CYTOLOGICAL DIAGNOSTIC ACCURACY IN SKIN TUMOR

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ABSTRAK

*Modalitas pemeriksaan yang sering digunakan untuk mendiagnosis berbagai tumor kulit adalah pemeriksaan histopatologi dari bahan biopsi punch serta shave. Metode pemeriksaan sitologi yang memiliki kelebihan diagnosis lebih cepat dan non-invasif diharapkan memiliki peran penting dalam diagnosis tumor kulit. Tujuan dalam penelitian ini adalah membandingkan hasil pemeriksaan sitologi preoperatif dengan hasil pemeriksaan histopatologi untuk mengetahui akurasi, sensitifitas dan spesifisitas pemeriksaan sitologi pada tumor kulit. Dilakukan pengumpulan data arsip pemeriksaan histopatologi tumor kulit antara bulan Januari 2008 hingga Desember 2010 di Patologi Anatomi RSUD Dr. Soetomo. Diperoleh 530 kasus histopatologi tumor kulit. Sebanyak 201 (35,89%) kasus tersebut telah dilakukan pemeriksaan sitologi preoperatif. Penelitian retrospektif dilakukan dengan membaca ulang 201 kasus tersebut dan membandingkan hasil sitologi preoperatif dan histopatologinya untuk menentukan akurasi, sensitifitas, dan spesifisitas pemeriksaan sitologi pada diagnosis tumor kulit. Didapatkan nilai akurasi diagnosis pemeriksaan sitologi tumor kulit adalah 96,52%, nilai sensitifitas 94,92% dan spesifisitas 98,80%. Sebagai kesimpulan, modalitas pemeriksaan sitologi memiliki peran dalam diagnosis tumor kulit terutama dalam menyingkirkan keganasan.**(FMI 2013;49:66-71)***

Kata kunci: *tumor kulit, sitologi, akurasi*

ABSTRACT

Examination modalities that are often used to diagnose a variety of skin tumors is histopathologic examination of punch and shave biopsy material. Cytological examination method that has the advantages of faster diagnosis and non-invasive expected to have an important role in the diagnosis of skin tumors. The purpose of this study was to compare the results of preoperative cytology with histopathological examination to determine the accuracy, sensitivity and specificity of cytology in skin tumors. Archival data collection histopathological examination of skin tumors between January 2008 to December 2010 at the Hospital Dr. Anatomical Pathology. Atopic Dermatitis. Retrieved 530 cases of skin tumor histopathology. A total of 201 (35.89%) cases had a preoperative cytologic examination. A retrospective study was conducted with 201 re-read the case and compare the preoperative cytologic and histopathologic results to determine the accuracy, sensitivity, and specificity of cytology in the diagnosis of skin tumors. Accuracy values obtained cytology diagnosis of skin tumors was 96.52%, 94.92% and a sensitivity value of 98.80% specificity. In conclusion, cytologic examination modalities have a role in the diagnosis of skin tumors, especially in getting rid of malignancy. ***(FMI 2013;49:66-71)***

Keywords: skin tumor, cytology, accuracy

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INTRODUCTION

Skin tumors, especially malignant tumors of the skin, is one of the health problems in the community which is quite important, although the mortality rate is low. There are various types of skin tumors. Based on the classification of WHO (World Health Organization) in 2003, skin tumors are grouped into: keratinocytic tumors, melanocytic tumors, tumor appendageal, haematolymphoid tumors, soft tissue tumors, and neural tumors (LeBoit et al 2006). Various types of skin tumors that would have a different behavior and management, so often the clinician often require pathological examination.

Anatomical pathology examination methods on a variety of skin lesions commonly use histopathologic examination of the punch biopsy samples, and superficial shave biopsy, incisional biopsy in, complete excision and scrapings. Skin biopsy is especially necessary in cases with suspicion of malignancy or to clarify cases have limited the clinical picture. Selection of anatomical pathology examination methods require different considerations, including diagnosis, lesion location, lesion morphology, the general condition of the patient, even in terms of cosmetics (Elenitsas & Ming 2008, Lin & Zakowski 2008, Orell & Domanski 2005).

