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Cervical sarcoma botryoides and ovarian Sertoli–Leydig cell tumor: a case report and review of literature

P. Rosenberg · S. Carinelli · M. Peiretti · V. Zanagnolo · A. Maggioni

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Introduction

The diagnosis of two or more conditions in the same patient and in particular of the same system is always noteworthy because it raises the possibility to see a common etiopathogensis. A not very well known example is the association between cervical sarcoma botryoides and ovarian Sertoli–Leydig cell tumor. Daya and Scully [1] reported two cases of cervical rhabdomyosarcoma on 207 patients with ovarian Sertoly-Leydig cell tumors. Goldbang et al. [2] referred a case report of a 14-year-old patient, who had a sarcoma botryoides and who 13 years later developed an early ovarian Sertoli–Leydig. McClean et al. reported an other case of a 13-year-old patient with a cervical rhabdomyosarcoma concomitant of ovarian Sertoli–Leydig cell tumor; but none of these authors refer to a clear answer about a common pathogenesis [3]. In this report, we describe the case of a patient with a cervical relapse of sarcoma botryoides originally diagnosed in our hospital when she was 20 years old and 1 year before she had developed an ovarian Sertoli–Leydig cell tumors. A systematic review contained in a table of the published literature about this association is also showed. Although this is the fifth published case, the basis for this association is not clear.

P. Rosenberg (✉) · S. Carinelli · M. Peiretti · V. Zanagnolo · A. Maggioni
Unit of Gynecology, European Institute of Oncology, Via Ripamonti, 239, Milan, Italy
e-mail: piergiorgio.rosenberg@ieo.it

Case report

In June 2002, a 20-year-old girl came to our hospital for a suspected vaginal neoformation. It was a cervical polyp of about 7 cm. We made a polypectomy and histological exam showed cervical sarcoma botryoides with positive immuno-fenotype for myogenin, desmin and protein S-100. From May 2002 to July 2002 we administered three cycles of chemotherapy based on ifosfamide 3000 mg/mq and epiadriamycin 30 mg/mq every 21 days. Subsequently a leep of anterior uterine cervix, on which there was the basis of implant of sarcoma was made. Histology was negative.

In January 2002, the patient went to another hospital for some investigations. An ultrasound scan noted the presence of a right ovarian cystis measuring 8 cm in the largest diameter. Preoperative hormonal levels and tumoral markers were normal excepted for elevated serum levels of prolactin and testosterone (PRL: 57.1 ng/ml; test: 0.7 ng/ml). The patient in fact showed clinical evidence of virilisation.

At laparotomy, a right ovarian Sertoli–Leydig tumor of intermediate grading was confirmed and salpingoophorectomy with staging were made. Peritoneal washing was negative.

After 6 years of negative follow up, in 2008 we diagnosed a cervical polyp of 3–4 cm protruding from the external uterine orifice and mechanic polypectomy was performed. Histology was compatible with a recurrence of rhabdomyosarcoma and positive immunofenotype for desmin and CD 10. After a month we made hysteroscopy with endometrial biopsies and cold-knife conization. All histological exams were negative. The patient is alive without evidence of disease, 8 years after diagnosis of ovarian Sertoli–Leydig tumor and 2 years after diagnosis

of recurrence of sarcoma botryoides. A systematic review on cervical rhabdomyosarcoma with synchronous ovarian Sertoli–Leydig tumor from medline is given in Table 1.

Pathological findings

Cervical tumor

The cervical mass measured 2 cm and was yellowish and edematous. On microscopic examination, the polyp was lined by endocervical epithelium with focal immature squamous metaplasia. The stroma was extensively myxoid and focally hyalinized with nodules of immature cartilage. Hypercellular hyperchromatic stroma was distributed under the epithelial layer of the surface and glands in scattered stromal aggregates. The hyperchromatic cells had scanty cytoplasm and elongated small nuclei. Mitoses were scattered. Rhabdomyoblasts with varying degree of maturation, ranging from rounded to ribbon-like cells with abundant eosinophilic cytoplasms and cross striations were also present. Tumor cells were immunoreactive for desmin and myogenin.

The recurrent polyp showed features similar with the primary. However, the stroma was extensively fibrous and cartilage nests were not found (Fig. 1).

