Three years of retrospective evaluation of skin biopsy results in childhood

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ABSTRACT

OBJECTIVE: In our study, we aimed to evaluate retrospectively histopathological diagnoses of children based on their skin biopsies, and determine the prevalence of the disease in question.

METHODS: Among patients who applied to Medeniyet University Goztepe Training and Research Hospital between January 2011 and February 2014, we retrospectively evaluated demographic data and histopathological diagnoses of patients aged between 0-17 years whose skin punch biopsy samples were obtained.

RESULTS: The study population (n=566) with skin biopsy results consisted of 287 (50.7%) male, and 279 (49.2%) female patients with a mean age of 10.04±4.84 years. Biopsy materials were obtained from the various age groups as follows: 0-2 years, n=31 (5.4%); 3-5 years, n=67 (11.8%) 6-11 years, n=165 (29.1%), and 12-17 years, n=303 (53.5%). Among all age groups, we took biopsies mostly from patients with noninfectious erythematous squamous (24%) and vascular (21.2%) diseases. The determined histopathological diagnoses were leukocytoclasis vasculitis (18.9%), psoriasis (7.4%), melanocytic nevus (5.4%), and contact dermatitis (5.1%) respectively.

CONCLUSION: We determined that skin punch biopsy examinations were done most frequently during adolescence and are mostly necessary for diagnosis of erythematous squamous and vascular diseases. If clinical evidence-based prevalence studies are supported with histopathological data, more significant results can be obtained.

Key words: Biopsy; childhood dermatoses; epidemiology.
MATERIALS AND METHODS

Among patients applied to Medeniyet University Goztepe Training and Research Hospital, between January 2011, and February 2014, those aged less than 18 years who had punch skin biopsy materials were determined. Approval of Ethics Committee of our hospital was obtained. The most diagnostic sample among multiple biopsy materials from the same patient was included in the study. The patients were analyzed in groups of infancy (0-2 years), preschool age (3-5 years), school age (6-11 years), and adolescence (12-17 years) [1]. Histopathological diagnoses were classified based on the criteria indicated in the textbook “Lever’s Histopathology of the Skin” [7]. According to this classification, the disease groups were indicated as follows: Genodermatoses, Non-infectious erythematos-squamous diseases, Vascular diseases, Non-infectious vesiculobullous vesiculo-pustulous diseases, Non-infectious Granulomas, Infectious Diseases, Pigmented Lesions, Histiocytosis, Nevod Lesions, Connective tissue diseases, Diseases related to drugs/physical factors/photosensitivity, Degenerative Metabolic Diseases, Inflammatory diseases of epidermal appendix, Tumors of the epidermal appendix, Cutaneous lymphoma/leukemia/mastocytosis, Fibrous/fibrohistiocytic/vascular tumors. Demographic data of all patients, and histopathological diagnoses were retrospectively evaluated.

RESULTS

In our survey lasting for a period of 3 years, skin biopsies had been obtained from 401 (1.8%) of 22,277 patients aged 0-17 years who applied to the dermatology polyclinic. During the same period, skin biopsies had been obtained from 3,685 out of 68,240 (5.4%) patients aged over 18.

When all clinics were considered in the evaluation of pediatric age group, punch biopsy materials from a total of 566 patients had been sent to the pathology laboratory for analysis. Study population consisted of 287 male (50.7%), and 279 (39.2%) female patients with a mean age of 10.04±4.84 years. Skin biopsy materials obtained from different age groups had been sent for histopathological evaluation as follows: 0-2 years, n=31 (5.4%), 3-5 years, n=67 (11.8%); 6-11 years, n=165 (29%), and 12-17 years, n=303 (53.5%). These biopsy materials had been sent from clinics of dermatology (n=401; 70.8%), pediatrics (n=158; 27.9%), pediatric surgery (n=5; 0.8%), and plastic, and esthetic surgery (n=2; 0.3%).