In the field of pathology is also known cytology method which has been widely applied to a variety of pathological lesions. Cytology has several advantages, namely a short time, non- invasive, reliable, safe, patient tolerated the procedure very easy and efficient (Lin & Zakowski 2008, Orell & Domanski 2005, Koss & Melamed 2005, Daskalopoulou 2000). Similarly, in skin tumor lesions, cytologic examination is expected to have an important role in the diagnostics. The expectation proved the existence of demand for cytology of skin tumors clinician.

Samples lesions involving the skin surface scrapings obtained by method (scraping) or imprint, whereas when forming a mass lesion or nodule, FNA samples obtained by method-B with 25-27 G needle (Lin & Zakowski 2008, Orell & Domanski 2005, Aryya et al 1992). Cytology methods of skin tumors has been widely applied in various centers of pathology, as well as in the Anatomical Pathology Hospital Dr. Atopic Dermatitis. However, there is a lot of literature that analyzes the accuracy of cytology methods in skin tumors (Orell & Domanski 2005). There are various skin tumors cytology requests from clinicians from time to time, but not a lot of discussion about the accuracy, sentitifitas and specificity of cytology in skin tumors. That's why this study was conducted to determine the accuracy, sensitivity and specificity of cytology in the diagnosis of skin tumors in Anatomical Pathology Hospital Dr Atopic Dermatitis.

MATERIALS AND METHODS

Observations were made retrospectively by collecting the entire archive histopathological examination of skin tumors at the Hospital Dr. Anatomical Pathology. Atopic Dermatitis, Faculty of Medicine Airlangga University, Surabaya, in January 2008 until December 2010. We obtained 560 cases of skin tumors. A total of 201 cases have been performed before preoperative cytologic examination at the Hospital Anatomical Pathology DR. Atopic Dermatitis. Three hundred and fifty- nine cases no preoperative cytologic examination were excluded from the analysis. Cytology results categorized as benign when in cytology showed a lesion is benign or non-neoplastic, or without malignancy, and malignant if it showed malignancy cytology. Then, the diagnosis of preoperative cytology compared with histopathologic diagnosis as the gold standard, using a diagnostic test and analysis made by Pusponegoro 2x2 table (Pusponegoro et al 2002). Statistical analysis was performed to determine the accuracy, sensitivity, and specificity.

RESULTS

Data request from the preoperative cytologic examination of the entire archive collection histopathology of skin tumors showed an increase in each year (Figure 1).

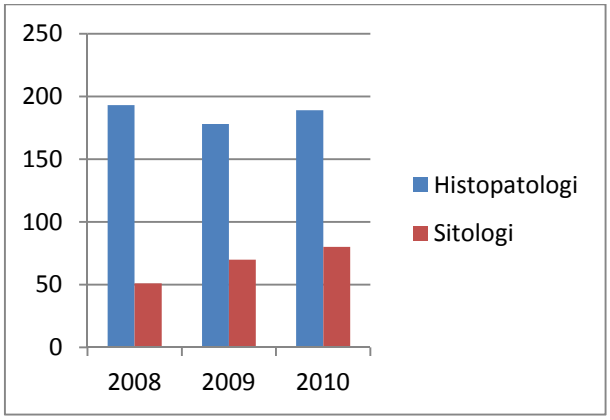

Figure 1. Comparison demand cytology and histopathology of skin tumors in 2008-2010 at the Hospital Dr. Atopic Dermatitis

