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ORIGINAL ARTICLE

Frequency of Expression of D240 in Dermatofibroma – A diagnostic study

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ABSTRACT

Aim: To establish the diagnostic utility of D2-40 IHC stain in dermatofibroma, by determining its positivity of expression.
Study design: It was a Cross-sectional study
Setting: The study was conducted in Department of Histopathology, Chughtai Institute of Pathology
Duration of study: Six months (1st August 2018 to 31st January 2019)
Methods: A total 70 samples were included. The clinical parameters like age and gender were recorded. The histological preparation was performed by classic method for inclusion in paraffin followed by haematoxylin-eosin staining. The immunohistochemical analysis was performed on serial sections using immune-enzymatic soluble complex method. The antibody used was D2-40 polyclonal antibody from DAKO. Diffuse crisp cytoplasmic D2-40 staining was considered positive.
Results: The mean age was 32.76±10.65 years and male to female ratio was 1:1.4. There were 70% cases have D2-40 positivity for dermatofibroma and 30% have no D2-40 positivity for dermatofibroma and mean duration of disease was 9.05±6.33 months. There were significant difference (P<0.05) between age and duration of disease with respect to D2-40 positivity for dermatofibroma;
Conclusion: D2-40 immunoreactivity is sensitive and is useful in the differential diagnosis of dermatofibroma.
Keywords: Dermatofibroma, Haematoxylin, Immunohistochemical, Positivity of D2-40

INTRODUCTION

Dermatofibroma (DF) is a benign fibro-histiocytic lesion predominantly involving lower extremities, commonly occurring in women. It usually appears in early to mid-adult life and occurs in response to trauma and insect bite.[1] There are multiple variants of DF and it is important to diagnose them because they can be mis-diagnosed as malignant tumors. These variants include epithelioid DF, lipidized DF, clear cell DF, cellular DF, myxoid DF, atrophic DF, hemosiderotic DF, granular cell DF, DF with intracytoplasmic eosinophilic globules and cholesteric DF. Other variants include aneurysmal, atypical, palisading, keloidal, balloon cell and signet ring cell type.[2] Few DF can involve the sub-cutis[3].

Some dermatofibromas can be extremely cellular and some may have large atypical nuclei and can be mistakenly diagnosed as DFSP. It is important to differentiate these two lesions because of difference in their behavior and treatment as DF is treated by excision, cryosurgery or laser therapy while wide local excision with extended margins is recommended for DFSP.[4]

Currently, CD34 is used to differentiate between the two lesions, being positive in DFSP. However, CD34 can be positive in cellular variants of DF. D2-40 is a membrane mucoprotein that reacts with the O-linked, 40-KDa sialo-glycoprotein present on lymphatic epithelium, fetal testis and on surface of germ cell tumors[5]. There are international studies, one showing 100% expression of D2-40 in DF[6], while other showing 76% cases of DF positive for D2-40.[7] However, to best of our knowledge, no national data is available on this subject.

The objective of the study was to establish the diagnostic utility of D2-40 IHC stain in dermatofibroma, by determining its positivity of expression.

MATERIALS AND METHODS

It was designed as a cross-sectional study performed in histopathology department of Chughtai institute of pathology in the duration of six months from 1st August 2018 -31st January 2019. A total of 70 cases were collected which included all diagnosed cases of dermatofibroma of both genders with age range of 15-55 years along with blocks from outside laboratories. The clinical parameters like age, gender and duration were recorded from the form sent from the sample site.

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The histological preparation was performed by classic method for inclusion in paraffin followed by haematoxylin-eosin staining. The immunohistochemical analysis was performed on serial sections using immune-enzymatic soluble complex method. The antibody used was D2-40 polyclonal antibody from DAKO. Diffuse crisp cytoplasmic D2-40 staining was considered positive. One consultant histopathologist (minimum experience of 5 years)examined each case and his/her diagnosis was taken as confirmatory.