Ovarian tumor

The ovarian mass was predominantly solid and yellow on sectioning and smooth and whitish on surface. Microscopically the tumor was lobulated and more cellular masses were separated by loose oedematous tissue. Hypercellular tumor tissue consisted of closely packed elongated cells with scattered rounded cells with abundant eosinophiloic cytoplasm corresponding to Leydig cells. Epithelioid cells were distributed in cords and single file in either hypercellular or oedematous tissue; focal luminal differentiation was also present. Atypia was mild and mitotic figures were rare with the highest activity corresponding to three mitotic figures per 10 FPF (Fig. 2).

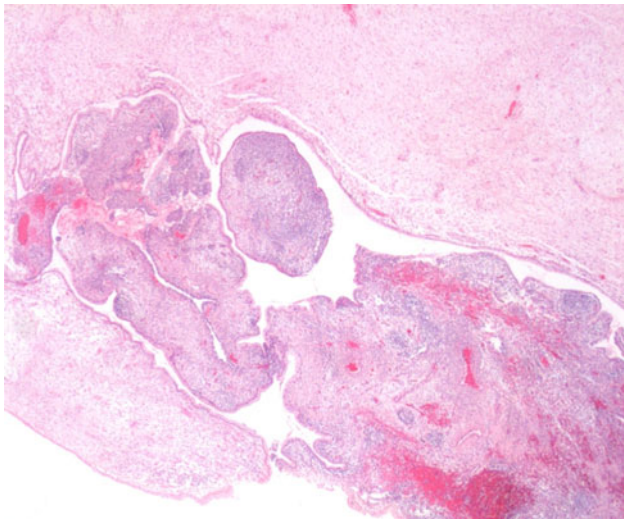

Fig. 1 Embryonal rhabdomyosarcoma of uterine cervix. A cellular subepithelial cambium layer contrasts with the underlying stroma and hypercellular subepithelial layer

Discussion

As far as we know, this is the fifth associated case of Sertoli–Leydig cell tumor with a botryoid sarcoma of uterine cervix.

Sex cord stromal tumors are a rare pathology and there are few examples of association with other tumors and

Table 1 SLCT: Sertoli-Leydig cell tumor; SB: Sarcoma botryoides

Case	Sarcoma botryoides			Sertoli–Leydig		
	Age	Clinical and surgery	Pathology	Age	Clinical and surgery	Pathology
Daya, case 6 [1]	23	Vaginal bleeding; polyp 4 cm; TAH + pelvic nodes	SB	24	Not known	SLCT G2
Daya, case 9 [1]	15	Vaginal bleeding; polyp 3 cm; polypectomy + chemotherapy	SB with heterologus cartilage	18	Not known	SLCT G2
Golbang [2]	14	Vaginal bleeding; polyp 4 cm; radical hysterectomy + pelvic nodes	SB with heterologus cartilage	27	Abdominal pain, hirsutism; 1–2 cm solid and cystic right ovarian mass; unilateral oophorectomy	SLCT G2
McClean [3]	13	Polyp 3 cm; polypectomy	SB	13	Hirsutism; amhenorrea; change in voice; unilateral oophorectomy	SLCT G2
Present case	20	Polyp 7 cm; polypectomy + chemotherapy.	SB	19	Hirsutism; amhenorrea; abdominal pain; unilateral oophorectomy	SLCT G2

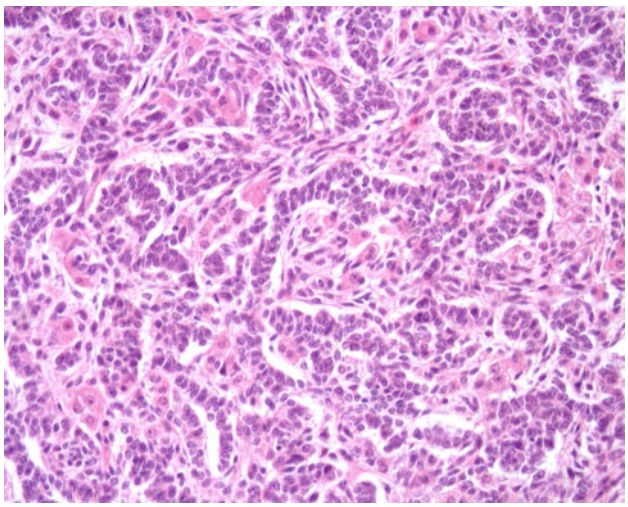

Fig. 2 Sertoli–Leydig cell tumor of intermediate differentiation. Cords and clusters of Sertoli cells with scan cytoplasm are admixed with nests of Leydig cells

syndromes. About one-third of a rare type of sex cord stromal tumor with uncertain male or female differentiation of tumor cells, the sex cord tumor with annular tubules, is a component of the Peutz-Jeghers syndrome [4]. Sertoli–Leydig cell tumor was found to occur in some families, particularly with thyroid diseases.

