ISSN: 0975-833X

Available online at http://www.journalcra.com

International Journal of Current Research
Vol. 8, Issue, 06, pp.33448-33452, June, 2016

INTERNATIONAL JOURNAL OF CURRENT RESEARCH

RESEARCH ARTICLE

BASAL CELL LESIONS OF MAXILLOFACIAL REGION

***,[1]Dr. Ajinkya Amritrao Deshmukh, [2]Dr. Kirti Balkrishna Buva, [3]Dr. Atul Deshmukh and [4]Dr. Vaishali P. Chaskar**

[1]III yr Post Graduate Fellow, Bharti Vidyapeeth Deemed University Dental College, Hospital and Research Centre, Pune
[2]MDS (Oral Pathology) Pune
[3]Director. Oral & Maxillofacial Pathology & Pre-Clinical Research Centre Mumbai, Director of centre for Interdisciplinary Research D Y Patil University Navi Mumbai
[4]D.N.B. Anaesthesiology, Assistant Professor, Department of Anaesthesiology, Seth G.S.M.C. and K.E.M. Hospital Parel, Mumbai

ARTICLE INFO

Article History:
Received 24th March, 2016
Received in revised form
10th April, 2016
Accepted 25th May, 2016
Published online 30th June, 2016

Key words:
Basal cells,
Maxillofacial region,
Basal cell lesions.

ABSTRACT

Basal cells which are located at the basement membrane have an important function to differentiate at proliferating the cells, they have a typical appearance cuboidal to high cuboidal with a basophilic round to oval nuclei. This review focuses on the lesions which are termed after the suffix "Basal". They are merged together merely on the basis of the suffix. Few may show a histogenesis from the basal layer cells and few of them shows resemblance to the basal cell morphology. Thus, this is a segregation of basal cell lesions and there histopathological differential diagnosis.

Citation: Dr. Ajinkya Amritrao Deshmukh, Dr. Kirti Balkrishna Buva, Dr. Atul Deshmukh and Dr. Vaishali P. Chaskar, 2016. "Basal cell lesions of maxillofacial region", *International Journal of Current Research*, 8, (06), 33448-33452.

INTRODUCTION

Basal cells are supported by basement membrane, basal cells are cuboidal to high cuboidal, nucleus is round to ovoid situated furthermost from basal lamina giving a polarized appearance to the cell. These cells have different cell organelle ratio at a different site for example gingiva buccal mucosa or epidermis. (Garant, 2003) In this review article we compiled the different lesions of maxillofacial region with different histopathogenesis but sharing same basal cell appearance and utmost important in oral pathology practice. Basal cell lesions are few but most important aspect of oral pathology as they show a wide array of prognosis. It's important to diagnose these basal cell lesions. Clinicopathologically we can exclude differential diagnosis which gives a same basal cell appearance.

Corresponding author: Dr. Ajinkya Amritrao Deshmukh,
III yr Post Graduate Fellow, Bharti Vidyapeeth Deemed University Dental College, Hospital and Research Centre, Pune.

Basal Cell Adenoma

Basal cell adenoma (BCA) is a benign neoplasm. And it accounts for 1% to 2% of all salivary gland epithelial tumors. (Kratochvil, 1991; Seifert and Sobin, 1991) Kleinsasser and Klein first separated this entity from other lesions in 1967. (Kleinsasser and Klein, 1967) These authors also explained three basic patterns of BCA, solid, tubular and trabecular. And they also reported the monomorphic and isocellular nature of cells which are present in this tumor. Further, they reported that this tumor is different from pleomorphic adenoma because it lacks myoepithelial cells and myxochondroid component. Histologically, it is divided into four subgroups based on predominant growth pattern solid, tubular, trabecular and membranous. Some BCA shows a mixture of these growth patterns. (Nagao *et al*., 1982; Chaudhary *et al*., 1983; Seifert, and Sobin, 1991; Kratochvil, 1991) BCAs mainly occur in adults and the average age is 57 years. (Kratochvil, 1991) The majority of BCAs affects to a major salivary gland that is a parotid gland. This tumor can also found at the minor salivary