In 2008 found 193 cases of skin tumors in which 51 cases of previous cytologic examination (26.42%). In 2009 found 178 cases, 70 cases (39.33%) and cytological examination in 2010 found 189 cases. A total of 80 cases (42.33%) cytology done beforehand. The study includes 201 cases of skin tumors, consisting of 84 men and 117 women. Two hundred and one cases observed in this study shows the results of a total of 119 cases of malignant histopathology (59.20%) and benign histopathology of 82 cases (40.80%). One hundred nineteen cases of skin tumors in this study revealed histopathological malignancy, 113 cases diagnosed malignant on cytology results (true positives). While the 6 cases diagnosed benign on cytology results (false negatives). Eighty- two cases of skin tumors in this study showed benign histopathology results. Eighty-one cases diagnosed benign on cytology results (true negatives). One case of acquired benign skin tumor with malignant cytology results (false positives). Based on these results, obtained sensitivity and specificity of cytology towards malignancy in skin tumors was 94.92% and 98.80%. While the diagnostic accuracy reached 96.52%. The positive predictive value of cytology of the skin malignancy in tumors was 99.12% while the negative predictive value of 93.18%. Value was also obtained positive likelihood ratio of 79 and a negative likelihood ratio of 0.05.

Table 1. Table 2x2 cytology with histopathologic diagnosis of skin tumors

Cytological results	Histopathological results		Total
	Malignant	Benign	
Malignant	112	1	113
Benign	6	82	88
Total	118	83	201

Histopathological examination results obtained various types of tumors. Basal cell carcinoma is a type of skin tumors majority, namely 93 cases (46.27%).Eighty-five cases showed basal cell carcinoma cytology results, with the remainder being diagnosed as different tumor types. Squamous cell carcinoma and malignant melanoma are the next most tumor types, each obtained 11 cases (5.47%). Other tumor types are ecrine Sebaceous Mucinous adenocarcinoma, neuroendocrine tumors DDX Merkel cell tumors, actinic keratosis, verruca vulgaris, Seborrheic keratosis, nevus, Nodular hidradenoma, Ecrine Poroma, syringocystadenoma, benign epidermal cyst, hemangioma, pyogenic granuloma, Dermatofibromas, neurofibromas, benign Mesenchymoma, Lipoma, Squamous papilloma, papilloma, Condyloma accuminata and Sebaceous Adenocarcinoma.

DISCUSSION

This study shows demand cytology compared histopathological examination of skin tumors increased from 2008 to 2010, ie 26.42%, 39.33%, and 42.33%. This suggests that pre -operative cytology clinicians increasingly necessary, especially in getting rid of malignancy. Diagnostic accuracy of cytology to malignancy in skin tumors in this study was 96.52%. Not many reports on the observation of a correlation between the results of cytology and histopathology of skin tumors. Research by Daskalopoulou along with that of Maounis and Gourgiotou prove that cytology in the diagnosis of a variety of primary skin tumors have high accuracy (Daskalopoulou et al 1993, Daskalopoulou et al 1997). Layfield and Glasgow reported cytological diagnosis of primary skin tumors 89% correct in distinguishing benign and malignant tumors (Orell & Domanski 2005). Research conducted Rodriguez proves cytological diagnosis of tumors had a sensitivity of 86% and specificity of 93% (Rodriguez et al 2007).

This study obtained 6 false negative cases. Three false negative cases are basal cell carcinoma diagnosed by cytology results showed atypic cells and epidermal hyperplasia and papilloma lesions suspicious of granulation tissue. Three other cases of false negatives are well differentiated squamous cell carcinoma with cytologic results of chronic ulcer and 2 cases with benign epidermal lesion cytology results.