Statistical analysis: SPSS-20 was used to enter and analyse the data. Mean and standard deviation was calculated for quantitative variable like age. Frequency and percentage were calculated for qualitative variables like gender and D2-40 positivity for DF in the samples. Effect modifiers like age, gender, duration of the disease were controlled through stratification. Post stratification chi-square test was applied by taking P value equal to 0.05 significant.

RESULTS

There were 46 patients (65.7%) in age group 18-36 years and 24 patients (34.3%) in age group 37-55 years. The mean±SD age was 32.76±10.65 years (Table 1).

Regarding genders, 29 patients (41.4%) were males and 41 (58.6) were females with male to female ratio was 1:1.4 (Table 2).

According to D2-40 positivity for dermatofibroma, there were 49 patients (70%) have D2-40 positivity for dermatofibroma and 21 (30%) have no D2-40 positivity for dermatofibroma (Table 3).

When the patients were distributed according duration of disease, 64 patients (91.4%) between 1-15 months and 6 patients (8.6%) between 16-36 months with mean duration of disease was 9.05±6.33 (Table 4).

When the D2-40 positivity for dermatofibroma was stratified according to age, statistically significant difference (P<0.05) was found between age and D2-40 positivity for dermatofibroma (Table 5). There were statistically no significant difference (P>0.05) was found between gender and D2-40 positivity for dermatofibroma (Table 6). Regarding duration of disease stratified with D2-40 positivity for dermatofibroma, the results showed significant difference (P<0.05) (Table 7).

Table 1: Frequency and percentage of age(n = 70)

Age (years)	No.
18 – 36	46(65.7%)
37 – 55	24(34.3%)
Mean±SD	32.76±10.65

Table 2: Frequency and percentage of gender(n = 70)

Gender	n
Male	29(41.4%)
Female	41(58.6%)
Male to Female Ratio	1:1.4

Table 3: Frequency and percentage of D2-40 positivity for dermatofibroma(n = 70)

D2-40 positivity for dermatofibroma	n
Yes	49(70%)
No	21(30%)

Table 4: Frequency and percentage of duration of the disease (n = 70)

Duration of disease(months)	No.	%
1 – 15	64	91.4
16-36	6	8.6
Mean±SD	9.05±6.33	

SD = Standard deviation

Table 5: Stratification of D2-40 positivity for dermatofibroma according to age(n = 70)

Age (years)	Positive	Negative
18 – 36	38	8
37 – 55	11	13

χ^2 = 10.157 df. = 1 P = 0.001

Table 6: Stratification of D2-40 positivity for dermatofibroma according to gender (n = 70)

Gender	Positive	Negative
Male	21	8
Female	28	13

χ^2 = 0.137 df. = 1 P = 0.711

Table 7: Stratification of D2-40 positivity for dermatofibroma according to duration of the disease(n = 70)

Duration of disease	Positive	Negative
1 – 15	47	17
16 – 36	2	2

χ^2 = 4.201, df. = 1, P = 0.040

DISCUSSION

Dermatofibroma also known as fibrous histiocytoma is one of the most common types of benign cutaneous as well as soft tissue tumors.When present below the skin,they are termed as 'Dermatofibroma' and when centered in the deeper soft tissue, the variant is named as 'Deep fibrous histiocytoma'.It is usually found in young to middle-aged adults and is more common in females. It frequently develops on extremities and trunk and is asymptomatic in majority of the cases.Clinical presentation of DF varies from plaques to nodules or polyps of less than 1 cm in diameter with a red-brown to purple discolouration. Etiology of DF is not known however, associations with minor injury and insect bites have been reported.[10] The lesions are most often solitary, but multiple lesions are documented in approximately 10% of individuals, especially in patients with altered immunity. In the current study, most of the presenting features were consistent with those of the previous reports.[11,12] The results showed that most of the lesions presented within the age range of 18-36 years with an overall female predominance. About 70% of the cases occurred on the extremities, with a dusky brown smooth surface.