gland sites, followed by an upper lip and buccal mucosa. (Kratochvil, 1991) Microscopically BCAs are encapsulated and well-circumscribed tumors. The cystic formation can be seen. Two types of cells are present luminal cells and basal cells. Component of the basal cell is the important diagnostic criteria. Round to oval small tumor cells are present in less cytoplasm. The nucleus is generally darkly stained which gives the basaloid appearance. In two cell types, basaloid cells are present periphery to the luminal cells or tumor cells. In nests of basaloid cells, cuboidal or columnar cells which are present in the outer layer have a tendency of palisaded arrangement. There is a sharp boundary between stroma and tumor cells. Stroma is thin and vascular activity is rarely seen. (Salivary gland tumor pathology. Irving Dardick) Tubular type microscopically shows tumor cells are present in cords and they are interconnected and contain duct or acinar-like structures. Lumens are present within the cords and contain secretions. The outer layer consists of single and smaller cells and slightly larger central cells responsible for lumen formation. The thin stromal tissue is present in between the cords of tumor cells. (Salivary gland tumor pathology. Irving Dardick) Trabecular type microscopically shows two or more cells thick narrow interconnecting cords. Tumor cell cords are uniform in thickness. The central portion of trabeculae shows larger cells with increased cytoplasm. Lumens are smaller in size or absent. (Salivary gland tumor pathology. Irving Dardick) Solid type microscopically shows tumor cells are present in the nests and these nests are bulbous, closely associated, variable in shape and angular. And arrangements of these nests are complex. Peripheral cells are cuboidal to columnar and palisaded. Centrally placed tumor cells are lighter than the peripheral tumor cells because of more cytoplasm. Nest consists of basaloid cells and absence of lumen. Sometimes central part of nests shows squamoid appearance. Circular clear deposits can be present in tumor cell nodules. Stroma is minimum between nodules. (Salivary gland tumor pathology. Irving Dardick) Membranous type microscopically usually shows non-capsulated, multilobular and multifocal. It resembles the solid variant and histologically resembles the tubulo-trabecular variant. Small basaloid tumor cells are present with outer palisaded arrangement of cells. Thick eosinophilic bands are seen at the borders of the nests or cords of cells. (Salivary gland tumor pathology. Irving Dardick) The differential diagnosis for BCA is pleomorphic adenoma (PA) and adenoid cystic carcinoma (ACC). But ACC shows perineural and perivascular invasion which is absent in the BCA. Ductal elements and nests of tumor cells are small in ACC than in BCA. Basosquamous whirling is absent in ACC. BCA show sharp separation between epithelium and stroma component which is not so clear in PA. chondroid differentiation is rare in BCA while it is seen in PA. Basal cells in PA are numerous and slightly separated than BCA.

Basal cell adenocarcinoma

Ellis and Wiscovitch reported basal cell adenocarcinoma (BCAC) is a low-grade carcinoma of salivary gland origin. (Ellis and Wiscovitch, 1990) It is considered a malignant counterpart of BCA, and show demographic and histologic features same as BCA, BCAC may arise either new or from a preexisting BCA. (Batsakis and Luna, 1991) mostly 90% of BCAC found in the parotid gland and account for 0.6% of parotid tumors. (Nagao *et al*., 1998) This tumor accounts for 1.6% of all salivary gland tumors and 2.9% of malignant salivary gland tumors. (Ellis and Auclair, 1996) No gender predilection and occurs in third to tenth decades of life. BCAC usually shows the features same as the solid or tubulo-trabecular type of BCA. Microscopically basic growth pattern same as solid and tubule-trabecular type of BCA, the solid type is most common and show a mosaic-like pattern. This tumor shows pushing borders or frank infiltration. The bulk of solid aggregates contain small dark staining basaloid cells. Some ductal structures also present. Nuclei are small, irregular and vary in size. Peripheral palisaded tumor cells are less as compared to BCA. Mitotic figures are present. Poorly differentiated variant show more nuclear and cytoplasmic pleomorphism and increased mitotic activity. Infiltration occurs into peri-glandular fat, muscle, and dermis. Perineural invasion is seen and intravascular invasion is rare. The eosinophilic hyaline material is seen. Necrosis and hemorrhage can also be seen. (Salivary gland tumor pathology. Irving Dardick) Differential diagnosis consists of basal cell adenoma, adenoid cystic carcinoma, polymorphous low-grade adenocarcinoma, and small cell undifferentiated carcinoma. Invasion and the increased mitotic activity is the differentiating factor between BCA and BCAC. Hyaline droplets are absent in ACC. BCA show another form of intercellular basal lamina than ACC. polymorphous low-grade adenocarcinoma does not show regular and mosaic-like growth pattern. And also shows the single type of tumor cells. Peripheral palisading is absent in polymorphous low-grade adenocarcinoma. In small cell undifferentiated carcinoma ductal differentiation and mosaic-like growth with or without peripheral palisading are not seen. Foci of tumor cells are very infiltrative in small cell undifferentiated carcinoma. (Salivary gland tumor pathology. Irving Dardick)