The first two cases of the association were included in a review of 13 cases of sarcoma botryoides of the cervix by Daya and Scully [1] and they were included in a review of 207 cases of Sertoli–Leydig cell tumors by Young and Scully [5]. These patients developed an intermediate ovarian Sertoli–Leydig cell tumor, respectively, 1 and 3 years later. The third case was reported by Goldbang et al. [2]. The patient was 14 years when she had cervical embryonal rhabdomyosarcoma treated by radical hysterectomy and bilateral pelvic lymphadenectomy and after 13 years she developed an intermediate ovarian Sertoli–Leydig cell tumor, treated by oophorectomy. McClean et al. reported the fourth case of literature of a 13-year-old girl with clinical evidence of hirsutism and changed voice, who had cervical embryonal rhabdomyosarcoma, avulsed by polypectomy concomitant with an intermediate ovarian Sertoli–Leydig cell tumor [3].

All five Sertoli–Leydig cell tumors have been of intermediate differentiation. Subunit α inhibin serum level was normal and only the serum levels of prolactin and testosterone were higher, in fact we excluded a tumor or dysfunction of pituitary through a magnetic resonance of brain.

Except for the first case described by Dally [1] and the Golbang's case [2], treated respectively by extrafascial and radical hysterectomy with pelvic lymphadenectomy, in the present and other cases a conservative treatment through polypectomy was performed. Adjuvant chemotherapy doesnot seem to improve the prognosis, in fact this patient had a recurrence of uterine disease after 6 years.

Polypectomy therefore seems to be a safe way to approach this pathology.

Sarcoma botryoides showed typical features. All reported tumors were polypoid and consisted of mostly edematous stroma with the presence of the hypercellular subepithelial cambium layer. Differently from McClean and Goldbang, mature classical rhabdomyoblasts with eosinophilic cytoplasm and cross-striations were also identified. Myogenin and desmin were positive on immunostains. Nests of fetal cartilage were present in two of the five cases [1, 2]. A cambium layer with condensation of stromal cells around epithelial elements is a characteristic feature [3] (Fig. 1). The differential diagnosis may include a usual cervical or endometrial polyp, a fibroepithelial polyp, an endometrial stromal or a leiomyomatous neoplasm. The morphological appearance of a polypoid lesion containing benign epithelial elements with a malignant stromal component, which condenses around the epithelium, may suggest an adenosarcoma, although in cervical embryonal rhabdomyosarcoma the glandular elements are considered to be entrapped rather than an integral component of the tumor [3].

Although not present in this case, immature cartilage and skeletal muscle are seen in 5% of Sertoli–Leydig tumors and suggest a potential link between cervical sarcoma and SLCT, because these elements may be seen in both [6].

Goldbang and McClean have suggested that the association of these rare neoplasms is more than coincidental and a genetic linkage can be speculated, in fact McClean observed the abnormality of chromosome 12 in both embryonal rhabdomyosarcoma and ovarian Sertoli–Leydig cell tumor [2, 3]. Conventional cytogenetic studies have suggested that trisomy 12 may be a characteristic nonrandom numerical chromosome anomaly in ovarian tumors, particularly sex cord-stromal tumors [7, 8]. Trisomy of chromosome 12 and more rarely monosomy 22 are observed in female genitourinary tract tumors and has been a recurrent and often unique anomaly in granulosa cell tumors, Sertoli–Leydig cell tumors and fibrotechomas using FISH and/or conventional cytogenetics suggesting a common mechanism of carcinogenesis within this diverse group of neoplasms [9–11]. Manegold et al. provided the first cytogenetic analysis of a metastasizing SLCT, identifying trisomy 8 as sole unbalanced aberration. Whereas the pathogenetic meaning of trisomy 8 in the development of the SLCTs remains unclear, the finding indicates that SLCTs are cytogenetically different from other sex-cord stromal tumors, particularly granulosa cell tumors of the ovary [12].

In summary, we have reported the fifth documented case of cervical sarcoma botryoides and ovarian Sertoli–Leydig cell tumor and although we think that this association is not coincidental, the pathogenetic mechanisms are not yet known.

Conflict of interest None.

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