

## Pediatric dermatopathology: an overview

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### ABSTRACT

Dermatopathology is a subspecialty of pathology and dermatology involving correlation of clinical information with microscopic observations of skin biopsies to provide diagnostic information. Pediatric dermatology is a subspecialty of dermatology for which specific points need to be known for evaluating and managing skin disorders in children. The histopathological approach and other important factors for definitive diagnoses in pediatric dermatopathology are reviewed. Skin diseases in children are not necessarily smaller versions of those that develop in adults and some diseases may be confined to pediatric age group. An experienced team of dermatology and pathology increases the success of skin biopsies in pediatric dermatology besides the excellent technical skills. The histopathologic findings of skin lesions in children should be evaluated by pediatric pathologists, who have a specific interest for pediatric dermatopathology, in close collaboration with pediatric dermatologists.

**Key words:** dermatology, dermatopathology, pediatrics, correlation, diagnosis.

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### INTRODUCTION

Dermatopathology has increasingly become a popular sub-specialty in the world.<sup>1</sup> It is a subspecialty of pathology and dermatology involving correlation of clinical information with microscopic observations of skin biopsies to provide diagnostic information to the treating physician.<sup>2</sup> It has experienced a dynamic development and acquired highly original aspects. Electron microscopy, immunofluorescence microscopy, and immunohistochemistry have greatly enhanced both diagnostic capabilities and understanding of the pathogenesis of them. Despite these technical and scientific advances, the dermatopathologist remains limited in the role of diagnostician by both the adequacy of biopsy specimens and the clinical information that accompanies them.<sup>3,4</sup>

### Dermatopathology

D e r m a t o l o g y a n d dermatopathology are subjects that can be mastered only by observing numerous cases and histopathology sections respectively along with conceptual understanding of the disease.<sup>5</sup> Pathologic examination of the biopsied specimen often serves as a complementary or confirmative part of the diagnosis.<sup>6</sup> In the past, the histological diagnosis of a disease was based only on examination of slides stained with hematoxylin and eosin (H&E) with the aid of a few histochemical stains. Cutaneous inflammatory conditions are usually only diagnosed with the use of slides stained with H&E and infectious diseases rely on histochemical stains, however, there are a number of immunohistochemical and molecular biology techniques to help in the diagnosis of infections. Mainly immunohistochemistry, an ancillary technique, has proven a great asset as an aid in histopathological diagnosis.<sup>1</sup> However, what has been learned over the years is that dermatopathology is macroscopic and microscopic pathology of the skin, and that evaluation of clinical presentation represents a crucial step in the diagnostic process.<sup>7,8</sup>

For more than twenty years, molecular biology has been developed in many medical fields. It has proven to be a great asset in understanding of mechanisms of disease and at a diagnostic level it has proven to be a great tool.<sup>1</sup> Particularly in dermatopathology, molecular diagnostics has and continues to contribute to the significant advances made in the diagnoses and subclassification of cutaneous tumors.<sup>9</sup> The diagnostic, prognostic, and therapeutic molecular biomarkers and targeted therapies envisaged

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in “Molecular Diagnostics in Melanoma” have become a reality.<sup>10</sup>

These advances can lead us to think whether newer techniques will replace the pathologist in diagnostic pathology. But this seems unlikely, as correlation between findings obtained with ancillary techniques and histopathology are crucial to avoid a misdiagnosis. In other words, correlation between histological features and immunohistochemical and molecular biology findings is paramount and the role of the pathologist has never been more crucial.<sup>1</sup>

### **Pediatric dermatology**

Pediatric dermatology may pose a challenge to pediatricians and dermatologists alike, because pediatricians may be unfamiliar with certain dermatologic diagnoses, and general dermatologists may not be accustomed to dealing with children and their parents.<sup>11</sup> Examination of the skin is made more challenging by how quickly the look of an eruption can change. Manipulation, natural time course, therapy, or even the underlying immune status can change the pattern of an eruption. The exact same lesion can look markedly different in different skin types, ages, and even body locations.<sup>12</sup> Skin biopsies are usually a last resort because they may be traumatic for young children and leave unnecessary scarring. If the diagnosis is truly in question and the information provided by a biopsy would alter management of the patient, then it is imperative to perform this diagnostic test.<sup>11</sup>

Skin diseases which are encountered in adults can also be seen in pediatric population. But their frequencies differ from those in adults.<sup>13-15</sup> Also, skin diseases in children are not necessarily smaller versions of those that develop in adults. There are some conditions, in fact, that are virtually confined to the pediatric age group. Many of these are inflammatory disorders or genodermatoses that clinicians who deal with adults primarily may not be readily familiar with. Others are rare neoplasms that present in childhood.<sup>16</sup>

