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Head and neck inflammatory myofibroblastic tumor (IMT): Evaluation of clinicopathologic and prognostic features

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SUMMARY

Owing to rarity and awareness deficiency towards inflammatory myofibroblastic tumor (IMT), we sought to review on its clinicopathological features; arising awareness to achieve early diagnosis; exploring prognostic factors and then establishing a treatment protocol. Retrospective study was performed on patients with histological proven IMT between January 2003 and December 2010. Their demographic data, clinical and histological presentations were recorded. Overall survival (OS) and progression-free-survival (PFS) were estimated via Kaplan–Meier method. Cox regression model was applied to determine the significant of prognostic factors. Logistic regression model was established to predict the probability of relapse. A total of 28 patients. Five-year PFS was 65%. Surgical margins primarily and independently determined the survival, followed by size, pseudocapsule of the lesion, intra-lesional necrosis and lastly Ki-67 and ALK overexpression. Logistic model in prediction of relapse was established, with the formula as probability of relapse = $1/(1 + e^{-z})$ where e = exponential function, z = constant value (3.9) + B*margin + B*size + B*immunohistochemical expression + B*pseudocapsule + B*intra-lesional necrosis. Immunohistochemical overexpression was significant if Ki-67 was strongly expressed with a conditioned ALK overexpression simultaneously. Staining intensity must be at least moderate for those ALK nuclear staining was less than 25%. Weak ALK staining intensity is only significant if nuclear staining was more than 25%. Diagnosis of IMT is achieved via exclusion. Radical resection and obtaining negative margins remains the mainstay of treatment. Both high and moderate-risk groups required post-operative radiotherapy. In low-risk group, post-operative radiotherapy was recommended if the lesion is larger than 5 cm in diameter with a conditioned ALK & Ki-67 overexpression.

Introduction

Inflammatory myofibroblastic tumor (IMT) is a relatively rare soft-tissue lesion. It has a distinctive histopathology of heterogeneous group of proliferating myofibroblastic spindle cells with infiltration of inflammatory cells predominantly plasma cells and lymphocytes.[1–6] The lesion predominated in lung and represents less than 1% of soft-tissue sarcoma. Head and neck IMT accounts for 14–18% of extra-pulmonary IMT.[5]

Several terms like inflammatory pseudotumor, plasma cell granuloma, histiocytoma, plasma cell histiocytoma complex, fibrohistiocytoma, xanthomatous granuloma, lymphoid hamartoma, myxoid hamartoma, xanthomatous pseudotumor, spindle cell pseudotumor, inflammatory fibrosarcoma, benign myofibroblastoma and inflammatory myofibroblastic proliferation were used.[1,7–15] In 1994, World Health Organization (WHO) had anthologized those terms as IMT. WHO declared IMT as a diagnostic classification for intermediate soft-tissue myofibroblastic neoplasm by its well reproducible histological morphology.[16–18]

Owing to its rarity, the conception of IMT altered with time, from a benign reactive process to an intermediate neoplasm. Multiple pathological manifestations, controversial biological origin and diversified radiological images had led to diagnostic dilemma. To date, most studies performed were case reports. Of interest, case reports provide limited information and overview on IMT. We sought to review the clinicopathological features;

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arising awareness to achieve an early diagnosis and establishing a treatment protocol for IMT.

Material and methods

Ethical approvals were obtained from Hospital Review Boards. This is a retrospective study. Data of histological proven IMT between 2003 and 2010 were retrieved from a sequential and prospectively maintained cancer database of Shanghai Ninth People's Hospital. Data collected include patient's demographic details, clinical features, medical history, treatment received, clinicopathological characteristics and follow-ups. Pathological slides were reviewed by two consultant pathologists independently and only similarly interpreted data were taken into account. We subdivided the primary tumor location into superficial (a) or deep (b) tumor. Superficial IMT are those exophytic lesions without involvement of superficial fascia or periosteum which periosteum must be histologically proven negative. Deep IMT was defined as either deeply situated tumor or those had invaded superficial fascia, surrounding muscle or bone.