Histopathological diagnoses were evaluated according to disease groups. In all age groups, biopsy materials were most frequently obtained from non-infectious erythematos-squamous lesions (24%), and vascular diseases (21.2%), and the most frequently detected histopathological diagnoses were leukocytoclastic vasculitis (18.9%), psoriasis (7.4%), melanoicystic nevi (5.4%), and contact dermatitis (5.1%). When these diagnoses were evaluated according to age groups, most frequently detected diseases in the infantile period were leukocytoclastic vasculitis (12.9%), urticaria (12.9%), and ichthyosis (9.6%) (0-2 years). During preschool age (3-5 years) leukocytoclastic vasculitis (17.9%), urticaria (5.9%), psoriasis (5.9%), PLEVA (5.9%), calcinosis cutis (5.9%), mastocytosis (5.9%) were detected. During the school age (6-11 years) leukocytoclastic vasculitis (36.3%), psoriasis (10.9%) granuloma annulare (5.4%) were noted. During adolescent period (12-17 age) melanocytic nevus (10.2%) leukocytoclastic vasculitis (10.2%), and acute folliculitis (6.9%) were found. Among most frequently seen diseases, melanocytic nevus was encountered especially in the 6-11 age group, while melanocytic nevus was predominantly seen between 12-17 years. Histopathological diagnoses, and their incidence rates in all patients according to age groups are indicated in Table 1.