Basal cell ameloblastoma

The basal cell ameloblastoma is an extremely rare subtype of ameloblastoma. (Neville *et al*., 2002) first it is thought to be present in peripheral location but also seen intraosseously. (Reichart *et al*., 1995) basal cell ameloblastoma grows in an island-like pattern. Color gradation is not appreciable like other ameloblastomas. Because the central portion of the tumor island is occupied by the basaloid appearing cells rather than stellate reticulum like cells. The basaloid cells usually stain dark basophilic. The cells which are present in the central portion of the tumor are polyhedral to spindle in shape. Stellate reticulum like cells is absent in basal cell ameloblastoma. The orientation of nuclei and morphology of peripheral cells are altered. Peripheral cells are columnar to cuboidal and does not show reverse nuclear polarity with subnuclear vacuole formation. Nuclei are hyperchromatic and palisading. Basal cell ameloblastoma is very similar to basal cell carcinoma. (Kessler, 2004)

Basal cell carcinoma

Basal cell carcinoma (BCC) is the most common malignancy in the humans. It develops most commonly on the sun-exposed parts of the skin. The appearance of basal cell carcinoma is a pearly wax-like nodule that eventually ulcerates. (Antonio

Cardesa and Pieter J Slootweg) The face and the scalp are the most common sites. It usually affects to older individuals but also seen in younger individuals. And it usually affects to fair skinned people rather than dark people. Male to female ratio is 3:2. It is a slow-growing tumor and metastasis is rare. It causes local destruction. Ultraviolet radiation is the most common etiology of this tumor. Radiations like x-ray and a chemical like arsenic are also responsible for it. It is thought that BCC arises from the pluripotent stem cell compartments of the basal layer of the epidermis and follicular structures. It does not arise from the oral cavity so never seen in the oral cavity unless infiltrated from skin to oral mucosa. (Shafer's textbook of oral pathology) BCC is divided into nodular, cystic, superficial, micronodular nodulocystic, superficial multifocal, adenoid, morpheaform, infiltrative, keratotic, and pigmented forms, and other rarer variants. (Shafer's textbook of oral pathology; McGibbon, 1985; Wade and Ackerman, 1978) Among these nodular is most common and small slightly elevated papule with a central depression. Pigmented BCC shows brown black pigments. Cystic BCC contains blue-gray cystic nodules. Superficial BCC appears scaly with a thread like border, red to brown in color. Micronodular and morpheaform are aggressive forms of BCC. (Shafer's textbook of oral pathology) Microscopically the nodular, pigmented and syndrome related BCC contains uniform ovoid, darkly stained basaloid cells with moderate size nucleus and less cytoplasm. Cells arranged into islands and strands and appear arise from the basal cell layer of the epidermis and invade into connective tissue. Islands show peripheral palisading of cells. At some areas, keratin is seen, duct formation seen because of interlacing strands of lesional cells. Cystic appearance is because of necrosis of the islands. Solar elastosis because of actinic damage seen in the stroma. Pigmented BCC shows melanocytes in tumor islands and melanophages in the stroma. Sclerosing BCC shows infiltrating thin strands of tumor cells and dense stroma in the background. Superficial BCC shows lobules of tumor cells which drop from epidermis in the multifocal pattern. (Neville *et al*., 2009) Differential diagnosis consists of conventional trichoepithelioma which mimics keratotic BCC (Neville *et al*., 2009), desmoplastic trichoepithelioma mimic morpheaform BCC (Lum and Binder,
2004), small cell squamous cell carcinoma (Wick *et al*., 1988), basaloid squamous carcinoma mimic nodulocystic BCC (Jimenez *et al*., 1995), and adenoid cystic eccrine carcinoma mimic adenoid or eccrine BCC (Wick and Swanson, 1986; Misago *et al*., 2004).