The primary end point was clinicopathological characteristics. Secondary end points were: (1) overall survival (OS), defined as time from surgery performed in our institute to death. (2) Progression-free survival (PFS), defined as time from surgery performed in our institute to death or first documented relapse or distant metastases. Death of unknown causes was censored.

Statistical analysis was performed using SPSS13.0 software. OS and PFS were estimated via Kaplan–Meier method. Univariate analysis on size, location, depth, surgical margin, duration of delay diagnosis, clinical manifestation (primary vs recurrent), provision of adjuvant treatments (radiotherapy/chemotherapy), mitotic figure, necrosis, immmunohistochemical results and pseudocapsule's status. Multiple regression analysis using Wald methodology was performed to assess the risk factors and prognostic factors. Logistic regression analysis was performed to predict relapse risk. Receiver operating characteristic (ROC) analysis was applied to determine the sensitivity and specificity of our logistic model. A p value of $\leqslant 0.05$ was considered statistically significant.

Results

Clinical findings

A total of 28 cases. Clinical characteristics were summarized in Table 1. In general, superficial lesions ($n = 11$,34.4%) were well demarcated and gain alertness at early stage. On the other hand, Computer tomography (CT) scans showed deep lesions ($n = 16$,57.1%) invaded into surrounding muscle with osteolytic bone-destructive growth pattern except the intraglandular IMT ($n = 13.6\%$). Similarly, deep lesion manifested as diffused heterogeneous lesions on magnetic resonance imaging (MRI). The lesion appears as iso-intense to hypo-intense signal on T1-weighted image but hyper-intense signal on both unenhanced and fat-suppression T2-weighted images. Only 1 case manifested bilateral lymphadenopathy without significant rim-enhancement in which subsequent histology showed lymphadenitis without metastasis. Overall, family history, cervical lymphadenopathy and malaise were unremarkable.

Pathological findings

Macroscopically, IMTs were pseudocapsulated, rubbery firm in consistency and focally hemorrhagic occasionally. Sectioned surfaces were homogeneously yellowish white. Microscopically, it is composed of spindle myofibroblastic cell with various

Table 1
Clinicopathological characteristics.

Characteristic	Value: *n*	%
Subjects	28	100
Female	12	42.9
Male	16	57.1
Median age (y) (IQ range)	37.3 (5–75), predominant at 20s and 30s	
Follows up (of June 2011)		
Median (mo)	30.5	
IQ range (mo)	4–82	
Manifestation		
Primary	22	78.6
Re-resection		
2nd attempt	4	14.3
3rd attempt	1	3.55
4th attempt	1	3.55
Median timing in achieving definitive		
Diagnosis (mo)	9	
(IQ range) (mo)	0.5–96	
Relapse after surgical resection in our institute		
Yes	8	28.6
No	20	71.4
Overall survival		
Survive	22	78.6
Death		
IMT related	4	14.3
Non-IMT related	2	7.1
Tumor size (cm)		
Median	3.3	
IQ range	0.5–7	
Local: overlying skin color		
Erythematic and elevated skin (°C)	9	32.1
Dullness	2	7.1
Systemic		
Low grade fever + leukocytosis	9	32.1
Low grade fever	3	10.7
Leukocytosis	1	3.6
Location		
Maxilla		
a	2	7.1
b	5	17.9
Skull base (b)	1	3.6
Nasal cavity (b)	1	3.6
Infratemporal fossa (b)	1	3.6
Mandible		
a	1	3.6
b	3	10.7
Buccal cheek		
a	1	3.6
b	3	10.7
Tongue		
a	2	7.1
b	1	3.6
Floor of mouth (a)	2	7.1
Submandibular gland (b)	1	3.6
Posterior auricle (a)	2	7.1
Neck		
a	1	3.6
b	1	3.6
Traumatic injury/extraction history		
Buccal cheek	2	7.1
Tongue	2	7.1
Maxilla	5	17.9
Mandible	2	7.1
Surgical procedure		
Conservative/endoscopic approach	2	7.1
Wide resection	26	92.9
Surgical margins		
Negative		
No residual R0	17 (2 relapse and re-resection performed)	60.7