DISCUSSION

Histopathological examination has a very important place in the diagnosis of skin diseases It espe-
| Disease groups and histopathological diagnosis | Age 0-2 | Age 3-5 | Age 6-11 | Age 12-17 | Total |
|-----------------------------------------------|---------|---------|----------|-----------|-------|
| | n | % | n | % | n | % | n | % | n | % |
| Genodermatoses | 5 | 16.1 | 0 | 0 | 3 | 1.8 | 4 | 1.3 | 12 | 2.1 |
| Ichthyosis | 3 | 9.6 | 0 | 0 | 0 | 0 | 1 | 0.3 | 4 | 0.7 |
| Epidermolysis bullosa | 2 | 6.4 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 0.3 |
| Keratosis pilaris | 0 | 0 | 0 | 0 | 1 | 0.6 | 0 | 0 | 1 | 0.1 |
| Palmoplantar keratoderma | 0 | 0 | 0 | 0 | 2 | 1.2 | 1 | 0.3 | 3 | 0.5 |
| Anhidrotic ectodermal dysplasia | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0.3 | 1 | 0.1 |
| Focal dermal hypoplasia | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0.3 | 1 | 0.1 |
| Noninfectious erythematous-scaly diseases | 6 | 19.3 | 18 | 26.8 | 42 | 25.4 | 70 | 23.1 | 136 | 24.0 |
| Urticaria | 4 | 12.9 | 4 | 5.9 | 5 | 3.0 | 3 | 0.9 | 16 | 2.8 |
| Psoriasis | 1 | 3.2 | 4 | 5.9 | 18 | 10.9 | 19 | 6.2 | 42 | 7.4 |
| Superficial perivascular dermatitis | 1 | 3.2 | 2 | 2.9 | 8 | 4.8 | 11 | 3.6 | 22 | 3.8 |
| Lichen spinulosus | 0 | 0 | 1 | 1.4 | 0 | 0 | 2 | 0.6 | 3 | 0.5 |
| Gianotti crosti | 0 | 0 | 3 | 4.4 | 0 | 0 | 3 | 0.9 | 6 | 1.0 |
| PLEVA | 0 | 0 | 4 | 5.9 | 4 | 2.4 | 5 | 1.6 | 13 | 2.2 |
| Lichen nitidus | 0 | 0 | 0 | 0 | 4 | 2.4 | 3 | 0.9 | 7 | 1.2 |
| Lichen striatus | 0 | 0 | 0 | 0 | 3 | 1.8 | 2 | 0.6 | 5 | 0.8 |
| Pityriasis lichenoides chronica | 0 | 0 | 0 | 0 | 0 | 0 | 4 | 1.3 | 4 | 0.7 |
| Lichen planus | 0 | 0 | 0 | 0 | 0 | 0 | 6 | 1.9 | 6 | 1.0 |
| Erythema dyschromicum perstans | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0.3 | 1 | 0.1 |
| Pityriasis rosea | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 0.6 | 2 | 0.3 |
| Pityriasis rubra pilaris | 0 | 0 | 0 | 0 | 0 | 0 | 6 | 1.9 | 6 | 1.0 |
| ILVEN | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 0.6 | 2 | 0.3 |
| Miliaria profunda | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0.3 | 1 | 0.1 |
| Vascular diseases | 6 | 19.3 | 14 | 20.8 | 65 | 39.3 | 35 | 11.5 | 120 | 21.2 |
| Urticarial vasculitis | 2 | 6.4 | 4 | 5.9 | 3 | 1.8 | 2 | 0.6 | 9 | 1.5 |
| Leucocytoclastic vasculitis | 4 | 12.9 | 12 | 17.9 | 60 | 36.3 | 31 | 10.2 | 107 | 18.9 |
| Pigmented purpuric dermatoses | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 0.6 | 2 | 0.3 |
| Noninfectious vesiculobulbous vesiculopustulous derm. | 5 | 16.1 | 11 | 16.4 | 17 | 10.3 | 39 | 12.8 | 72 | 12.7 |
| Allergic/contact dermatitis | 3 | 9.6 | 6 | 8.9 | 10 | 6.0 | 10 | 3.3 | 29 | 5.1 |
| Erythema multiforme | 1 | 3.2 | 2 | 2.9 | 0 | 0 | 0 | 0 | 3 | 0.5 |
| Infantile acropustulosis | 1 | 3.2 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0.1 |
| Atopic dermatitis | 0 | 0 | 2 | 2.9 | 0 | 0 | 0 | 0 | 2 | 0.3 |
| Bullous pemphigoid | 0 | 0 | 1 | 1.4 | 0 | 0 | 3 | 0.9 | 4 | 0.7 |
| Seborrheic dermatitis | 0 | 0 | 0 | 0 | 2 | 1.2 | 7 | 2.3 | 9 | 1.5 |
| Nummular dermatitis | 0 | 0 | 0 | 0 | 5 | 3.0 | 14 | 4.6 | 19 | 3.3 |
| Lichen simplex cronicus | 0 | 0 | 0 | 0 | 0 | 0 | 4 | 1.3 | 4 | 0.7 |
| Dermatitis herpetiformis | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0.3 | 1 | 0.1 |
| Noninfectious granulomas | 1 | 3.2 | 0 | 0 | 9 | 5.4 | 9 | 2.9 | 19 | 3.3 |
| Granuloma annulare | 1 | 3.2 | 0 | 0 | 9 | 5.4 | 8 | 2.6 | 18 | 3.1 |
| Foreign body reaction | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0.3 | 1 | 0.1 |
| Disease groups and histopathological diagnosis | Age 0-2 | Age 3-5 | Age 6-11 | Age 12-17 | Total |
|-----------------------------------------------|--------|--------|----------|-----------|------|
|                                               | n  | %     | n   | %     | n   | %     | n  | %     |
| Infectious diseases                           |     |       |     |       |     |       |     |       |
| Insect bites                                  | 1  | 3.2   | 2   | 2.9   | 2   | 1.2   | 13  | 4.2   | 18  | 3.1   |
| Tinea                                         | 0  | 0     | 1   | 1.4   | 0   | 0     | 2   | 0.6   | 3   | 0.5   |
| Molluscum contagiosum                        | 0  | 0     | 0   | 0     | 2   | 1.2   | 0   | 0     | 2   | 0.3   |
| Verruca vulgaris                              | 0  | 0     | 0   | 0     | 0   | 0     | 3   | 0.9   | 3   | 0.5   |
| Epidermodysplasia verruciformis              | 0  | 0     | 0   | 0     | 0   | 0     | 1   | 0.3   | 1   | 0.1   |
