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Case Report

Granular cell tumor of the male breast: a case report and review of literature

Min Yu[1], Yu-Nan Han[2], Liang Feng[2], Qing-Fu Zhang[3]

[1]Department of Cell Biology, Key Laboratory of Cell Biology, Ministry of Public Health, and Key Laboratory of Medical Cell Biology, Ministry of Education, China Medical University, Shenyang, People's Republic of China; [2]Department of Breast Surgery, The First Affiliated Hospital of China Medical University, Shenyang, People's Republic of China; [3]Department of Pathology, College of Basic Medical Sciences, China Medical University, Shenyang, People's Republic of China

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Abstract: Granular cell tumor of the breast is an extremely rare tumor which occurs in men. We reported a rare case of a male breast granular cell tumor and a review of the literature. A 43-year-old Asian man presented with a painless mass in his left breast two weeks ago. Clinically, this single, painless and immobile mass was resembled breast carcinoma. The patient underwent lumpectomy of left breast mass. Histopathologic staining best differentiates breast granular cell tumor from other breast tumors with their positive staining for S-100, vimentin, inhibin-α and CD68 and negative for cytokeratin (CK), CD34 and smooth-muscle actin (SMA).

Keywords: Granular cell tumor, breast carcinoma, immunohistochemistry

Introduction

Granular cell tumor (GCT) is a relatively rare soft tissue tumor with neurogenic origin which mostly occurs in tongue, head and neck. It can also occur in any sites of the body, such as skin, subcutaneous tissue, respiratory tract, gastrointestinal tract and genital tract [1, 2]. Granular cell tumor of the breast (GCTB) only accounts for 5% to 15% of GCT and [3]. The majority of GCTB were seen in African-American women which range from 30 to 50 years old [4]; however, 6.6% of GCTB occur in men [5]. As GCT often appeared to be a single, painless and immobile mass, which resembled breast cancer through clinical and imaging examinations, the diagnosis of GCT is really a challenge for clinicians. Up to the present, pathological examinations are the most frequently used and definite method for the final diagnosis of GCT. Herein, we reported a rare case of male benign GCTB which mimicked breast cancer by clinical examinations and imaging findings.

Case report

A 43-year-old Asian man presented with a painless mass in his left breast two weeks ago. Breast examination showed a palpable firm mass with poor mobility in the upper inner quadrant of the left breast. The mass measured pigeon-egg in size and protruded above surrounding surface of the skin. No color and temperature change in breast. No abnormal in opposite breast and both axillary lymph nodes. The patient had no history of malignant or other diseases including hypertension. Also, he had no family history of any malignancy. The patient underwent lumpectomy of left breast mass. The case was finally diagnosed as benign GCT by pathological examinations. Grossly, the solid tumor was 1.1×0.9×0.8 cm, with poor envelope and white in cut surface. No necrosis was found within the tumor. Hematoxylin and eosin (H&E) staining showed that the tumor located within the breast tissue and it had incomplete envelope and the margin was unclear. The tumor cells grew in an infiltrative pattern without necrosis (**Figure 1A**). The nest-like large and eosinophilic granular tumor cells exhibited an infiltrative growth pattern and the breast ducts were involved centrally (**Figure 1B**). The tumor cells infiltrated into the surrounding fat tissues (**Figure 1C**), without invading into the nerve tissue or vascellum. The tumor cells were polygo-

