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A case report



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Metrorrhagia in a child with an endodermal sinus tumor of the vagina. A case report

In a female child presenting with vaginal bleeding or a mass protruding through the vagina, it is mandatory to perform an endoscopic and laparoscopic examination and biopsy to establish the correct diagnosis and precise extent of the lesion. An endodermal sinus tumor (EST) of the vagina is a rare, malignant germ cell tumor that occurs primarily in infants. Clearly, the vagina is a critical site for treatment, and the surgeon should seek to preserve the reproductive and sexual function, if possible. We report our experience of a case of EST of the vagina in a 9-month-old female with a history of metrorrhagia. We employed minimally invasive procedures for diagnosis and then, after the administration of platinum-based chemotherapy (PEB regimen), removed a residual lesion during follow-up. These procedures resulted in tumor regression. At follow-up, after two years, the patient is alive and disease-free.

KEY WORDS: Minimally invasive surgery, Pediatric metrorrhagia, Vaginal endodermal sinus tumor.

Introduction

Malignant germ cell tumors (MGCT) are rare tumors of childhood and account for approximately 3% of all pediatric malignancies¹. In some cases an MGCT arises primarily from the vagina: in this case the histological subtype is almost always an endodermal sinus tumor (EST). The presence of "Schiller-Duvall bodies" in the biopsy specimens, as well as positive immunoperoxidase staining of

the tumor tissue for serum alpha fetoprotein, are the typical histological aspects of this extremely rare tumor, that has an incidence ranging from 3% to 8% of all germ cell tumors^{1,4,5}. A very high cure rate of MGCT has been achieved even in advanced stages of the disease, thanks to a multimodal approach based on chemotherapy and appropriate surgery². Surgical resection of any residual tumor, after first-line chemotherapy, is recommended because it helps to improve event-free and overall survival. Unfortunately, the vagina is a critical site as far as local treatment is concerned, and potentially mutilating surgery should be avoided, making every effort to preserve the reproductive and sexual function.

Case report

A 9-month old-female was referred to the Pediatric Surgery Department of the Pediatric Hospital Giovanni XXIII in Bari for a suspected pelvic neoplasm.

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Abdominal ultrasound scans were performed for hematuria of ten days' duration, revealing a pelvic neoplasm appearing as a "complex mass". At physical examination, a friable, bleeding mass arising from the vagina was observed, similar to a "botryoid sarcoma" of the vagina (Fig. 1). Results of routine laboratory tests and tumor markers were normal except for the serum alpha fetoprotein (α -FP) level, that was elevated (11379 IU/mL; normal 20 IU/mL). The presumed diagnosis was an EST of the vagina: subsequent total body Computerized Tomography (CT) and abdominal Magnetic Resonance



Fig. 1: Initial presentation: a bleeding, friable mass arising from the vagina.

Imaging (MRI) showed a pelvic mass, 3cm x3.2cm x2.8 cm in size, adhering to the perineal plane, involving the uterus and vagina, but it was not possible to determine its origin. The mass was causing dislocation of the rectum and imprinting on the bladder (Fig. 2), while no evidence of distant metastasis was found: the kidneys, liver and ovaries were disease-free.

With the patient under general anesthesia, vaginoscopy was performed and revealed a friable mass arising from the right wall of the vagina. Biopsy of the mass was done during vaginoscopy and histopathological examination of the specimens demonstrated an endodermal sinus tumor (EST) of the vagina. After consultation with a pediatric oncologist, the patient was administered 6 cycles of chemotherapy according to the PEB regimen every 4 weeks (cisplatin 20 mg/m²/day from days 1–5, etoposide 100 mg/m²/day from days 1–5, and bleomycin 18 mg/m²/day on days 2 and 16).

The α -FP returned within normal range after the second PEB cycle, but the patient was administered all 4 further cycles of chemotherapy. At the end of chemotherapy, MRI showed a regression of the pelvic mass, revealing only a residual lesion measuring 1.3cm x 0.6cm. (Fig. 3). Vaginoscopy showed the presence of a vegetating lesion, located on the right vaginal wall, which was completely excised with biopsy forceps during an endoscopic procedure. On the left wall of the vagina the mucosa appeared anomalous, so three biopsies were performed. The cervix had a normal appearance but despite this evidence, biopsies were taken around the circumference.