| Viral rash                                    | 0  | 0     | 0   | 0     | 0   | 0     | 3   | 0.9   | 3   | 0.5   |
| Scabies                                       | 0  | 0     | 0   | 0     | 0   | 0     | 2   | 0.6   | 2   | 0.3   |
| Bacterial pustulosis                          | 0  | 0     | 0   | 0     | 0   | 0     | 1   | 0.3   | 1   | 0.1   |
| Pigmented lesions                             |     |       |     |       |     |       |     |       |
| Vitiligo                                      | 1  | 3.2   | 0   | 0     | 1   | 0.6   | 1   | 0.3   | 3   | 0.5   |
| Postinflammatory pigmented lesions           | 1  | 3.2   | 3   | 4.4   | 4   | 2.4   | 12  | 3.9   | 20  | 3.5   |
| Addison's disease                             | 0  | 0     | 0   | 0     | 0   | 0     | 1   | 0.3   | 1   | 0.1   |
| Histiocytosis                                 |     |       |     |       |     |       |     |       |
| Generalised eruptive histiocytosis            | 2  | 6.4   | 3   | 4.4   | 2   | 1.2   | 1   | 0.3   | 8   | 1.4   |
| Juvenile xanthogranuloma                      | 1  | 3.2   | 2   | 2.9   | 3   | 1.8   | 1   | 0.3   | 7   | 1.2   |
| Langerhans cell histiocytosis                 | 0  | 0     | 1   | 1.4   | 0   | 0     | 0   | 0     | 1   | 0.1   |
| Nevroid lesions                               |     |       |     |       |     |       |     |       |
| Congenital nevus                              | 1  | 3.2   | 0   | 0     | 0   | 0     | 0   | 0     | 1   | 0.1   |
| Mongolian spot                                | 0  | 0     | 1   | 1.4   | 0   | 0     | 0   | 0     | 1   | 0.1   |
| Linear whorled hypermelanosis                 | 0  | 0     | 1   | 1.4   | 0   | 0     | 0   | 0     | 1   | 0.1   |
| Spitz nevus                                   | 0  | 0     | 0   | 0     | 2   | 1.2   | 1   | 0.3   | 3   | 0.5   |
| Blue nevus                                    | 0  | 0     | 0   | 0     | 1   | 0.6   | 3   | 0.9   | 4   | 0.7   |
| Dysplastic nevus                              | 0  | 0     | 0   | 0     | 0   | 0     | 6   | 1.9   | 6   | 1.0   |
| Becker's nevus                                | 0  | 0     | 0   | 0     | 0   | 0     | 1   | 0.3   | 1   | 0.1   |
| Melanocytic nevus                             | 0  | 0     | 0   | 0     | 0   | 0     | 31  | 10.2  | 31  | 5.4   |
| Connective tissue diseases                    |     |       |     |       |     |       |     |       |
| Collagen tissue nevus                         | 0  | 0     | 2   | 2.9   | 4   | 2.4   | 8   | 2.6   | 14  | 2.4   |
| Morphoe                                       | 0  | 0     | 1   | 1.4   | 0   | 0     | 0   | 0     | 1   | 0.1   |
| Lichen sclerosus et atrophicus               | 0  | 0     | 0   | 0     | 4   | 2.4   | 4   | 1.3   | 8   | 1.4   |
| Dermatomyositis                               | 0  | 0     | 0   | 0     | 0   | 0     | 1   | 0.3   | 1   | 0.1   |
| Drug/physical/photosensitive related diseases |     |       |     |       |     |       |     |       |
| AGEP                                          | 0  | 0     | 0   | 0     | 0   | 0     | 1   | 0.3   | 1   | 0.1   |
| Drug eruption                                 | 0  | 0     | 0   | 0     | 4   | 2.4   | 3   | 0.9   | 7   | 1.2   |
| Erythema ab igne                              | 0  | 0     | 0   | 0     | 0   | 0     | 1   | 0.3   | 1   | 0.1   |
| Polymorphous light eruption                   | 0  | 0     | 0   | 0     | 0   | 0     | 1   | 0.3   | 1   | 0.1   |
| Pernio                                        | 0  | 0     | 0   | 0     | 0   | 0     | 1   | 0.3   | 1   | 0.1   |
| Degenerative/metabolic diseases               |     |       |     |       |     |       |     |       |
| Calcinosis cutis                              | 0  | 0     | 4   | 5.9   | 0   | 0     | 7   | 2.3   | 11  | 1.9   |
| Mucinosis                                     | 0  | 0     | 0   | 0     | 0   | 0     | 1   | 0.3   | 1   | 0.1   |
cially carries diagnostic importance in atypical lesions whose clinical diagnosis can not be made or mimic other dermatoses. In dermatology polyclinics “punch biopsy” method is accepted as a practical, and reliable method, and it is used prevalently in patients at every age. It is frequently applied in pediatric dermatology. In our study the incidence of biopsy procedures in polyclinics in the pediatric age group was detected as 1.8% which was in compliance with the incidence rate of 1.7% cited in the literature [4]. The rate of performing biopsy procedures was lower in the pediatric age group relative to that indicated in adults. Indeed, some types of dermatoses such as skin neoplasias whose diagnosis