In general dermatology practice, the most frequent pattern of skin diseases diagnosed by skin biopsies were reported to be benign tumors, drug related dermatoses, infectious diseases, eczema, papulosquamous disorders, malignancies, connective tissue diseases, vasculitis, non-infectious bullous disorders, lymphatic disorders, and folliculitis.<sup>17</sup> On

the other hand, Henoch-Schönlein purpura, pityriasis lichenoides, pityriasis rosea, lichen planus, pityriasis rubra pilaris, erythema multiforme, atopic dermatitis, granuloma annulare, and pigmented purpuric dematosis were the most common skin disorders confirmed dermatopathologically in descending order of frequency in pediatric dermatology practice.<sup>18</sup>

The rates of skin biopsies were reported to be 1.7% and 3.7% in outpatient pediatric dermatology practices;<sup>19,20</sup> however, the rates were higher (17.5% and 35%) in pediatric dermatology consultation series.<sup>21,22</sup> While clinical features of skin diseases may not be as well known to many dermatologists, histologic features are likely to be even less well known, given that the number of skin biopsies performed on children is far less than the number performed on adults.<sup>16</sup> For example, the management of dysplastic nevi in the pediatric population has been largely derived from the studies of adults. Biopsies are usually performed on this young age group because of lesion change or abnormal appearance. One might therefore assume that the frequency of histologically diagnosed dysplastic nevi would be higher in children than in adults. But, it has been reported that there is an extremely low frequency of histologically confirmed dysplastic nevi within the general pediatric population when compared with adult population.<sup>23</sup> Another skin disorder, pityriasis lichenoides et varioliformis acuta (PLEVA) that is commonly thought of a disease of young adults can also be seen in pediatric population. Although the clinical and histological features of PLEVA are similar to those reported in adults, a high index of suspicion and biopsy specimens are often needed to differentiate PLEVA from other papular and crusted eruptions seen in the pediatric age group. These include reactions to arthropods, Gianotti-Crosti syndrome, varicella, and erythema multiforme. Histologically, papular eczema and pityriasis rosea may be misdiagnosed as PLEVA.<sup>24</sup>

The skin biopsy is simpler than renal biopsy for Henoch-Schönlein vasculitis (HSV) and remains the most reliable tool to diagnose HSV.<sup>25</sup> Therefore, all skin biopsy samples with pre-diagnosis of HSV are transported to pathology laboratory in Michel's medium for direct immunofluorescence examination.<sup>18</sup> In pediatric population, skin biopsy may be applied for psoriasis in case of doubtful diagnosis.<sup>26</sup> Although the variety of vesiculobullous disorders seen in childhood is vast, most of these disorders are

rare and they need histopathological assessment involving immunofluorescence examination.<sup>27</sup> The skin biopsies are taken from pediatric patients by incisional method after application of local anesthesia by pediatric dermatologists just after examination without a need for further appointment for this procedure.<sup>18</sup>

### Clinicopathologic correlation

Despite the fact that pathologists have always handled tumor pathology with ease, there has always been an almost knee-jerk reaction to being presented with biopsy specimens dealing with inflammatory skin conditions. This is just an acknowledgement that skin specimens in inflammatory conditions can be interpreted adequately only with a thorough knowledge of clinical dermatology.<sup>1</sup> Lack of clinical information is one of the largest limitations in interpretation of biopsies of inflammatory skin diseases. Certain clinical clues may prompt closer examination of subtle histological signs.<sup>28</sup> This is particularly true in a general surgical pathology practice where skin biopsies are seen less frequently and appropriate clinical terminology and/or dermatologic entities are often not well known.<sup>29</sup> Similarly, the dermatologist is also presented with a clinical differential diagnosis prompting the biopsy. Assimilating all of the information is challenging yet rewarding when accurate diagnosis is made.<sup>30</sup> Hence, the histological diagnoses of inflammatory and other skin diseases requires clinicopathologic correlation, and there is evolution of skin lesions into different stages as the diseases progress.<sup>6</sup> In many inflammatory processes, the stage of the disease may determine whether or not the histological features are diagnostic.<sup>28</sup> The histopathological approach seems to be more important in pediatric dermatology than many other fields of pathology.<sup>18</sup>

On the other hand, there is nothing more dreadful for a dermatologist to obtain a specimen from a patient with an inflammatory skin condition and receive back a report from a general pathologist reading 'chronic non-specific dermatitis'. But this situation has gradually changed over the years as the specialty has steadily expanded and developed, attracting physicians in the fields of both dermatology and pathology. Consequently, many countries have endeavoured to create societies devoted to the specialty.<sup>1</sup>