Basaloid squamous cell carcinoma

Basaloid squamous cell carcinoma (BSCC) is a poorly differentiated squamous cell carcinoma which consists of basaloid cells and squamous cell carcinoma. Clinically it shows aggressive behavior. First described by wain *et al* in 1986. (Wain *et al*., 1986) It is an extremely rare histological variant of squamous cell carcinoma. Also called as basaloid carcinoma and adenoid cystic-like carcinoma. Commonly affects to the base of tongue, supraglottic larynx, and hypopharynx. Clinically aggressive and systemic and lymph nodes metastasis seen. (Wain *et al*., 1986) This is a mucosa based tumor and till date common sites are the base of the tongue, supraglottic larynx, and hypopharynx. (Wain *et al*., 1986; Tsang *et al*., 1991; Banks *et al*., 1992; Cadier *et al*., 1992; Campman *et al*., 1994; Coppola *et al*., 1993; Gartlan *et al*., 1992; Ereno *et al*., 1994; Hellquist *et al*., 1994; Klijanienko *et al*., 1993; Lovejoy and Matthews, 1992; Luna *et al*., 1990; McKay *et al*., Bilous *et al*., 1989; Muller and Barnes, 1995; O'Malley, 1992; Raslan *et al*., 1994; Seidman *et al*., 1991; Shvili *et al*., 1990; Wan *et al*., 1992) Mostly affects to older individuals age range 27-88 yrs. and commonly affects to males than females and show high-grade presentation that is stage III-IV. The etiology of BSCC is tobacco and alcohol use and also other risk factors. (Raslan *et al*., 1994) Clinical presentation shows an exophytic mass, flat lesion, central ulceration and marginal submucosal induration. (Coppola *et al*., 1993; Gartlan *et al*., 1992; Lovejoy and Matthews, 1992; Luna *et al*., 1990; McKay and Bilous, 1989) It may infiltrate deeply and laterally, submucosal soft tissue infiltration is seen. (McKay and Bilous, 1989; Barnes *et al*., 1996) Microscopically BSCC consists of small closely packed basaloid cells with hyperchromatic nuclei. Central necrosis seen called comedo necrosis. Small cystic spaces are present which contain PAS and alcian blue positive material and stromal hyalinization. (Wain *et al*., 1986; Banks *et al*., 1992) BSCC is also associated with squamous cell carcinoma component. BSCC very rarely show malignant spindle cell component. (Muller and Barnes, 1995; Barnes *et al*., 1996) Differential diagnosis consists of neuroendocrine carcinoma, adenoid cystic carcinoma, adenocarcinoma and adenosquamous carcinoma. Neuroendocrine carcinoma positive for various neuroendocrine markers which help to differentiate from BSCC. (Banks *et al*., 1992; Cho *et al*., 2000) Adenoid cystic carcinoma very rarely show squamous differentiation and tumor cells are positive for S-100 protein and vimentin whereas they are negative in BSCC. (Klijanienko *et al*., 1993; Barnes *et al*., 1996) Adenocarcinoma and adenosquamous carcinoma show gland formation and mucin secretion in tumor cells which is absent in BSCC. Radical neck dissection followed by supplemental radio and chemotherapy is the treatment of choice. (Wain *et al*., 1986; Barnes *et al*., 1996; Wenig, 2002)

Conclusion

Till now there was no compilation of basal cell lesions of maxillofacial region. Clinically the locations of these lesions are different, Clinical and radiographical appearance is also vary from each other histogenesis also differ from each other, all these lesions are different from each other in all aspect except sharing one common histopathological finding that is 'basal cells'. So there was a need to compile these lesions under one heading to simplify the study of basal cell lesions of maxillofacial region.

REFERENCES

Banks ER, Frierson HF, Mills SE, *et al*. 1992. Basaloid squamous cell carcinoma of the head and neck. *Am J Surg Pathol*., 16:939–946.

Barnes L, Ferlito A, Altavilla G, *et al*. 1996. Clinicopathological consultation. Basaloid squamous cell carcinoma of the head and neck. Clinicopathological features and differential diagnosis. *Ann Otol Rhinol Laryngol*., 105:75–82.

Batsakis JG, Luna MA: 1991. Basaloid salivary carcinomas. *Ann Otol Rhinol Laryngol*., 100:785–787.

