Report of two cases of granular cell tumor, a rare tumor in children

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ARTICLE INFO

Article history:
Received 28 May 2016
Received in revised form 7 August 2016
Accepted 10 August 2016

Key words: Granular cell tumor Recurrent granular cell tumor Pediatric masses

ABSTRACT

Granular cell tumor (GCT) is a rare soft tissue neoplasm. It was first named as “granular cell myoblastoma” in 1926 by Abrikossof. GCT often manifests as a single, painless nodule that shows a slow enlargement in the cutaneous, subcutaneous, or submucosal tissues. It mostly affects adults between ages 30 and 60 years, and is very rare in children. We herein report two children with GCT; the first patient with a tumor in the neck is presented due to the rare occurrence of the tumor in children. The other patient with a tumor in the leg is presented due to the rare occurrence of the tumor in children and the relatively less common site of occurrence. Both of the patients were female. The mean tumor size was 2.5 × 2 cm. Histopathological examination of the specimens revealed benign granular cell tumor. One of the patients who had positive margin did not follow-up after the first excision of the tumor and she presented with a local recurrence in a year. Then a wide excision was performed and the defect was closed primarily. The second patient had negative margin and had no recurrence during the follow-up period. Granular cell tumor is rare in children. Although it is mostly benign, it may be malignant in approximately 2% of the cases and metastasize. The local recurrence in a year is characteristic for malignant GCT before metastasis. Positive surgical margins are associated with high recurrence rates, therefore total excision of the tumor is crucial for local recurrence. GCT should be included in the differential diagnosis of head and neck masses. It should be remembered that the tumor may arise in atypical locations and there is a possibility of malignancy.

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Granular cell tumors (GST) are rare soft tissue neoplasms with a general benign course [1,2]. It was first named as “granular cell myoblastoma” in 1926 by Abrikossof who, based on the microscopic appearance of the tumor, thought that the tumor originated from myofibroblasts [3,4]. In 1935, Feyrter proposed a neural origin for the tumor and named it as “granular cell neuroma”. In 1948, Fust and Custer confirmed this theory, and named it as “granular cell neurofibroma”. In 1962, by immunohistochemical studies, Fisher and Wechles confirmed the neural origin of the tumor [4].

GCT often manifests as a single, painless nodule that shows a slow enlargement in the cutaneous, subcutaneous, or submucosal tissues [5]. The tumor often originates from the gastrointestinal mucosa, and it is seen most commonly in the tongue and the oral cavity [6]. It mostly affects adults between ages 30 and 60 years, and is very rare in children [7]. Women are affected 2–3 times more commonly than men [8]. Although most lesions are solitary, 5–25% are multiple. Multiple lesions are reported to be less common in children, and more commonly associated with a positive family history [1]. Malignant GCT was first described by Ravich et al. in 1945 [8]. GCT may be malignant in 1–2% of the cases, and shows a very poor prognosis [4].

We herein report two children with GCT. The first patient with a tumor in the neck is presented due to the rare occurrence of the tumor in children. The other patient with a tumor in the leg is presented both due to the rare occurrence of the tumor in children and the relatively less common site of occurrence.

1. Case 1

A 16 year old girl presented with a mass in the anterolateral aspect of the 1/3 distal neck. The mass was present for approximately 6 years. A 2 × 2 cm subcutaneous solitary mass was palpated...
on physical examination. Plain radiographs were normal. An excisional biopsy of the mass was performed under local anesthesia and the defect was closed primarily.

Macroscopically, the mass measured 2 cm in diameter, it was firm, yellow, limited to the subcutaneous tissue and did not invade the surrounding tissues. There were no postoperative complications. Histopathologic examination of the specimen revealed granular cell tumor (Fig. 1-A,B), therefore the patient was transferred to the plastic surgery department where she underwent a wide resection with 2 cm distance from the previous incision. The defect was closed primarily. The final pathology report showed negative surgical margins. Immunohistochemical studies showed NSE (⁺), Vimentin (⁺) (Fig. 2-A), S-100 (⁺) (Fig. 2-B), CD68 weak (⁺), and Ki67 proliferation index was 2%. Microscopic examination showed wide and polygonal cells that were interspersed between collagen fibers, forming nests and cords. Their nuclei were centrally located, small, and round, and the cytoplasmas were eosinophilic. The cellular borders were indistinct, and there were no mitoses or necroses. The patient did not have any recurrence during the follow up period.

2. Case 2

A 14 year old girl presented with a lump and pain in the middle 1/3 of the posterolateral aspect of her right leg that was present for 1 year. Physical examination showed a 3 × 2 cm subcutaneous mass, painful on palpation. Radiographs did not show any bone pathologies. The tumor was excised under local anesthesia, and the defect was closed primarily. Macroscopically the mass had a yellow-gray appearance, measured 3 cm in diameter, was confined to the subcutaneous tissue, and did not invade the neighboring structures. Although the patient was told to attend her regular follow ups after she received the pathology report, she did not come back. One year later she presented with pain in the same area. Her pathology report from the previous excision showed the diagnosis of granular cell tumor, with a positive side margin. On physical examination, she had a recurrent mass in the same area. Wide local excision and primary repair were performed. The margins were negative in the pathology report. There were no recurrences during the follow up period.