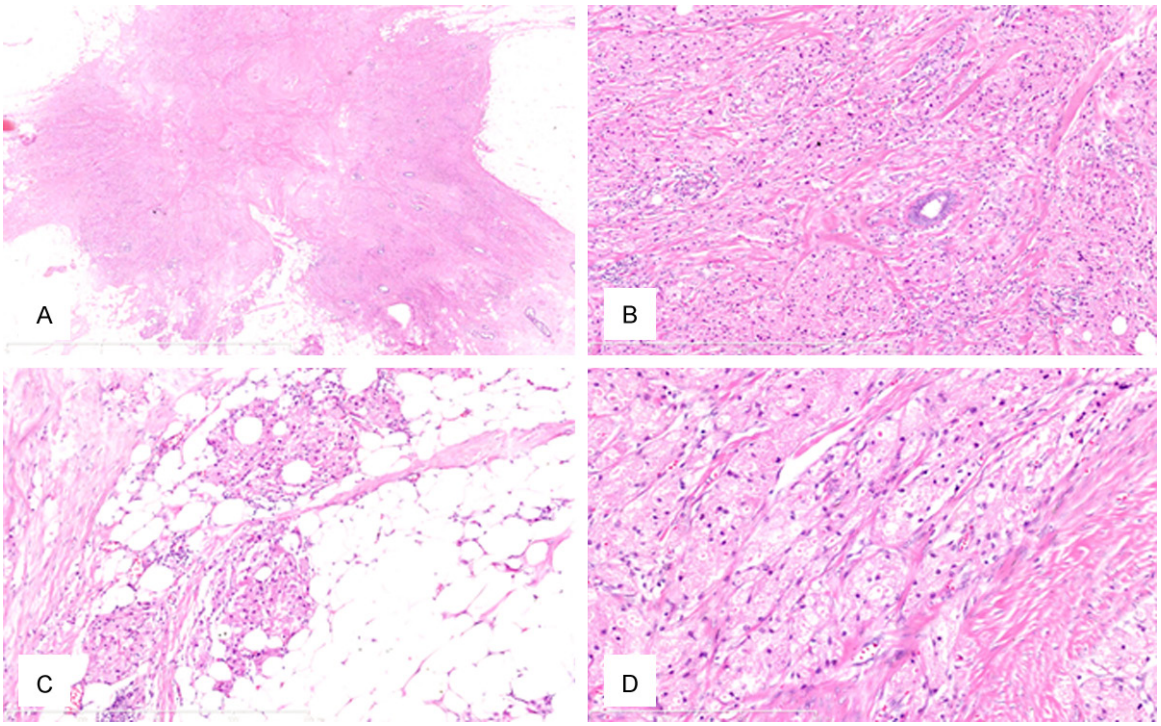

Figure 1. Hematoxylin and eosin (H&E) staining findings. A. At low magnification, the tumor had incomplete envelope and the margin was unclear. The tumor cells grew in an infiltrative pattern without necrosis. ×12.5. B. The nest-like large and eosinophilic granular tumor cells exhibited an infiltrative growth pattern and the breast ducts were involved centrally. ×100. C. The tumor cells infiltrated into the surrounding fat tissues. ×100. D. The tumor cells were polygonal or oval in shape with clear border. They presented small nucleoli and abundant eosinophilic granular in cytoplasm. Mitotic figures were very rare. ×100.

nal or oval in shape with clear border. They presented small nucleoli and abundant eosinophilic granular in cytoplasm. Mitotic figures were very rare (**Figure 1D**). Immunohistochemical (IHC) staining displayed the tumor cells were positive for S-100 (**Figure 2A**), vimentin (**Figure 2B**), inhibin-α (**Figure 2C**) and CD68 (**Figure 2D**). They were negative for cytokeratin (CK), CD34 and smooth-muscle actin (SMA). The Ki-67 index was about 5% positive. The patient was free of disease for 18 months after excision.

Discussion

GCT was firstly alluded by Weber in 1854 and fully described by Abrikossoff et al. in 1926 [6]. Abrikossoff proposed GCT was origin from striated skeletal muscle cells and he termed it as myoblastoma. Subsequently, some authors showed evidence that GCT was origin from smooth muscle cells. Currently, most scholars accept that GCT is origin from Schwann cells because of positive S-100 and ultrastructural features of the tumor cells [7].

The current evidence of prevalence of GCTB suggests 1:617 in screened population and 6.7:1000 among total clinical population [3]. The case we reported here was a benign GCTB occurred in a male patient which was extremely rare. To our knowledge, cases of male GCTB in English-language literatures which could be obtained enough data were demonstrated in **Table 1** [8-42].

GCTB typically presents as a firm, painless, slow growing mass, ranging from regular well defined to irregular poor defined [3]. GCTB may cause retraction or ulceration of the overlying skin or may be fixed to the pectoralis major muscle [3]. Men suffer GCTB are extremely rare, the majority of these patients are pre-menopausal women. And a hypothesis that hormones had relationship with the pathogenesis of GCTB, however no relative receptors have been found on the tumor [31]. GCTB can occur in any sites of the breast and the predominant quadrant is upper inner quadrant of the breast, as in our case, where parallels the distribution

