neck Pathology and Bone and Soft Tissue Pathology. I had not had the opportunity to read any of these books until now; therefore, I cannot provide a comparison within the series.

Neoplastic Mimics in Dermatopathology is well organized. It starts with a concise, basic overview, and then is divided into five sections addressing imitators of epithelial tumors; regressed and regressing melanocytic neoplasms; mesenchymal lesions; neurocutaneous rests and ectopias; and lymphoreticular infiltrates. The final section of the book provides a table of "pseudo-pseudotumors" and the lesions they mimic. Pseudo-pseudotumors are the more common malignant neoplasms than imitate benign and reactive proliferations.

The book is 155 pages with appropriate references (pages 157-187) and an index (pages 189-194). The text is concise and easy to follow, which made it a quick read. There are many useful tables outlining neoplastic and pseudoneoplastic lesions with corresponding imitators. Many high quality photomicrographs are included, comparing tumors and their mimics. Some clinical photos are also present.

This book is ideal for residents or fellows, as it highlights histopathologic clues and immunohistochemical stains that can be used to distinguish between entities. It describes the difficulties in establishing various diagnoses including desmosplastic melanoma, cutaneous lymphoma, angiosarcoma, Kaposi's sarcoma, and squamous cell carcinoma. General pathologists who do not interpret dermatopathology slides regularly would also derive benefit from this book. Additionally, it is a wonderful tool for dermatologists as it describes specific situations where clinical information can help the dermatopathologist provide a more definitive diagnosis. For example, pathologists are familiar with pseudoepitheliomatous (pseudocarcinomatous) hyperplasia and how it can mimic squamous cell carcinoma. While the authors give histopathologic features distinguishing between the entities, they point out that sometimes it is difficult to be definitive, especially when examining a superficial biopsy specimen. Another example is the discussion of verrucous carcinoma, where macroscopic information may be critical for an accurate diagnosis.

This book is meant to be an easy-to-use reference and it serves this purpose well. It compactly describes histopathologic characteristics that distinguish entities from one

another. It is not intended to include comprehensive discussions of difficult entities. Instead, readers are provided references to textbooks devoted to such topics, such as cutaneous lymphoma. That said, I think there could have been some expansion or a short table describing other mimics for some lesions such as epidermal nevi. The authors point out that these lesions imitate seborrheic keratosis. In the absence of clinical information, additional considerations include acanthosis nigricans, terra ferma forme dermatosis and acrokeratosis verruciformis of Hopf.

As a relatively young pathologist (practicing dermatopathology for 5 years), I was aware of most of the entities and mimics discussed. However, I did learn some new facts and was reminded of some tidbits of information, as well as differential diagnoses, in conditions that I do not see commonly in my practice. For example, the authors discuss "Der Wulst" to describe a condition for which I had used the term "central facial folliculcentric basaloid proliferation." Additionally, I thought I knew all of the terms for pseudolymphoma, but learned of another: Spiegler-Fendt sarcoid.

I typically do not use p53 immunohistochemical stain, and was pleasantly reminded that p53 is positive in acantholytic actinic keratoses while re-epithelialized bullae and warty dyskeratoma are negative, and Paget disease is variably positive.

In my practice, clinical information is often scarce. For cases that look like scar, I typically call the clinician to find out if a prior biopsy was performed, and if so, what the initial lesion was. If I am told there was no prior biopsy, I typically order an S-100 to rule out desmoplastic melanoma. However, Drs. Wick and Patterson have reminded me that ordering an HHV-8 to exclude Kapsoi sarcoma also may be prudent. Additionally, they provided a photomicrograph of a keloidal Kaposi sarcoma mimicking keloid, and I will from now on think of this entity in the back of my mind when looking at mundane keloids.