Brownstein MH, Shapiro L: 1977. Desmoplastic trichoepithelioma. *Cancer*, 40:2979–2986.

Cadier MA, Kelly SA, Parkhouse N, *et al*. 1992. Basaloid squamous carcinoma of the buccal cavity. Head Neck 14:387–391.

Campman SC, Gandour-Edwards RF, Sykes JM: 1994. Basaloid squamous carcinoma of the head and neck. *Arch Pathol Lab Med*., 118:1229–1232.

Chaudhary AP, cutler LS, Satchidanand S, Sunder Raj M, Lin C-C: 1983. Monomorphic adenomas of the parotid gland: Their ultrastructure and histogenesis. *Cancer*, 52:112-120.

Cho KJ, Jang JJ, Lee SS, Zo JI 2000. Basaloid squamous carcinoma of the oesophagus: a distinct neoplasm with multipotential diff erentiation. *Histopathology,* 36:331–340.

Coppola D, Catalano E, Tang CK, *et al*. 1993. Basaloid squamous cell carcinoma of floor of mouth. *Cancer,* 72:2299–2305.

Ellis GL, Auclair PL: 1996. Malignant epithelial neoplasms. In Ellis GL, Auclair PL (eds): Atlas of Tumor Pathology. Tumors of the Salivary Glands. Washington, DC: Armed Forces Institute of Pathology, pp 337–343.

Ellis GL, Wiscovitch JG: 1990. Basal cell adenocarcinomas of major salivary glands. *Oral Surg Oral Med Oral Pathol*., 69:461–469.

Ereno C, Lopez JI, Sanchez JM, *et al*. 1994. Basaloid-squamous cell carcinoma of the larynx and hypopharynx. A clinicopathologic study of 7 cases. *Pathol Res Pract*., 190:186–193.

Garant P. 2003. Oral cells and tissues. Chicago: Quintessence Pub. Co.

Gartlan MR, Goetz SP, Graham SM: 1992. Basaloid-squamous carcinoma (BSCC) of the larynx. *Arch Otolaryngol Head Neck Surg*., 118:998–1001.

Hellquist HB, Dahl F, Karlsson MG, *et al*. 1994. Basaloid squamous cell carcinoma of the palate. *Histopathology*, 25:178–180.

Jimenez FJ, Burchette JL Jr, Grichnik JM, *et al*. 1995. BER-EP4 immunoreactivity in normal skin and cutaneous neoplasms. *Mod Pathol*., 8:854–858.

Kessler HP, 2004. Intraosseous ameloblastoma. *Oral Maxillofac Surg Clin N Am*., 16: 309-322.

Kleinsasser O, klein HJ: 1967. Basalzelladenome der speicheldrusen. Archive Klin Exper Ohren- Nasen- und Kehlkopfheilk, 189:302-316.

Klijanienko J, El-Naggar A, Ponzio-Prion A, *et al*. 1993. Basaloid squamous carcinoma of the head and neck. Immunohistochemical comparison with adenoid cystic carcinoma and squamous cell carcinoma. *Arch Otolaryngol Head Neck Surg*., 119:887–890.

Kratochvil FJ: 1991. Canalicular adenoma and basal cell adenoma. In Ellis GL, Auclair PL, Gnepp DR, eds., surgical pathology of the salivary glands. Philadelphia; W.B. Saunders Co., 202-224.

Kratochvil FJ: 1991. Canalicular adenoma and basal cell adenoma. In Ellis GL, Auclair PL, Gnepp DR (eds): Surgical Pathology of the Salivary Glands. Philadelphia: WB Saunders, pp 202–224.

Lovejoy HM, Matthews BL: 1992. Basaloid-squamous carcinoma of the palate. *Otolaryngol Head Neck Surg*., 106:159–162.

Lum CA, Binder SW: 2004. Proliferative characterization of basal-cell carcinoma and trichoepithelioma in small biopsy specimens. *J Cutan Pathol*., 31:550–554.

Luna MA, El Naggar A, Parichatikanond P, *et al*. 1990. Basaloid squamous carcinoma of the upper aerodigestive tract. *Cancer*, 66:537–542.

McGibbon DH: 1985. Malignant epidermal tumors. *J Cutan Pathol*., 12: 224–238.