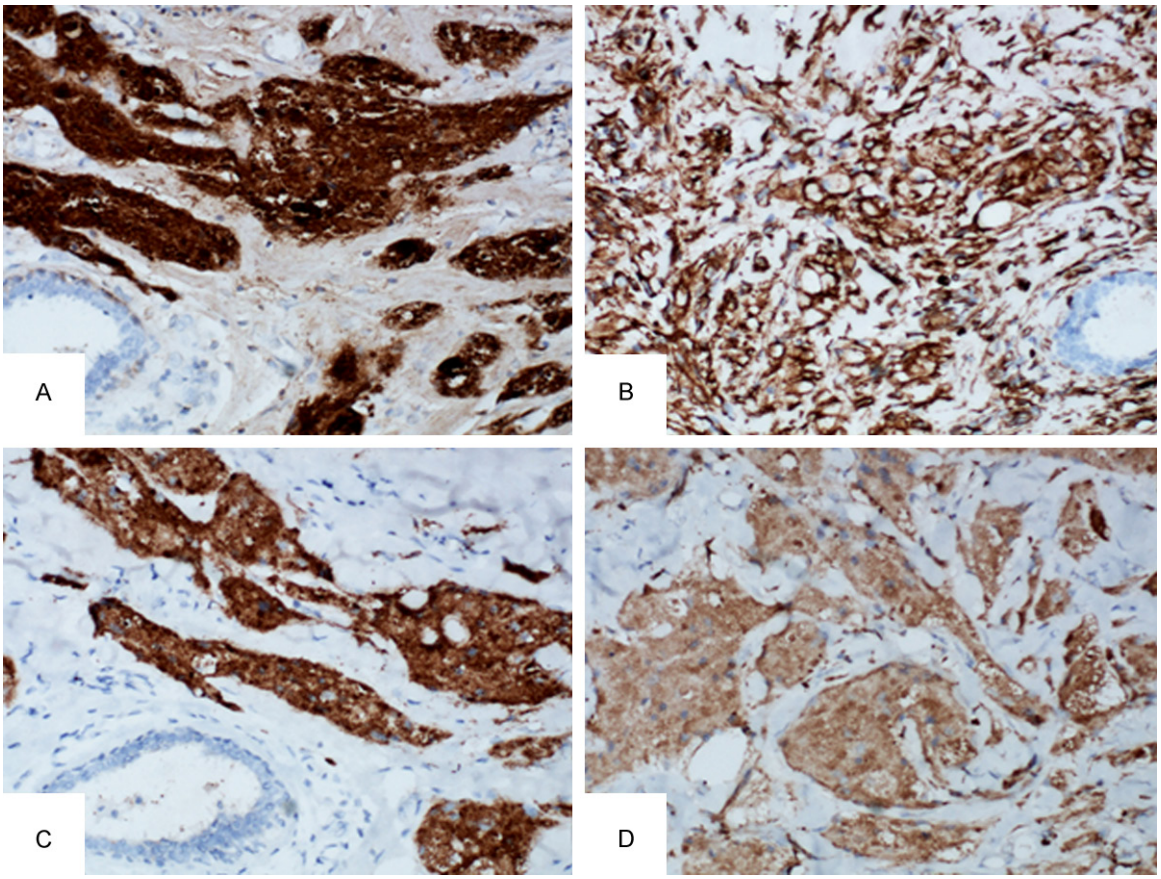

Figure 2. Immunohistochemical staining findings. A. The tumor cells were strong positive for S-100. ×200. B. The tumor cells were moderate to strong positive for Vimentin. ×200. C. The tumor cells were moderate positive for Inhibin-α. ×200. D. The tumor cells were weak positive for CD68. ×200.

of cutaneous sensory branches of the supraclavicular nerve [31]. Compared with breast cancer, the most common quadrant is outer upper quadrant. GCTB is difficult to differentiate with breast malignancies through both breast ultrasound and mammography because of heterogeneity, irregularity, spiculation, poor boundary and so on [3]. Up to the present, pathological examinations including H&E and IHC stains are the most accurate diagnostic techniques.

Microscopically, tumor cells are usually described as large, polygonal cells with nests, cords or clusters-like patterns. They contain characteristic abundant granular eosinophilic cytoplasm and uniform small, round or oval nuclei [32]. GCT does not display mitoses, nuclear multiplicity, atypia and pleomorphism [32]. Immunohistochemically, S-100 is a sensitive marker for GCT, however it is not specific as 10% of breast malignancies display S-100 positive [33]. CD68 is a distinctive feature for GCT and associates with abundant phagolysomes existed in cytoplasm [33]. Moreover, vimentin, inhibin-α and are reported to be positive in some cases [34-37]. Periodic acid-Schiff stain (PAS) is often positive [15]. Cytokeratin, carcinoembryonic antigen (CEA), epithelial membrane antigen (EMA), estrogen receptor (ER), progesterone (PR) and gross cystic disease fluid protein (GCDFP-15) are generally negative [3, 4, 34].