Some other facts that I learned or which I was reminded include the following:

- Rosai Dorfman disease can mimic regressed malignant melanoma.
- Angiokeratoma is not a true hemangioma and is thought to represent reactive telangiectasias. (From a philosophical standpoint, Drs. Patterson and Wick have done a thorough job categorizing and considering many entities such as this.)
- Epithelioid sarcoma does not express the INI1 gene product, while isolated necrobiotic granuloma retains it.
- Rhabdomyomatous mesenchymal hamartoma should be distinguished from adult or fetal-type rhabdomyoma. I do not think about these entities very often. The histopathologic features described by Drs. Patterson and Wick are useful.

While the authors have done a great job with creating this reference, I have a few recommendations should there be a second edition. The authors mention that Bcl-2 does not offer much in the assistance of cutaneous B-cell infiltrates. I do not agree with this statement and would appreciate if the authors would re-consider this statement or further support this statement. Bcl-2 can be helpful in diagnosing primary cutaneous marginal zone lymphoma, which is usually positive for this marker. It helps to distinguish it from primary cutaneous follicle center lymphoma, which is typically negative for Bcl-2. Additionally, reactive germinal centers are also typically Bcl-2 negative. It is important to note that nodal follicle center lymphoma, secondary cutaneous follicle center lymphoma and primary cutaneous large B-cell lymphoma, leg type are usually positive for Bcl-2. However, the latter typically has a different histomorphology, and the other lymphomas mentioned can be excluded by clinical work-up.

The authors discuss reactive and malignant angioendotheliomatosis (i.e., angioendotheliomatosis proliferans systemisata). Given the differences is the histopathology, they suggest using the term "intravascular lymphomatosis" for the malignant variant of this non-Hodgkin lymphoma. I think they should consider using the term "intravascular large B-cell lymphoma" which is current classification of this disorder according to the World Health Organization (WHO). Additionally, it should be noted that rare cases of T-cell and NK cell phenotypes have been described, but should be considered different entities according to the WHO.

Additionally, there is movement toward dropping "s" from entities termed by proper names. For example, Kaposi's sarcoma, should now be called Kaposi sarcoma and Paget's disease should be termed Paget disease, etc. I would suggest updating these terms.

Finally, an index of acronyms would be useful. While I use acronyms heavily, there were some of which I was not aware, such as ING (isolated necrobiotic granuloma). I found myself searching the text to find the initial acronym many times. Also, some of the acronyms were different from the ones that I use. For instance, PSCN is a post-operative spindle cell nodule within the text; whereas, I know it as pigmented spindle cell nevus of Reed. It was a bit difficult to re-learn the new acronym, as I found myself reading the acronym the way I learned it, which did not make sense. Considering this is my major critique, I think the authors can commend themselves on a job well done.

My last recommendation is to create an electronic application for mobile devices for residents and fellows to use when learning dermatopathology. Having a list (and such great photomicrographs) of microscopic differential diagnoses for neoplastic mimics at our fingertips would be useful to many practicing physicians, as well as to pathologists in training.

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Drs. Wick and Patterson respond

We are grateful to Dr. Puri for her careful review of our monograph, and for helpful comments that can be applied in the future. We are pleased that she found our book to be a worthy effort!

Mark Wick & James Patterson

Review by Mark A. Hurt, MD

This is a book about cutaneous non-neoplastic proliferations that mimic neoplastic ones. As the authors note in the Preface:

> … with particular reference to this monograph, it is also possible for nonneoplastic proliferations to assume the guises of neoplasms at a macroscopic level, a microscopic, one or both….

There are 7 chapters, which are as follows:

1. Neoplastic Mimics: Overview
2. Pseudoneoplastic Mimics of Epithelial Tumors in the Skin
3. Imitators of Regressing and Regressed Melanocytic Neoplasms
4. Pseudoneoplastic Mesenchymal Lesions
5. Pseudoneoplastic Neurocutaneous Rests and Ectopias
6. Pseudoneoplastic Lymphoreticular Infiltrates of the Skin
7. "Pseudo-Pseudoneoplasms" of the Skin

There is an index preceded by all references in one location rather than after each chapter.