Table 2. Suitability cytology and histopathology diagnosis of skin tumors

Histopathology	Cytology	Total
Basal Cell Carcinoma	*Basal Cell Carcinoma*	85
Basal Cell Carcinoma	*Squamous Cell Carcinoma*	1
Basal Cell Carcinoma	*Adenocarcinoma*	1
Basal Cell Carcinoma Morphea Type	*Carcinoma Poorly Differentiated*	1
Basal Cell Carcinoma	*Adenoid Cystic Carcinoma*	2
Basal Cell Carcinoma	*Atypiccells apparent*	1
Basal Cell Carcinoma	*Benign Epidermal Lesion*	1
Basal Cell Carcinoma	Jaringan Granulasi	1
Squamous Cell Carcinoma	*Squamous Cell Carcinoma*	7
Squamous Cell Carcinoma	*Carcinoma*, imp.*Adenocarcinoma*	1
Squamous Cell Carcinoma	*Ulcus Chronic*	1
Squamous Cell carcinoma, Well Differentiated	*Benign Epidermal Lesion*	2
Melanoma Maligna	*Melanoma Maligna*	10
Melanoma Maligna	*Malignant, Epidermal Carcinoma*	1
Mucinous Ecrine Sebaceous Adenocarcinoma	*Adenocarcinoma, Mucinous Type*	1
Neuroendocrine Tumor DDx Merkel Cell Tumor	*Malignant Small Round Cell tumor*	1
Actinic Keratosis	*Benign Epidermal Lesion*	1
Verruca Vulgaris	*Benign Epidermal Lesion*	3
Seborrhoeic Keratosis	*Benign Epidermal lesion*	23
Keratoacantoma	*Benign Epidermal Lesion*	1
Nevus	*Benign Lesion, kesan Nevus*	32
Nevus	*Benign Lesion*	1
Nodular Hidradenoma	Kesan *Squamous Cell Carcinoma*	1
Nodular Hidradenoma	*Benign Adnexa Tumor*	1
Eccrine Poroma	*Benign Adnexa Tumor*	1
Syringocystadenoma	*Benign Adnexa Tumor*	1
Benign Epidermal Cyst	*Benign Epidermal Cyst*	5
Hemangioma	*Benign Epidermal Lesion*	2
Pyogenic Granuloma	Granulated tissue	1
Dermatofibroma	*Benign Epidermal Lesion*	1
Neurofibroma	*Benign Spindle Mesenchymal Tumor*	1
Benign Mesenchymoma	*Hemangioma*	1
Lipoma	*Lipoma*	1
Squamous Papilloma	*Benign Epidermal Lesion*	2
Papilloma	*Benign Epidermal Lesion*	2
Condyloma Accuminata	*Benign Epidermal Lesion*, resembling *Condyloma accuminata*	2
Sebaceous Adenocarcinoma	*Adenocarcinoma*	1
	TOTAL	201

Three cases of false negative with basal cell carcinoma histopathology results entirely cytology showed a less representative sample. The case shows the cytology results only a few small groups of basal cell atypia, enlarged nuclei with little background contains a lot of blood. Cases of basal cell carcinoma with benign cytology results epidermal lesion, suspicious papilloma obtained from tumor -shaped bulge, diameter 8 mm with an intact surface. In such cases the lesions are too small, so it is difficult to obtain a representative sample FNA. Intact surface does not allow the sample obtained by scraping techniques. The false negative cases of basal cell carcinoma by cytology results obtained in the granulation tissue of ulcerative lesions were partially coated surface granulation tissue. Cytologic preparations in the case of many shows the distribution of inflammatory cells in the background contains a lot of blood.

Three other cases showed false negative results of cytologic diagnosis of chronic ulcer 1 and 2 benign epidermal lesion. The third case shows a picture of a Verrucos carcinoma histopathology. Based on the WHO classification, Squamous cell carcinoma of skin tumors has several variants, namely Acantholitic Squamous cell carcinoma, spindle cell-Squamous cell carcinoma,

verrucous squamous cell carcinoma, Squamous cell carcinoma and Pseudovascular Adenosquamous Carcinoma (LeBoit et al 2006). Based on the WHO classification, three cases showed histopathologic picture verrucous variant of squamous cell carcinoma squamous cell carcinoma, which shows the growth of tumor composed of squamous cells with mild atypia with few mitosis. Exo and endophytic growth pattern with picture suppress tumor growth in the stroma (LeBoit et al 2006, Rosai 2011). Based on the histopathological picture of course on cytology preparations will only be obtained squamous epithelial cells with mild atypia, whereas that suppress tumor growth pattern surrounding tissue does not allow derived from cytology preparations. A sign of malignancy in squamous cell carcinoma verrucous variant of squamous cell carcinoma is often not obtained from cytologic preparations (Lin & Zakowski 2008).