As part of clinicopathologic correlation, the histopathological findings need to be evaluated in conjunction with the clinical picture, laboratory findings and the history and clinical course of the disease.<sup>6</sup> A study evaluating the results of the biopsies performed in pediatric dermatology clinic reported that the rate of providing a definite diagnosis was satisfactory (61.0%) due to clinicopathologic correlation and the biopsy diagnosis was present among the pre-diagnoses in 56.3% of the cases.<sup>18</sup> In pediatric dermatology, an experienced team of dermatology and pathology increases the success of skin biopsies. Now, digital photography is available and the pathologist can reach to this data whenever it is needed.<sup>15</sup> In a study performed on 100 consecutive skin biopsies in which an inflammatory dermatosis was queried, the rates of accurate diagnoses were 53% in cases which were history blind and 78% in cases in which clinical information was available.<sup>31</sup> In another study which compared the results of the biopsies taken by dermatologists and nondermatologists, it was found that inflammatory skin diseases were correctly diagnosed in 71% of the cases by dermatologists but in only 34% of the cases by nondermatologists emphasizing that the histopathological diagnosis will be limited or restricted without sufficient clinical data.<sup>32</sup>

### Factors important for accurate dermatopathologic diagnosis

Biopsies are properly accepted as definitive tests providing diagnoses and, from them, management and prognostic guides, but have the critical limitation that not all of the lesional tissue is actually examined. The physician may choose to biopsy only part of the lesion, using a destructive mode for the remainder or even leaving it alone, and the pathologist can never section everything submitted, since each section is typically only four or five microns in thickness.<sup>33</sup> Other factors important for accurate dermatopathologic diagnosis are optimum time, best location and preferred techniques of skin biopsy. The most characteristic microscopic picture is likely to be obtained from a specimen taken from a well-developed lesion.<sup>6</sup> The issue of whether a lesion or tissue reacting to it is biopsied is very much of a discussion between the dermatopathologist and the clinician, because, unless an excisional biopsy is performed, the clinician chooses which portion of the lesion to biopsy. In addition to obtaining

diagnostic tissue, this decision is influenced by factors such as cosmetic result and other disabilities resulting from the biopsy. If a lesion is biopsied at its edge, or at another special site, this information needs to be communicated to the pathologist.<sup>34</sup>

As the dermatopathology laboratory continues to become more remote from clinical setting, the lines of communication between clinician and dermatopathologist may become more tenuous.<sup>34</sup> A repeat biopsy should be obtained, when there is a discrepancy between the microscopic findings and the clinical manifestation. It is often necessary to make repeat biopsies during the course of a disease. If an earlier biopsy specimen exists, it should always be re-examined and considered together with the new material.<sup>6</sup>

Although all those data mentioned for accurate dermatopathologic diagnoses belong to general dermatopathology literature, pediatric dermatopathology should depend on their procedures and requirements completely and maybe more strictly.

## CONCLUSION

In pediatric dermatology, skin biopsy is very helpful for the differential diagnosis. An effective designation of biopsy indication, a good dermatopathologic correlation, a pathology tissue processing supported by the immunofluorescence technique in vasculitic and bullous lesions, and an experienced team of pediatric dermatopathology increase the success of skin biopsies.<sup>18</sup>

Dermatopathology is a strong and ultimate diagnostic tool in clinical dermatology in most instances. Thus, dermatopathology is an area for which pediatric dermatologist and pediatric pathologist should consider themselves in the same team in case of skin disorders in pediatric age groups. The pediatric dermatologist should know when biopsy is indicated, choose the appropriate lesion for biopsy and provide the pediatric pathologist a satisfying clinical information and clinical differential diagnoses. The pediatric pathologist should have a fundamental understanding and specific interest for pediatric dermatopathology and be cautious for interpreting histopathological patterns in communication with the clinician for accurate dermatopathologic diagnosis. ■