McKay MJ, Bilous AM: 1989. Basaloid-squamous carcinoma of the hypopharynx. *Cancer*, 63:2528–2531.

Misago N, Satoh T, Narisawa Y: 2004. Basal cell carcinoma with ductal and glandular differentiation: A clinicopathologic and immunohistochemical study of 10 cases. *Eur J Dermatol*., 14:383–387.

Muller S, Barnes L: 1995. Basaloid squamous cell carcinoma of the head and neck with a spindle cell component. *Arch Pathol Lab Med*., 119:181–182.

Nagao K, Matsuzaki O, Saiga H, Sugano I, Shigematsu H, Kaneko T, Katoh T, Kitamura T: 1982. Histopathologic study of basal cell adenoma of the parotid gland. *Cancer,* 50:736-745.

Nagao T, Sugano I, Ishida Y, *et al*. 1998. Basal cell adenocarcinoma of the salivary glands: Comparison with basal cell adenoma through assessment of cell proliferation, apoptosis, and expression of p53 and bcl-2. *Cancer*, 82:439–447.

Neville BW, Damm DD, Allen CM, Bouquot JE, 2002. Oral and maxillofacial pathology. 2nd edition. Philadelphia:WB Saunders, p 611-9.

Neville BW, Damm DD, Allen CM, Bouquot JE, 2009. Oral and maxillofacial pathology. 3rd edition. Philadelphia:WB Saunders.

O'Malley BW Jr: 1992. Pathologic quiz case 2: Basaloid-squamous carcinoma of the right pyriform sinus. *Arch Otolaryngol Head Neck Surg*., 118:212–215.

Pathology of head and neck. Antonio Cardesa, *Pieter J Slootweg*.

Raslan WF, Barnes L, Krause JR, *et al*. 1994. Basaloid squamous cell carcinoma of the head and neck: A clinicopathologic and flow cytometric study of 10 new cases with review of the English literature. *Am J Otolaryngol*., 15:204–211.

Reichart PA, Philipsen HP, Sooner S, 1995. Ameloblastoma: biological profile of 3677 cases. *Eur J Cancer B Oral Oncol*., 31B(2):86-99.

Salivary gland tumor pathology. Irving Dardick.

Seidman JD, Berman JJ, Yost BA, *et al*. 1991. Basaloid squamous carcinoma of the hypopharynx and larynx associated with second primary tumors. *Cancer*, 68:1545–1549.

Seifert G, Sobin LH: 1991. Histological Typing of Salivary Gland Tumours. World Health Organization International Histological Classification of Tumours, 2nd ed. New York: Springer-Verlag.

Seifert, G. and Sobin, L.H: 1991. World health organization international histologic classification of tumors: Histologic typing of salivary gland tumors. 2nd edition. Berlin; Springer-verlag.

Shafer's textbook of oral pathology.

Shvili Y, Talmi YP, Gal R, *et al*. 1990. Basaloid-squamous carcinoma of larynx metastatic to the skin of the nasal tip. *J Craniomaxillofac Surg*., 18:322–324.

Tsang WYW, Chan JKC, Lee KC, *et al*. 1991. Basaloid-squamous carcinoma of the upper aerodigestive tract and so-called adenoid cystic carcinoma of the oesophagus: The same tumour type? *Histopathology*, 19:35–46.

Wade TR, Ackerman AB: 1978. The many faces of basal cell carcinoma. *J Derm Surg Oncol*., 4:23–28.

Wain SL, Kier R, Volmer RT, Bossen EH 1986. Basaloidsquamous carcinoma of the tongue, hypopharynx, and larynx. Report of 10 cases. *Hum Pathol*., 17:1158–1166.

Wan SK, Chan JKC, Tse KC: 1992. Basaloid-squamous carcinoma of the nasal cavity. *J Laryngol Otol*., 106:370–371.

Wenig BM 2002. Squamous cell carcinoma of the upper aerodigestive tract: precursors and problematic variants. *Mod Pathol*., 15:229–254.

Wick MR, Manivel JC, Millns JL: 1988. Histopathologic considerations in the management of skin cancer. In Schwartz RA (ed): Skin Cancer: Recognition and Management. New York: Springer-Verlag, pp 246–275.

Wick MR, Swanson PE: 1986. Primary adenoid cystic carcinoma of the skin. *Am J Dermatopathol*., 8:2–13.

****