One case of false positives obtained with the results of the histopathological diagnosis of nodular hidradenoma impression cytology squamous cell carcinoma. Hidradenoma based on histopathologic picture consisted of a variety of epithelial cell types, including epithelial cells with clear or pale real cell membranes, but may also consist of epithelial cells squamoid shaped polygonal with vesicular nuclei and eosinophilic cytoplasm. Other epithelial cells in mucinous cell hidradenoma ie, columnar and Cuboid, also have apocrine differentiation. Combinations of various types of epithelial cells are often found (LeBoit et al 2006). In this case, obtaining cytological preparations of tumor cells composed of epithelial cells squamoid very similar to squamous epithelial cells, resulting in incorrect interpretation of the diagnostic impression of squamous cell carcinoma. Careful interpretation is needed to pay attention to the characteristics of malignancy in the cell nucleus. This study obtained 93 cases with histopathological results Basal Cell Carcinoma. Ninety (96.77%) cases diagnosed malignancy. This is not much different from the results of the study by 95.45% Fang X (Fang & Ma 1999). A total of 85 cases (88.54%) according diagnosed between cytology and histopathology. A total of 5 cases of malignant diagnosed with different types. While 3 cases of false negatives with the above explanation.

Five cases of malignant Basal cell carcinoma diagnosed by cytology type does not match that of adenoid cystic carcinoma, 2 cases, squamous cell carcinoma, adenocarcinoma and poorly differentiated carcinoma, 1 case each. Based on the WHO classification, basal cell carcinoma, obtained several variants, namely superficial basal cell carcinoma, nodular basal cell carcinoma, micronodular basal cell arcinoma, infiltrating basal cell carcinoma, fibroepithelial basal cell carcinoma, basal cell carcinoma with adnexal differentiation, basosquamous carcinoma, basal cell keratotic carcinoma as well as other variants include cystic, adenoid, sclerosing/morpheiform, infundibulocystic, pigmented and miscellaneous (LeBoit et al 2006). Two cases diagnosed adenoid cystic carcinoma with histopathological results of a nodular basal cell carcinoma and a variant form cribiform structure. Cytologic preparations in the case of matrix components showed eosinophilic hyaline globules resembling, but the components of the basal cells arranged a meeting with palisading edge. Basal cell carcinoma with squamous basosquamous variant can also be accompanied tumor cells containing keratin that resemble squamous cell carcinoma (Lin & Zakowski 2008, Orell & Domanski 2005, Koss & Melamed 2005). Although rare, Basal cell carcinoma can also demonstrate that the glandular component may resemble adenocarcinoma (Koss & Melamed 2005). One case of Basal cell carcinoma with cytologic results showed poorly differentiated carcinoma with histopathological picture morhpeiform variant. At the cytological picture shows the groups and distribution anaplasi cells, round nuclei with prominent nuclei child. Three cases of Basal cell carcinoma diagnosed in this study atypic cells, epidermal hyperplasia lesions and granulation tissue. The third case shows the cytology unrepresentative picture (described above).

This study received 11 cases with histopathological results Squamous cell carcinoma. Seven cases (63.64%) diagnosed according between cytology and histopathology. Three cases of false negatives is verrucous carcinoma are often not able to diagnosis of cytologic preparations. While one case the diagnosis of carcinoma, adenocarcinoma impressive, with a microscopic picture of the group and the distribution anaplastic epithelial cells with prominent nuclei child shows some glandular structures. Based on the WHO classification of tumors of the skin, one variant of squamous cell carcinoma is Adenosquamous with histopathologic picture showed a tumor composed of epithelial cells in sheets resembling tongues, columnar and rows of the invasion of the stroma. The tumor cells are squamous cells bordering diskeratotik glandular structures composed of epithelial mucin -producing secretory material (LeBoit et al 2006). In preparation cytology Squamous cell carcinoma, Adenosquamous variants may show epithelial cells with glandular structures, as in this case so diagnosed carcinoma, Adenocarinoma impression (Lin & Zakowski 2008, Orell & Domanski 2005).