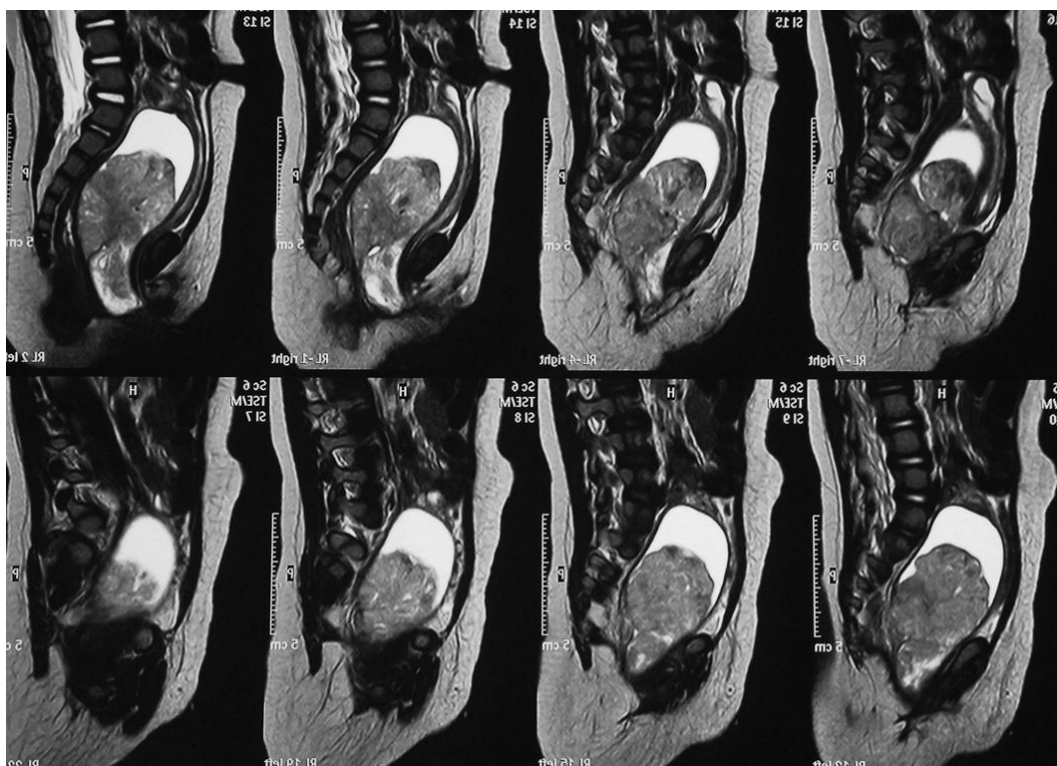


Fig. 2: MRI showed a 3cm pelvic mass with hydrocolpus, displacing the bladder and rectum.