Malignant granular cell tumor (MGCT) only accounts for 1-2% of all GCTs [3]. The widely accepted clinical features of MGCT of breast are large, rapid growing mass, which are associated with lymphadenopathy, aggressive local invasion and poor border [3]. Six histological criteria of MGCT was established by Fanburg-Smith et al. (FS criteria) [38], including necrosis, spindling of the tumor cells, vesicular nuclei with large nucleoli, increased mitotic rate (>2

Table 1. Cases of Male Granular cell tumor of the breast

No.	First Author	Year	Age (yo)	Side and quadrant	Size (cm)	Benign/ malignant	Treatment
1	Patel, 2013 [8]	2013	43	R, upper quadrant	2.2	Benign	Local excision
2	Lee, 2011 [9]	2011	42	L, subareola	NA	NA	NA
3	Taglietti, 2011 [10]	2011	54	R, outer quadrant	2.5	Benign	Wide local excision
4	Kim [11]	2011	50	R, subareola	1.7	Benign	Local excision
5	Kim [11]	2011	49	L, outer upper quadrant	1.7	Benign	Wide local excision
6	Irshad [12]	2008	59	R, inner quadrant	1.9	Benign	Local excision
7	Lauwers [13]	2008	44	R, nipple	1.3	Benign	Wide local excision
8	Adeniran [4]	2004	32	R	0.8	Benign	Local excision
9	Adeniran [4]	2004	36	L	1.0	Benign	Local excision
10	Adeniran [4]	2004	42	L	2.5	Benign	Local excision
11	Lee, 2000 [14]	2000	35	R, subareolar	3.0	Benign	Wide local excision
12	McCluggage [15]	1999	28	R	1.4	Benign	Local excision
13	Calò [16]	1998	64	L, upper quardrant	1.0	Benign	Local excision
14	Chachlani [17]	1997	28	R	1.3	Benign	Local excision
15	Okuda [18]	1996	45	outer upper quadrant	2.0	Benign	Local excision
17	Reale [20]	1995	38	outer upper quadrant	2.7	Benign	Local excision
18	Mariscal [21]	1995	47	R, upper quadrant	1.7	Benign	Local excision
19	Placidi [22]	1995	30	L, upper quadrant	1.5	Benign	Wide local excision
20	Rogall [23]	1995	35	R, upper and outer upper quadrant	1.0	Benign	Local excision
22	Damiani [25]	1992	25	L	2.0	Benign	Local excision
23	Baeten [26]	1989	49	R, subareolar	2.0	Benign	Local excision
24	Khansur [41]	1987	NA	NA	>2.5	Malignant	Local excision and systemic chemotherapy
25	DeMay	1984	26	R, outer upper quadrant	1.5	Benign	NA
26	Sussman [42]	1973	56	L, outer upper quadrant	1.8	Benign	Local excision
27	Hart [27]	1973	36	L, subareola	3.0	Benign	Local excision
28	Umansky [28]	1968	55	L, subareola	NA	Malignant	radical mastectomy
29	Umansky [28]	1968	44	R, outer upper quadrant	2.5	Benign	Wide local excision
30	Mulcare [19]	1968	35	L, inner upper quadrant	2.0	Benign	Local excision
31	Peison [29]	1964	21	R, subareola	1.8	Benign	Local excision
32	Simon [30]	1947	60	R, upper quadrant	2.5	Benign	Local excision

Abbreviations: L, left; R, right; mo, months; NA, not available; yo, years old.

mitosis/10 HPF, ×200), high nuclear-to-cytoplasmic ratio and pleomorphism. GCTs have three or more of these features are classified as malignant; those have one or two criteria are classified as atypical; and those have none of features are classified as benign. The treatment for GCTB according to the literature is local excision with a large tumor-free margin, due to the review of Kazuhisa Akahane et al, four of five MGCTBs spread to the axillary lymph nodes, they suggested widely resection with local lymph nodes dissection was treated for MGCTB [39]. The prognosis of benign GCT is favorable, and the recurrence after wider local excision is 2-8% [37]. Follow-up annually of patients with GCT is advisable to rule out recurrences [40].

With the aim of preventing inappropriate and unnecessary treatments, GCTB should be considered more during the differential diagnosis, including scirrhous malignances, granulomatous mastitis, metastatic clear cell malignancies, histiocytoid-myoblastomatoid breast carcinoma (HMBC) and so on [3].