In chapter 1, the authors lay the groundwork for what is to follow. They layout a number of scenarios by which pseudoneoplasms mimic actual neoplasms based on cause rather than morphology: reparative/post-traumatic, developmental, "functional", iatrogenic, and infectious. This is followed by a detailed list of specific non-neoplastic cellular proliferations sorted by anatomic location.

Pseudoneoplastic mimics of epithelial tumors in the skin presents the basic problem of hyperplasia versus neoplasm versus hamartoma versus malformation. Again, there are detailed tables of specific lesions, not all of them epithelial. I take issue with some of the diagnoses in the photographs presented. For instance Figure 2.40, which is presented as a "basaloid follicular hamartoma" I think is a variation of basal cell carcinoma of the infundibulocystic type. I don't think it is a hamartoma, as it consists of germinative cells, which are not mature, maturity being the template for a hamartoma. Furthermore, I think that Figure 2.44 is a sebaceous carcinoma, not an adenoma. I understand that most readers of this review, including the authors, will disagree with me, but this lesion looks nothing like a sebaceoma, which is the only authentic sebaceous adenoma in the skin. These criticisms aside, the authors make relevant points about ductal proliferations, Monsel's reaction simulating sarcomatoid squamous cell carcinoma, and certain bullous diseases that can simulate solar keratoses and acantholytic squamous carcinomas.

In chapter 3, the authors present a series of conditions that can mimic partially or fully regressed melanocytic lesions. These include fixed drug reactions, lupus, lichen planus, and erythema multiforme. The authors include Destombes-Rosai-Dorfman disease in this differential, but I think it is somewhat spurious, as this condition is uncommon and not usually in the differential of melanocytic lesions. Lichenoid keratosis, however, is in this differential commonly, and it is not mentioned in this chapter. As a practical matter, one must be ever vigilant when using Melan-A to find the "hidden" melanocytic lesion in lichenoid inflammation. As the authors aver, regressed melanoma is regressed melanoma; one will not find evidence of it, and it is an impossible diagnosis. Only when a residual melanoma is in the field can one repeatedly and reliably make such a diagnosis.

The pseudoneoplastic mesenchymal lesions (chapter 4) is a very strong and useful compilation of a myriad of mesenchymal lesions hyperplasias, hamartomas, and malformations that confound many a reviewer of sections of skin lesions. Most of the photographs are of high quality, with minor exception. Moreover, there is a good mixture of clinical, scanning, and medium to high-power photomicrographs in this section.

Chapter 5 consists of a number of unusual proliferations that dermatopathologists encounter only rarely: meningotheliomatous hamartomas and cutaneous glial heterotopias. The photography is excellent throughout, and the discussion of the differential diagnosis includes fibrohistiocytic and vascular proliferations.

Chapter 6 addresses lymphoid hyperplasias that mimic lymphomas. "Pearls" are given, such as the situation in which there are nodular or diffuse mononuclear lymphoid infiltrates expressing CD20 and CD43 as suggestive of B-cell lymphoma. Another example that suggests lymphoma is the predominance of >75% of B-cells that label with CD20, CD79a, or PAX5. Other interesting and important mimics of malignancy include reactive angioendotheliomatosis and intralymphatic histiocytosis. The fact that most of the conditions cited are rare and in the differential diagnosis of lymphoma underscores their importance to the histopathologist; it is a credit to the authors for providing a sound discussion of them.

The final chapter, chapter 7, is but a single page; it is packed with a table of pseudo-pseudoneoplasms, meaning that they are really neoplastic.

I recommend enthusiastically this book for all who practice pathology, especially dermatopathology. There is a lot of valuable material presented here, and it is presented well. I hope the authors consider expanding this work in a second edition, as every dermatopathologist I know, including this one, fears the mimic he or she might misdiagnose as benign when malignant, and and vice versa. Lives hang in the balance when errors are made in either direction, so it is important to be right. I believe this book will aid its readers to move in the right direction.

Dr. Hurt is the Book Review Editor for Dermatology Practical and Conceptual. He practices dermatopathology in St. Louis, MO, at Cutaneous Pathology, WCP Laboratories. Contact him at markhurt@aol.com.