| Disease groups and histopathological diagnosis | Age 0-2 | Age 3-5 | Age 6-11 | Age 12-17 | Total |
|-----------------------------------------------|---------|---------|----------|-----------|-------|
|                                               | n       | %       | n        | %         | n     | %     |
| Acanthosis nigricans                           | 0       | 0.0     | 0        | 0.0       | 3     | 0.9   |
| Confluent reticulated papillomatosis           | 0       | 0.0     | 0        | 0.0       | 1     | 0.3   |
| Anetoderma                                     | 0       | 0.0     | 0        | 0.0       | 1     | 0.3   |
| Inflammatory diseases of epidermal appendix    | 0       | 0.0     | 0        | 0.0       | 23    | 7.5   |
| Acute folliculitis                              | 0       | 0.0     | 0        | 0.0       | 21    | 6.9   |
| Cronic folliculitis                             | 0       | 0.0     | 0        | 0.0       | 1     | 0.3   |
| Eosinophilic folliculitis                      | 0       | 0.0     | 0        | 0.0       | 1     | 0.3   |
| Tumours of epidermal appendix                  | 1       | 3.2     | 1        | 1.4       | 0     | 0.0   |
| Squamous papilloma                             | 0       | 0.0     | 0        | 0.0       | 1     | 0.3   |
| Sebaceous nevus                                | 0       | 0.0     | 0        | 0.0       | 1     | 0.3   |
| Epidermal nevus                                | 0       | 0.0     | 1        | 1.4       | 0     | 0.0   |
| Keratoacanthoma                                | 0       | 0.0     | 0        | 0.0       | 1     | 0.3   |
| Seborrheic keratosis                           | 0       | 0.0     | 0        | 0.0       | 2     | 0.6   |
| Pilomatrixoma                                  | 1       | 3.2     | 0        | 0.0       | 1     | 0.3   |
| Comedon                                       | 0       | 0.0     | 0        | 0.0       | 3     | 0.9   |
| Trichoepitelioma                               | 0       | 0.0     | 0        | 0.0       | 1     | 0.3   |
| Eruptive vellus hair cysts                     | 0       | 0.0     | 0        | 0.0       | 1     | 0.3   |
| Cutaneous lymphoma/leukemia/mastocytosis       | 0       | 0.0     | 4        | 5.9       | 6     | 3.6   |
| Mastocytosis                                   | 0       | 0.0     | 4        | 5.9       | 6     | 3.6   |
| Mycosis fungoides                              | 0       | 0.0     | 0        | 0.0       | 2     | 0.6   |
| Lymphomatoid papulosis                         | 0       | 0.0     | 0        | 0.0       | 1     | 0.3   |
| Fibrous/fibrohistiocytic/vascular tumours      | 0       | 0.0     | 0        | 0.0       | 9     | 2.9   |
| Scar                                          | 0       | 0.0     | 0        | 0.0       | 2     | 0.6   |
| Dermatofibroma                                 | 0       | 0.0     | 0        | 0.0       | 1     | 0.3   |
| Fibrous papule of the face                     | 0       | 0.0     | 0        | 0.0       | 1     | 0.3   |
| Angiokeratoma                                  | 0       | 0.0     | 0        | 0.0       | 1     | 0.3   |
| Pyogenic granuloma                              | 0       | 0.0     | 0        | 0.0       | 2     | 0.6   |
| Lymphangiomia                                  | 0       | 0.0     | 0        | 0.0       | 1     | 0.3   |
| Kaposi’s sarcoma                               | 0       | 0.0     | 0        | 0.0       | 1     | 0.3   |
| Inflammatory diseases of the fat tissue        | 0       | 0.0     | 0        | 0.0       | 1     | 0.3   |
| Erythema nodosum                               | 0       | 0.0     | 0        | 0.0       | 1     | 0.3   |
| Total                                         | 31      | 5.4     | 67       | 11.8      | 165   | 29.1  | 303   | 53.5  | 56    | 100   |
can be made only with histopathological examination of biopsy specimens are seen especially in the advanced age, and parents' reservations towards biopsy procedures which can be considered as a semi-invasive method can put off biopsy till adulthood. In addition, we think that multiple number of patients who present to the pediatry clinics with skin lesions are treated by pediatricians with the indication of nonspecific diagnoses, and so dermatology consultation is not requested which all can contribute to the lower incidence of biopsy procedures performed. In the literature, limited number of prevalence studies which generally encompassed all age groups have evaluated prevalence of biopsies. Gimbell et al. reviewed 2342 skin biopsies performed in Ethiopia, and reported that biopsy procedures had been most frequently performed for inflammatory dermatoses [6]. Engin et al. [5] evaluated biopsy specimens of 2128 patients aged between 2, and 91 years, and most frequently detected melanocytic nevi (27%). This phenomenon suggests that nevi are being excised in peripheral hospitals for cosmetic concerns. Similar to our study Afsar et al. evaluated 213 biopsy specimens taken from patients in the pediatric age group, and reported that they detected most frequently leukocytoklastic vasculitis, and psoriasis [4]. Especially in tertiary healthcare institutes, even though some dermatoses are clinically diagnosed, for definitive diagnosis histopathological evaluations are performed.