In this case, the tumor mass was very suspicious of malignancy clinically. The pathological examination revealed that tumor cells have abundant granular cytoplasm. Immunohistochemical staining revealed that the S-100 protein was strongly positive while cytokeratin was negative. CD68, vimentin and inhibin-α are all useful for further diagnosis to a benign GCT. Above all, the tumor reported in this case was diagnosed benign, and the patient only received a local resection and free of reoccurrence during the follow-up period.

In conclusion, GCTB is a very rare benign disease occurred in male which mimics breast

malignancy clinically and radiologically. The definitive diagnosis is through histopathological and immunohistochemical findings. Clinicians and pathologists should keep in mind this rare benign tumor occur in men in order to avoid over-treating.

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Disclosure of conflict of interest

None.

Address correspondence to: Dr. Qing-Fu Zhang, Department of Pathology, College of Basic Medical Sciences, China Medical University, 77 Puhe Road, Shenyang North New Area, Shenyang 110122, Liaoning Province, People's Republic of China. E-mail: qfzhang@mail.cmu.edu.cn

References

[1] Paul SP and Osipov V. An unusual granular cell tumour of the buttock and a review of granular cell tumours. Case Rep Dermatol Med 2013; 2013: 109308.

[2] Chen Q, Li Q, Guo L, Li S and Jiang Y. Fine needle aspiration cytology of a granular cell tumor arising in the thyroid gland: a case report and review of literature. Int J Clin Exp Pathol 2014; 7: 5186-5191.

[3] Brown AC, Audisio RA and Regitnig P. Granular cell tumour of the breast. Surg Oncol 2011; 20: 97-105.

[4] Adeniran A, Al-Ahmadie H, Mahoney MC and Robinson-Smith TM. Granular cell tumor of the breast: a series of 17 cases and review of the literature. Breast J 2004; 10: 528-531.

[5] Heinzerling NP, Koehler SM, Szabo S and Wagner AJ. Pediatric Granular Cell Tumor of the Breast: A Case Report and Review of the Literature. Case Rep Surg 2015; 2015: 568940.

[6] Abrikossoff A. Uber Myome ausgehend von der quergestreiften willkurlichen Muskulatur. Virchows Archiv 1926; 260: 215-233.

[7] Filipovski V, Banev S, Janevska V and Dukova B. Granular cell tumor of the breast: a case report and review of literature. Cases J 2009; 2: 8551.

[8] Patel HB and Leibman AJ. Granular cell tumor in a male breast: mammographic, sonographic, and pathologic features. J Clin Ultrasound 2013; 41: 119-121.

[9] Lee SJ and Mahoney MC. The protean manifestations of granular cell tumor of the breast. Breast J 2011; 17: 201-203.

[10] Taglietti L, Vettoretto N, Blanzuoli L and Giovanetti M. Granular cell tumor of the male breast. Updates Surg 2011; 63: 139-142.

[11] Kim EY, Kang DK, Kim TH, Jung YS, Kim KS and Yim H. Granular cell tumor of the male breast: two case descriptions and brief review of the literature. J Ultrasound Med 2011; 30: 1295-1301.

[12] Irshad A, Pope TL, Ackerman SJ and Panzegrau B. Characterization of sonographic and mammographic features of granular cell tumors of the breast and estimation of their incidence. J Ultrasound Med 2008; 27: 467-475.

[13] Lauwers K, Bestman TJ, Bergmans G and Molderez C. Granular cell tumour of the male breast. Acta Chir Belg 2008; 108: 112-114.

[14] Lee S, Morimoto K, Kaseno S, Katsuragi K, Hosono M, Wakasa K and Kinoshita H. Granular cell tumor of the male breast: report of a case. Surg Today 2000; 30: 658-662.

[15] McCluggage WG, Sloan S, Kenny BD, Alderdice JM, Kirk SJ and Anderson NH. Fine needle aspiration cytology (FNAC) of mammary granular cell tumour: a report of three cases. Cytopathology 1999; 10: 383-389.

[16] Calo PG, Porcu C, Pollino V, Cabula C and Malloci A. [Granular cell tumor of the male breast. A case report]. Minerva Chir 1998; 53: 1043-1046.

[17] Chachlani N, Yue CT and Gerardo LT. Granular cell tumor of the breast in a male. A case report. Acta Cytol 1997; 41: 1807-1810.

[18] Okuda I KT, Suzuki N, Nakazawa H, Yamazaki S. A case of granular cell tumor in the male breast (in Japanese with English abstract). Jpn J Clin Radiol 1996; 41: 471-474.