3. Discussion

Granular cell tumors are rare soft tissue neoplasms [8]. When they were first described they were thought to originate from the muscle, and therefore described as myoblasts [1,9]. However, advanced ultrastructural analyses and immunohistochemical studies have shown that, by immunohistochemical staining of the S-100 protein, the granular cell tumor actually originated from the Schwann cell [10]. Histologically, the tumor consists of a well demarcated dermal proliferation of round or polygonal cells with a small centrally located nucleus and granular eosinophilic cytoplasm. The characteristic wide cytoplasmic granules are named pustulo-ovoid bodies. The granules are PAS positive however they are diastasis resistant. The epithelium that covers the tumor shows pseudoepitheliomatous hyperplasia. This feature of the tumor mandates inclusion of squamous cell carcinoma in the differential diagnosis [1,10]. Rarely, a plexiform and perineural growth pattern is present [11]. The diagnosis is confirmed by immunohistochemical staining, which shows positivity for S100 and Neuron Specific Enolase. The tumor shows varying degrees of staining with Inhibin-a, Calretinin, Galectin-3 and mesothelioma marker antibody (HBME). It also expresses vimentin, protein gene product (PGP 9.5), melanoma directed monoclonal antibody NKI/C3 and CD68 [12].

Although GCTs may occur anywhere in the body; it is most common in the head and neck area, constituting 45–65% of all cases. Seventy percent of the tumors in the head and neck are in the oral cavity, and most commonly in the tongue. Other common sites are the breast (15%), respiratory system (10%), and the gastrointestinal system (4–6%) [13]. Granular cell tumors generally occur in adults, and rarely in children. Most of the reported cases are between ages 30 and 60. In previous reports, there are only 40 patients under age 19. In 2004, Brannon et al. made an analysis of 34 patients, and found that the mean age was 14.5 and female/male ratio was 3.1/1 [14]. According the study done by Alemayehu et al., 13 of 31 pediatric patients had GCT with extremity localization, therefore the GCT should be included in the differential diagnosis in the pediatric patients [15].

In the article reported by Abraham et al., a benign GCT was excised in a 5-year-old patient’s toe with Mohs Surgery to provide negative margin. According to the current literature, the local recurrence rate is related with insufficient excision [16,17].

Cutaneous GCT often has a nonspecific appearance, and it is difficult to diagnose clinically. It is mostly seen as a hard nodule smaller than 3 cm, solitary, asymptomatic, occasionally sensitive and itchy, and it has a color ranging from skin color to brown-red. The overlying epithelium is generally intact [18]. GCT often has a benign course, only 1–3% of the cases are malignant. Malignancy develops mostly in visceral or deep lesions. Such lesions are greater than 5 cm in diameter, they show a rapid progression and carry a risk of metastasis [19]. Malignant GCTs affect the Afro-American race more commonly than the Caucasian race, and it is twice as common in females. It develops typically in the lower extremity, and most commonly in the femur [20]. There is only one case report on a child with a malignant GCT, who had an intraneural GCT that

![Fig. 1. A: Acanthosis in the epidermis and the infiltration of the tumor with irregular border. B: Granular cytoplasm and large, round polygonal cell with a small nucleus in dermis.](image-url)
affected the lateral cutaneous nerve of the arm [21]. Six diagnostic criteria were described for malignant GCT, these are necrosis, spindle formation in the cells, a vesicular nucleus with a large nucleoli, increased mitotic activity (>2 mitoses/10–200× field), a high nuclear to cytoplasm ratio, and nuclear pleomorphism. The presence of 3 or more of these criteria supports the diagnosis of malignant GCT [22,23]. Recent studies have found that the p53 and Ki67 index were associated with an aggressive course. In benign tumors, the p53 is negative and Ki67 index is under 1%, whereas in malignant GCT the p53 and Ki67 index are positive in 10% and 30% of the cases, respectively [24,25]. In the cases presented above, none of the criteria for malignancy were present, also the ages of the patient and tumor sizes under 4 cm supported the diagnosis of benign GCT.

Total excision of the tumor is the treatment of choice in GCT when malignancy is not suspected [26]. Fine needle aspiration cytology may be helpful in the diagnosis, and if an early diagnosis can be made the surgical margins may be somewhat extended to cure the local microscopic infiltration [6]. Most of the GCTS have been successfully treated with wide local excision. In wide local excision, the recurrence rates after negative and positive surgical margins are 2–8% and >20%, respectively. Therefore assessment of surgical margins is crucial [27].

4. Conclusion

Granular cell tumor is rare in children. Although it is mostly benign, it may be malignant in approximately 2% of the cases and metastasize. Total excision of the tumor is crucial. Positive surgical margins are associated with high recurrence rates. GCT should be included in the differential diagnosis of head and neck masses. It should be remembered that the tumor may arise in atypical locations and there is a possibility of malignancy.

References