Histopathologically, dermatofibroma belongs to fibrohistiocytic group of lesions comprising of a variable mixture of population of cells. These include fibroblast-like cells, histiocytes either xanthomatous or multinucleated and blood vessels. Depending upon the predominent constituents, variants of DF have been designated in the past as 'nodular subepidermal fibrosis,' 'histiocytoma' and 'sclerosing hemangioma'. Currently,these lesions are renamed as the fibrocollagenous, histiocytic, and aneurysmal variants respectively which reflects their exact composition.[13]

Statistics showed that in our study, the mean age of DFs was significantly different but was consistent with the literature. The gender distribution and duration of disease was similar to what has been reported in the literature in past.[8,9]

D2-40 is a monoclonal sialoglycoprotein antibody. It is a useful marker of lymphatic endothelial origin helpful in establishing the lymphatic invasion of solid tumors. Tumors that show frequent expression of D2-40 include lymphangiomas and Kaposi sarcoma, chondroid tumors, seminomas, ependymomas & meningiomas.[14]

Studies have shown that D2-40 expression in soft tissue tumors is peculiar for follicular dendritic cells thus the tumors originating from these cells express D2-40. However, expression of D2-40 in DF has received little attention[6,15,16]. Our study strongly suggests that DF has originated from dermal dendritic cells.[6] According to Xu et al[16] D2-40 expression in cases of DF was100%,while all DFSPs were either negative or showed a focal weak positivity when present,thus establishing its diagnostic utility as a helpful immunostain in differentiating these two closely related lesions. Kaddu and Leinweber[15] conducted a study on 30 DFs and 15 cellular thekeomas. Here again the results proved that D2-40 expression can be helpful in separating cellular neurothekeomas and DFs from its close differentials. Our results also showed a statistically significant relationship between the D2-40 expression of DFs and DFSPs. However, controversial results from a study revealed that many malignant or benign subtypes of soft tissue tumors can show D2-40 positivity,which has no statistical value.[15]

Fig.1 dermatofibroma histology

Fig.2 a) H&E b,c,d) diffuse crisp cytoplasmic D240 staining in dermatofibroma on low & high powers

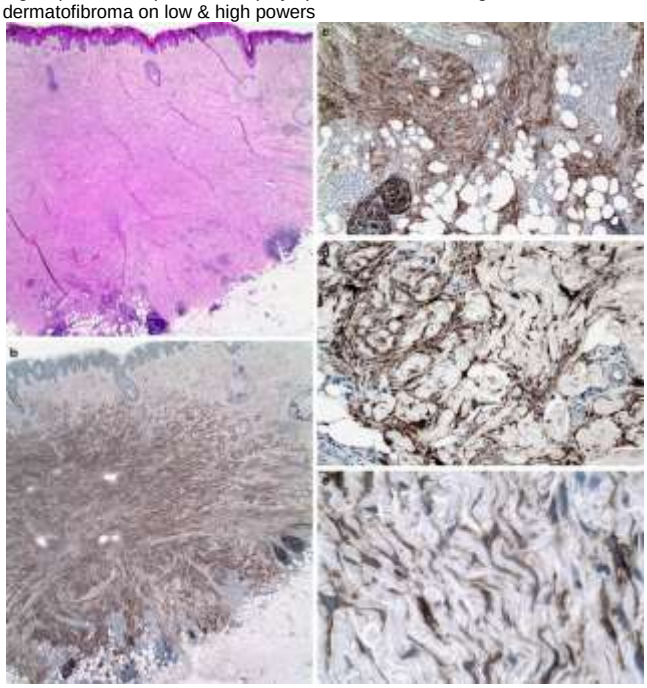

Fig. 3: Dermatofibrosarcoma protuberants showing absent D2-40 staining in the spindle cells, positive internal controls being the lymphatic endothelial cells and the basal layer of sebaceous glands

CONCLUSION

The clinical features and morphology of dermatofibroma and its variants is important to diagnose as to separate it from its possible differentials and to determine the prognosis, since the variants have different probabilities of local recurrence. Rare variants have the capability to metastasize as well.Thus,our study shows that D2-40 immunostain is helpful in diagnosing cases of dermatofibroma and confirming the diagnosis of those DFs which are difficult to be separated from all other agressive neoplasms,that can be considered in the differential diagnosis, on H&E alone.

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