This study received 11 cases with malignant melanoma histopathology results. Ten cases (90.91%) according diagnosed between cytology and histopathology. One

case with histopathologic results. Malignant melanoma is diagnosed as malignant, a carcinoma of the preparation cytology. Based on the type of tumor cells, malignant melanoma grouped into the types of epithelioid and spindle type. Epithelioid type shows a picture of the tumor cells resemble epithelial, large, round, wide cytoplasm, pleomorphic nuclei and vesicular nuclei with prominent child. Pigments can be found in the cytoplasm although it can also be minimal. While on the type of spindle cell shows a picture of nucleated cells spindle, length, cytoplasmic melanin pigment sometimes found (McKee et al 2005). In this case, melanoma including epithelioid cell type, but when sampling bleed easily, just gained some tumor cells with nuclei resembling epithelial and background contains a lot of blood.

Keratinocytic benign tumors found in this study is actinic keratosis, verruca vulgaris, condyloma accuminata, seborrheic keratosis and keratoacantoma. The entire case of the preparation cytology correctly diagnosed as benign lesions on the skin. However cytology methods have limitations in determining tumor type in benign tumors keratinocytic. All of these cases were cytologically diagnosed as benign epidermal lesion. Benign melanocytic nevus was found in 33 cases with varying types. A total of 32 cases were diagnosed with benign lesions impression nevus, 1 case of benign lesions diagnosed. Limitations of cytologic examination in such cases are that the small size of the lesion that is difficult to obtain a representative sample.

This study found two cases of sebaceous adenocarcinomas, diagnosed with an adenocarcinoma of the right cytology preparations. While the results of eccrine histopatology poroma, syringiocystadenoma and one case hidradenoma, in preparation cytology correctly diagnosed with a benign adnexal tumor. There are various types of appendageal skin tumors have limited cytologic examination to determine the type of tumor histopathology (Orell & Domanski 2005, the Slater & Reilly 1986, Rege & Shet 2001). To determine the exact type of tumor, it should be followed by histopathological examination of the excisional biopsy material (Layfield & Glasgow 1993). There is one case that is a false positive hidradenoma in this study and has been described above. Found also 5 cases of benign epidermal cyst diagnosed entirely correct on cytology.

Several cases of soft tissue tumors was also found that skin hemangioma, pyogenic granuloma, Dermato-fibromas, neurofibroma, and lipoma benign mesenchymoma. The whole case is really a benign mesenchymal tediagnosis tumor types but can not be identified precisely. There is one case with neuroendocrine tumors hisopatologi results DDX Merkel cell tumors. Cytologic preparations can recognize signs and diagnosed with a malignant round cell malignant tumor.

This study aims to determine the accuracy of cytology in all types of skin tumors. Kassi, who in his research assessing the diagnostic sensitivity and specificity of cytology is a special type of basal cell carcinoma tumors, showed results of 94.3% and 100%. Similarly Bakis in the meta-analysis showed a diagnostic sensitivity of cytology is a special type of basal cell carcinoma tumors by 97%. Naraghi Z also studied the specificity and sensitivity of diagnostic cytology of skin tumors on the type of basal cell carcinoma (Kassi et al 2012, Bakis et al 2004, Naraghi et al 2005).

In this study the positive predictive value of cytology in the diagnosis of malignant skin tumors was 99.12%, which means a 0.88% chance not suffering from malignant skin tumors where malignant cytology results. Negative predictive value in this study was 93.18%, which means a probability of 6.82% with a cytologic diagnosis of benign to malignant skin tumors suffer. Similarly, the positive likelihood ratio values was high (>10) in this study, suggesting that the role cytology in the diagnosis of skin tumors is important, especially in excluding malignancy.

CONCLUSION

Cytology method of skin tumors in Anatomic Pathology Department, Dr. Soetomo Hospital, has a sensitivity of 94.92%, specificity 98.80%, and 96.52% accuracy. These results indicate that skin tumor cytology method has a diagnostic role in excluding malignancy.

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