CASE REPORT

Neck metastasis of a juvenile granulosa cell tumour. A case report and literature review

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Received 22 June 2015; accepted 24 November 2015

Abstract Juvenile granulosa cell tumour (JGCT) is a rare tumour arising from the ovarian sex cord stroma (SCST) and comprising about 5 percent of all granulosa cell tumours. To our knowledge, a cervical metastasis has not been described before.

We report a case of a 19-year-old female who had a left supraclavicular mass with a previous history of a JGCT in 2010 and an abdominal recurrence in 2011 followed by radiotherapy and chemotherapy after surgery.

JGCT generally affects young women, can be hormonally active, and has malignant potential. The diagnosis is made by histopathology after surgical removal, although it should be suspected when there is a large adnexal tumour along with hyperestrogenism signs. Regional lymph nodes metastases are rare let alone extra-abdominal ones.

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KEYWORDS
Juvenile granulosa cell tumour (JGCT);
Neck–cervical metastasis

1. Introduction/background

Granulosa cell tumours (GCTs) are rare neoplasms arising from the sex cord stroma cells of the ovaries. They represent 1.2% of all primary ovarian cancers.1 They can be classified in two subtypes: the adult (95%) and the juvenile (5%), based on the clinical and histologic characteristics.2 The first mostly occurs in middle-aged women (mean age of 50–54 years), with generally a low degree of tumour cell atypia and mitosis. The latter generally affects teenagers or women of reproductive age, making it important to choose the right fertility-sparing treatment when there is a good long-term prognosis, but there is a relative high risk of recurrence with long disease-free intervals in between.3

From the histopathological point of view, adult granulosa cell tumour (AGCT) has round cells with scant cytoplasm and classic “coffee-bean” grooved nuclei. They may arrange themselves in small clusters around a central cavity, forming the Call-Exner bodies (although the lack of them is not frequent). JGCT has a high proliferative rate and a moderate to high degree of cell atypia.4 At early stages, these tumours have

http://dx.doi.org/10.1016/j.ejenta.2015.11.005
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a good prognosis, but later on the clinical course prognosis is less favourable with multiple relapses. They create a negative feedback system and have been found to be a more reliable marker for follicle (and inhibin B (produced by the developing follicles). Inhibin is a peptide hormone produced by granulosa cells in the ovarian follicles with two subtypes, inhibin A (produced by the dominant follicle) and inhibin B (produced by the developing follicles). They have been found to be a more reliable marker for GCT than estradiol. They create a negative feedback against the follicle-stimulating hormone (FSH) concealed in the anterior part of the pituitary gland. Serum inhibin B seems to be the predominant form of inhibin secreted by granulosa cell tumours and appears to reflect disease status more accurately than inhibin A. However, it is not completely specific for an ovarian sex cord tumour as sex cord stromal differentiation can be seen in other neoplasms, like ovarian endometrioid tumours and metastatic carcinomas to the ovary.

Clinically, GCT presents as an asymptomatic slow-growing abdominal mass. Hyperestrogenism symptoms such as breast tenderness, postmenopausal bleeding, menstrual abnormalities, and in children, sexual precocity, are often common. Generally sporadic, they can also be related with other clinical findings: in the presence of hemangiomas to Maffucci syndrome, or in the company of enchondromatosis, and Ollier’s disease. GCT is sometimes associated with hemangiomas and ambiguous genitalia with leprechaunism.

Treatment guidelines for GCT suggest surgical staging according to the FIGO (International Federation of Gynecology and Obstetrics) system. If the patient has fulfilled her fertility desires, abdominal hysterectomy and bilateral salpingo-oophorectomy are generally recommended with or without pelvic and para-aortic lymphadenectomy, omentectomy, peritoneal biopsy, and removal of any suspicious lesions. In early stages preservation of the healthy ovary and the uterus with an endometrial biopsy may be performed for young patients who desire to maintain fertility. Because of the slow growth of the tumour and the high rate of recurrence in advanced stages, secondary debulking may be an option and can improve the survival. Until now, there is no standardized treatment for adjuvant therapy. General consensus recommends no further treatment besides surgery for Stage IA. National Comprehensive Cancer Network (NCCN) guidelines advise platinum-based chemotherapy and or radiotherapy for stages II to IV. The most important prognostic factor is the disease stage and residual tumour.

2. Case presentation

We present a 19-year-old Egyptian female who came to our Head and Neck Multidisciplinary team meeting in Hamad Medical Corporation (Doha, Qatar) for evaluation of a left supraclavicular mass that could be related to a JGCT diagnosis and was initially treated in June 2010.