## REFERENCES

1. Calonje E. Dermatopathology in the age of molecular biology. *Histopathology* 2010;56(1):1-2.

2. Goldenberg G, Patel MJ, Sanguenza OP, et al. US dermatopathology fellows career survey: 2004-2005. *J Cutan Pathol* 2007;34(6):487-9.
3. Salem OS, Maize JC. Clinicopathologic correlation in diagnosis of diseases of the skin. *Am J Dermatopathol* 1986;8(1):53-6.
4. Kerl H. Dermatopathology today--current perspectives. *Wien Klin Wochenschr* 1983;95(23):835-8.
5. Boer A, Nischal KC. www.derm.101.com: a growing online resource for learning dermatology and dermatopathology. *Indian J Dermatol Venereol Leprol* 2007;73(2):138-40.
6. Sina B, Kao GF, Deng AC, et al. Skin biopsy for inflammatory and common neoplastic skin diseases: optimum time, best location and preferred techniques. A critical review. *J Cutan Pathol* 2009;36(5):505-10.
7. Cerroni L, Argenyi Z, Cerio R, et al. Influence of evaluation of clinical pictures on the histopathologic diagnosis of inflammatory skin disorders. *J Am Acad Dermatol* 2010;63(4):647-52.
8. Kerl H, Stadler R. Dermatopathologie im deutschen Sprachraum. Entwicklungen und Perspektiven. *Hautarzt* 2007;58(9):730-4.
9. Dadzie OE, Neat M, Emley A, et al. Molecular diagnostics-an emerging frontier in dermatopathology. *Am J Dermatopathol* 2011;33(1):1-13.
10. Carlson JA. On the cusp of a revolution: melanoma molecular diagnostics. *J Am Acad Dermatol* 2013;69(4):646-7.
11. Hanson SG, Nigro JF. Pediatric dermatology. *Med Clin North Am* 1998;82(6):1381-403.
12. Treat JR. Back to basics: steps in pediatric dermatologic diagnosis. *Pediatr Dermatol* 2015;32(2):297-9.
13. Tamer E, Ilhan MN, Polat M, et al. Prevalence of skin diseases among pediatric patients in Turkey. *J Dermatol* 2008;35(7):413-8.
14. Sardana K, Mahajan S, Sarkar R, et al. The spectrum of skin disease among Indian children. *Pediatr Dermatol* 2009;26(1):6-13.
15. Kutzner H, Kempf W, Schärer L, et al. Optimierung der dermatopathologischen Diagnostik durch digitale Fotografie und Internet. Bedeutung der klinisch-pathologischen Korrelation. *Hautarzt* 2007;58(9):760-8.
16. Essary LR, Hoang MP, Carder KR. Practical review and recent developments in pediatric dermatopathology. *Adv Dermatol* 2005;21:193-215.
17. Bin Yap FB. Dermatopathology of 400 skin biopsies from Sarawak. *Indian J Dermatol Venereol Leprol* 2009;75(5):518-9.
18. Afsar FS, Aktas S, Diniz G, et al. The role of biopsy in pediatric dermatopathology. *Turkderm* 2011;45(3):137-9.
19. Wenk C, Itin PH. Epidemiology of pediatric dermatology and allergology in the region of Aargau, Switzerland. *Pediatr Dermatol* 2003;20(6):482-7.
20. Afsar FS. Pediatric dermatology in practice: spectrum of skin diseases and approach to patients at a Turkish pediatric dermatology center. *Cutan Ocular Toxicol* 2011;30(2):138-46.
21. Srinivas SM, Hiremagalore R, Venkataramaiah LD, et al. Pediatric dermatology inpatient consultations: a retrospective study. *Indian J Pediatr* 2015;82(6):541-4.
22. McMahon P, Goddard D, Frieden IJ. Pediatric dermatology inpatient consultations: a retrospective study of 427 cases. *J Am Acad Dermatol* 2013;68(6):926-31.
23. Haley JC, Hood AF, Chuang TY, et al. The frequency of histologically dysplastic nevi in 199 pediatric patients. *Pediatr Dermatol* 2000;17(4):266-9.
24. Longley J, Demar L, Feinstein RP, et al. Clinical and histologic features of pityriasis lichenoides et varioliformis acuta in children. *Arch Dermatol* 1987;123(10):1335-9.
25. Davin JC, Weening JJ. Diagnosis of Henoch-Schönlein purpura: renal or skin biopsy? *Pediatr Nephrol*

- 2003;18(12):1201-3.
26. Tollefson MM, Crowson CS, McEvoy MT, et al. Incidence of psoriasis in children: a population-based study. *J Am Acad Dermatol* 2010;62(6):979-87.
  27. McKay RM. Vesiculo-bullous disorders of childhood. *Can Fam Physician* 1987;33:2593-7.
  28. Mehregan DR, Dooley VN. How to get the most out of your skin biopsies. *Int J Dermatol* 2007;46(7):727-33.
  29. Brinster NK. Dermatopathology for the surgical pathologist: a pattern based approach to the diagnosis of inflammatory skin disorders (part I). *Adv Anat Pathol* 2008;15(2):76-96.
  30. Anderson EB, Draft KS, Lee RA, et al. Update in dermatopathology. *Am J Clin Pathol* 2006;125 Suppl:S50-70.
  31. Rajaratnam R, Smith AG, Biswas A, et al. The value of skin biopsy in inflammatory dermatoses. *Am J Dermatopathol* 2009;31(4):350-3.
  32. Sellheyer K, Bergfeld WF. A retrospective biopsy study of the clinical diagnostic accuracy of common skin diseases by different specialties compared with dermatology. *J Am Acad Dermatol* 2005;52(5):823-30.
  33. Sarkissian N, Patel PP, Fleeger EJ, et al. Anatomically correct, histopathologically correct, diagnostically disastrous biopsies. *Skinmed* 2010;8(2):98-9.
  34. Rojas J, Sarkissian N, Heller DS, et al. Newtonian dermatopathology: when the reaction to a lesion obfuscates the diagnosis. *Skinmed* 2010;8(4):231-3.