Majority of biopsies sent from pediatry clinics have been apparently obtained from patients with vascular diseases. This phenomenon demonstrates that even patients with vascular diseases demonstrating skin lesions consult more frequently to pediatry polyclinics. Besides especially pediatricians require histopathological confirmation for ruling out dermatoses like cutaneous vasculitis which are considered in the differential diagnosis. Cutaneous vasculitis courses from time to time with systemic findings, and pediatric patients' consultation priorly to pediatry polyclinic for every type of disease can explain the need for histopathological confirmation.

Studies investigating prevalences of pediatric dermatoses are generally based on clinical evidence [1, 2, 3]. Some types of dermatoses have been diagnosed based on clinical evidence without resorting to histopathological findings. Therefore their prevalence rates do not parallel with those based on histopathological evidence. In studies aiming at determination of incidence rates of pediatric dermatoses in our country, authors reported different rates for various types of most frequently seen diseases (Tekin et al.: eczema/dermatitis [25.9%], and Bilgili et al.: infections, and infestations [24.5%]) [2, 3]. In a survey study which screened the same geographical region as ours eczema group of diseases was the most frequently detected dermatoses [1]. Although we evaluated the population of the same geographical region as indicated by the abovementioned authors, in our study on based on histopathological findings, dermatitis group diseases eczema (contact dermatitis, atopic dermatitis, nummular dermatitis, seborrheic dermatitis, and superficial perivascular dermatitis) were seen at a rate of 14% which was lower than those reported in the above-mentioned study. This finding indicates that diagnosis of dermatitis is mostly based on clinical manifestations. Biopsies are more often requested for patients referred by pediatricians and biopsy procedures are not frequently preferred in eczematous diseases which may be the underlying rationale of this attitude.

In our study, contrary to other prevalence studies, the incidence rates of not only disease groups, but also each established histopathological diagnosis in different age groups were determined. Accordingly differences in the distribution of diseases in various age groups were observed.

Evaluation of the biopsies obtained only within the last 3 years, and categorization of biopsy results have constituted limitations of our study. Since histopathological classification was mainly considered in the grouping of biopsy results vasculitis which is clinically a disease group by itself, was analyzed in the category of vascular diseases.

In conclusion, as observed in our study, skin punch biopsies during pediatric age were most frequently performed during adolescent period, and most often it was required for the diagnosis of erythematous-squamous skin lesions, and vascular diseases. Our study emphasizes diagnostic value of
histopathological examinations, and its significance in epidemiological studies. Besides, closer cooperation between pediatriticians, and dermatologists will increase the chances of accurate diagnosis, and more precise data can be obtained about the diagnosis of the diseases. It is possible to obtain more elucidative results in larger series based on clinico-pathological evaluation.

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