[19] Mulcare R. Granular cell myoblastoma of the breast. Ann Surg 1968; 168: 262-268.

[20] Reale D, Guarino M, Squillaci S, Bianchini E, Forloni B, Merisio I, Pascale M and Micoli G. [Granular cell tumor of the male breast. Case report and review of the literature]. Minerva Chir 1995; 50: 717-720.

[21] Mariscal A, Perea RJ, Castella E and Rull M. Granular cell tumor of the breast in a male patient. AJR Am J Roentgenol 1995; 165: 63-64.

[22] Placidi A, Aversa A, Foggi CM, Foggi P, Ricci G and Salvatori V. Granular cell tumour of breast in a young man preoperatively diagnosed by fine needle aspiration (FNA) cytology. Cytopathology 1995; 6: 343-348.

[23] Rogall B and Propeck P. Granular cell tumor of the breast in a male. AJR Am J Roentgenol 1995; 165: 230.

[24] Takahashi N TK, Sato T, Monma N. A case of granular cell tumor of male breast. Journal of

the Japanese Society of Clinical Cytology 1993; 420: 219-226.
[25] Damiani S, Koerner FC, Dickersin GR, Cook MG and Eusebi V. Granular cell tumour of the breast. Virchows Arch A Pathol Anat Histopathol 1992; 420: 219-226.
[26] Baeten CG, Weidema WF, Willebrand D and De Jong R. Granular cell tumor of the breast. Neth J Surg 1989; 41: 111-113.
[27] Hart S and Sisely L. Granular cell tumour in a male breast. Med J Aust 1973; 2: 1010-1011.
[28] Umansky C and Bullock WK. Granular cell myoblastoma of the breast. Ann Surg 1968; 168: 810-817.
[29] Peison BB. Granular cell myoblastoma of the male breast. NY State J Med 1964; 64: 1753-1754.
[30] Simon MA. Granular cell myoblastoma (myoblastic myoma, rhabdomyome granulo-cellulaire). Am J Clin Pathol 1947; 17: 302-313.
[31] Patel A, Lefemine V, Yousuf SM and Abou-Samra W. Granular cell tumour of the pectoral muscle mimicking breast cancer. Cases J 2008; 1: 142.
[32] Qian X, Chen Y and Wan F. Granular cell tumor of the breast during lactation: A case report and review of the literature. Oncol Lett 2014; 8: 2565-2568.
[33] Montagnese MD, Roshong-Denk S, Zaher A, Mohamed I and Staren ED. Granular cell tumor of the breast. Am Surg 2004; 70: 52-54.
[34] Pergel A, Yucel AF, Karaca AS, Aydin I, Sahin DA and Demirbag N. A therapeutic and diagnostic dilemma: granular cell tumor of the breast. Case Rep Med 2011; 2011: 972168.
[35] De Simone N, Aggon A and Christy C. Granular cell tumor of the breast: clinical and pathologic characteristics of a rare case in a 14-year-old girl. J Clin Oncol 2011; 29: e656-657.
[36] Ventura L, Guadagni S, Ventura T, Di Silvestre K, Coletti G and Leocata P. Benign granular cell tumor of the breast: a misleading disease. Tumori 1999; 85: 194-198.
[37] Quiroz-Rodriguez G, Robles-Vidal C, Guzman-Navarro L and Ortiz-Hidalgo C. Granular cell (Abrikossof) tumor of the breast. Breast J 2006; 12: 494.
[38] Fanburg-Smith JC, Meis-Kindblom JM, Fante R and Kindblom LG. Malignant granular cell tumor of soft tissue: diagnostic criteria and clinicopathologic correlation. Am J Surg Pathol 1998; 22: 779-794.
[39] Akahane K, Kato K, Ogiso S, Sakaguchi K, Hashimoto M, Ishikawa A, Kato T, Fuwa Y, Takahashi A and Kobayashi K. Malignant granular cell tumor of the breast: case report and literature review. Breast Cancer 2015; 22: 317-323.
[40] Gupta N, Sanchety N, Verma PS and Verma G. Malignant granular cell tumor of the breast; literature review. Indian J Pathol Microbiol 2015; 58: 238-240.
[41] Khansur T, Balducci L and Tavassoli M. Granular cell tumor. Clinical spectrum of the benign and malignant entity. Cancer 1987; 60: 220-222.
[42] Sussman EB, Hajdu SI and Gray GF. Granular cell myoblastoma of the breast. Am J Surg 1973; 126: 669-670.