There was no remarkable medical history besides thrombocytopenia of 51,000 platelets when she was 6 years old that recovered spontaneously with no specific treatment. She approached the gynaecology clinic with abdominal pain and excessive menstrual bleeding where an abdominal mass was detected related to the right ovary. The patient underwent a right salpingo-oophorectomy, omentectomy, and a peritoneal biopsy that reported negative. Histopathology reported a JGCT localized in the right ovary. She received adjuvant chemotherapy in September 2010: 5 cycles per week × 5 weeks of carboplatin. The patient recovered from treatment but in July 2011 she presented again with abdominal pain and continuous vomiting, and a retroperitoneal mass between the lower segments of the aorta and the inferior vena cava was noticed, suggesting a recurrence. This time, a midline laparotomy was done with bilateral pelvic, paraaortic, and lower vena cava lymphadenectomy that showed a metastatic JGCT tumour. Peritoneal wash was again negative for malignancy. Postoperative radiotherapy at a dose of 45 Gy (25 sessions × 1.8 Gy) was given to the lower paraaortic region.

In May 2013, the patient returned to the hospital with night sweats and a left moderately painful supraclavicular mass of three months of duration. Ultrasound showed multiple left lower jugular adenopathies, the biggest measuring 19.7 × 14.8 mm and showing a hypoechogenic pattern. A PET scan with F-18 fluorodeoxyglucose (FDG) showed a pathological ring-like uptake in the lower left parajugular area of approximately 2 × 2.5 cm proximal to the left internal jugular vein joining the left subclavian vein (Fig. 1). Excisional biopsy was done but in November 2013, another ovoid mass was noted at the root of the neck on the same side, posterior to the carotid sheath, displacing vascular structures mildly anteriorly. Again, a biopsy was taken.

Histologic examination of the first mass showed a replacement of lymphoid tissue by a malignant neoplasm with morphologic and immunohistochemical features similar to the earlier ovarian tumour (Figs. 2 and 3). The neoplasm shows a solid nodular configuration with focal trabecular and abundant necrosis. The cells are medium to large size, focally having a leuatinized appearance. There was marked hyperchromasia and frequent mitosis was identified. Immunoperoxidase stains were performed with appropriate controls which showed the tumour cells to stain with CD99 and WT-1. The cells were negative for carcinoma markers including cytokeratins (CKs) and epithelial membrane antigen (EMA). Germ cell markers including PLAP and CD117 were also negative, as were S-100 and LCA, excluding melanoma and lymphoma. Although no staining was noted with inhibin, the morphologic features and immunoprofile were most compatible with a juvenile granulosa cell tumour. The second biopsy did not show significant differences from the first.

During the multidisciplinary tumour meeting, after the patient refused chemotherapy, it was decided to give adjuvant...
radiotherapy since there were no signs of disease activity elsewhere by PET/CT scan after surgery. 60 Gy to the grossly enlarged nodes, 54 Gy (30 fractions) to the lower neck nodal station and surgical bed and 50.4 Gy to the adjacent unin- volved region. Radiotherapy was delivered in 30 fractions using Simultaneous integrated boost (SIB) technique. This study was approved by Hamad Medical Corporation Research Department. A waiver of informed consent was obtained.

3. Discussion

GCTs tend to have an indolent growth, especially during the first stage, and recurrences appear late (a mean of 4–6 years after initial diagnosis). Lymph node metastases are rare and therefore some surgeons omit paraaortic lymphadenectomy during the surgical staging for these tumours, following these patients closely afterwards. Most authors suggest that unilateral salpingo-oophorectomy and uterine preservation may provide a similar survival rate to other more aggressive treatments according to recent papers. Zhang et al. compares 132 patients with sex cord stromal tumours (SCSTs) younger than 50 diagnosed with stage I disease: 61 (46%) underwent standard surgical treatment including hysterectomy, and 71 (54%) had a uterine-sparing procedure. The prognosis for both groups seems to be good with equivalent 5-year survival rates of 97% and 98% (p = 0.61). Removal of lymph nodes during the initial surgery might not predict the pattern of recurrence or have a clear benefit to the patient. Complete removal of the primary tumour seems to be the most important prognostic factor.

Our patient underwent two excisional biopsies of a left supraclavicular metastatic node in June and November 2013 without any complications. Following the second surgery, she received radiotherapy to the surgical bed and adjacent lymph node regions.

4. Conclusion

JGCT is a rare ovarian tumour that usually spreads by direct extension and through the lymph nodes. The decision for the type of surgical excision at its primary site is debatable due to the few number of cases and follow-ups reported in the literature, but fertility sparing surgery seems to be the treatment of choice in young patients in the majority of the cases reviewed in this study. A distant cervical metastasis is an adverse situation that has not been described in the literature until now.

Conflict of interest statement

No conflict of interest.

References