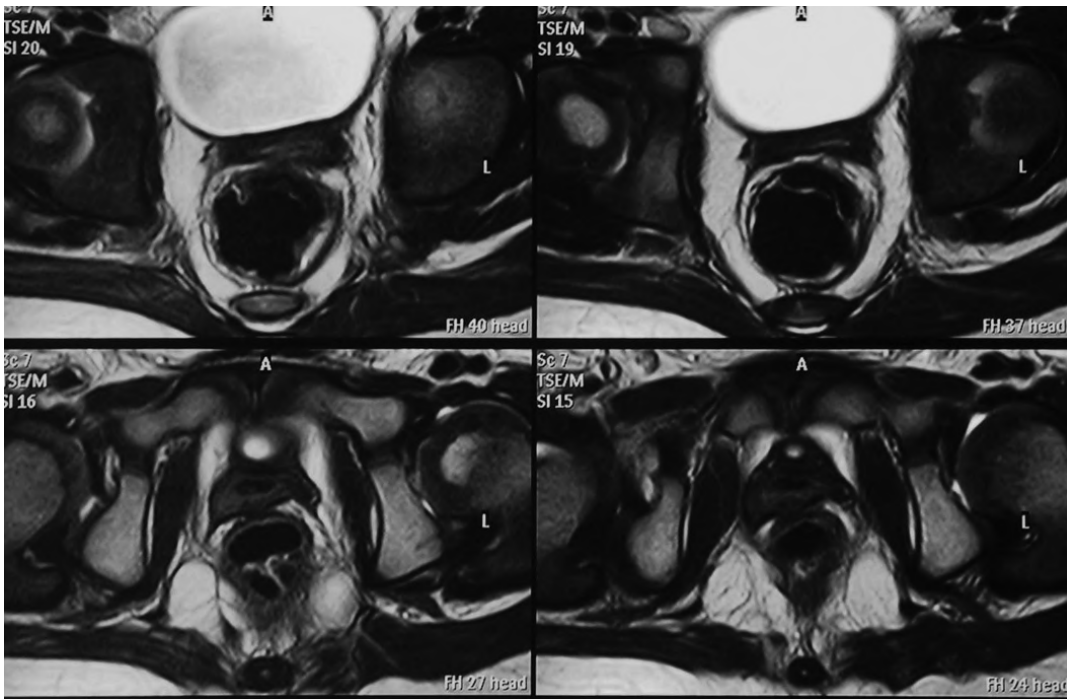


Fig. 3: MRI control after Chemotherapy showed a residual mass.



Fig. 4: Vaginoscopy and biopsy of the residual mass located in the right vaginal wall: "cervix normal".



Fig. 5: Clinical monitoring: normal appearance of the genital region.

The vaginal fornices were free. Histological examination of the residual mass revealed only tissue abnormalities due to chemotherapy, without neoplastic cells (Fig. 4). An exploratory laparoscopy was performed and no tumor penetrating the uterus and /or intra-abdominal metastases were evident. Nevertheless, biopsies of the uterus with tru-cut 16 G were performed laparoscopically using 3 mm instruments, and histopathological study of the specimens showed no viable malignant cells. The patient had an uneventful recovery after the procedure. Serum α -FP remained normal in the following months.

Considering the site of the disease and the optimal response to PEB, we scheduled follow-up by pelvic ultrasound and α FP level monitoring (Fig. 5); after two years, all findings are normal.

Discussion

The vagina is one of the rare sites of origin of MGCT, and presents almost exclusively under the age of 3 years, most frequently with vaginal bleeding as the first symp-

tom of the disease⁴. The most common histology is an endodermal sinus tumor, and α FP is considered a reliable marker to evaluate treatment response and remission status^{6,7}. EST is an aggressive tumor with a very poor prognosis, and in the past most patients died. Previously the typical treatment protocol consisted of radical surgery (i.e., pan-hysterectomy plus partial vaginectomy),¹⁶⁻¹⁹ with adjuvant radiotherapy (external radiation or vaginal brachytherapy) and /or chemotherapy, leaving no hope for future fertility^{4,7,8}. Since the introduction of platinum-based chemotherapy, the percent of survival has reached 70% and now, like their counterpart in adulthood, childhood MGCT have a good prognosis when platinum-based chemotherapy is employed⁵. In the current state-of-the-art, surgery is used mainly to make the histological diagnosis and to evaluate the presence of residual disease during follow-up after chemotherapy.

However, in advanced stage tumors and cases of failure of chemotherapy, surgical excision of primary tumors and of residual disease could be necessary, although late effects in children are always a major concern and potentially mutilating surgery should be avoided.

For vaginal MGCT, some Authors suggested conservative surgery involving at least a partial vaginectomy and subsequent chemotherapy^{10,11}. Unfortunately, fibrosis and growth impairment of the vagina have been observed secondary to "conservative" surgical procedures and radiotherapy¹². In our experience, local tumor excision with minimally invasive endoscopic and laparoscopic procedures, combined with platinum-based chemotherapy (PEB regimen) resulted in tumor regression without causing iatrogenic lesions, and preserving sexual and reproductive functions. Serum α FP is confirmed to be a useful marker for diagnosis and for monitoring the recurrence of vaginal EST: a delayed decrease of α FP levels should be a signal warning of the need for further evaluation. It has been observed that vaginal EST and germ cell tumors generally tend to recur early, within two years following first-line chemotherapy^{1,5}: serial determinations of α FP together with pelvic ultrasound monitoring are recommended in the first two years of follow-up.

Conclusion

In our experience and that of others, an initial biopsy followed by cisplatin-based chemotherapy, avoiding invasive surgical procedures, was shown to achieve complete tumor remission including α FP normalization; such an approach can be recommended in the treatment of vaginal EST⁵, as it preserves the reproductive and sexual organs and the potential for childbearing. In addition to radiological findings, cystovaginoscopy and a pelvic laparoscopic examination are essential to

detect lesions of the pelvic organs, and determine the precise location and extent of the lesion, as well as to obtain biopsies and allow excision by minimally invasive procedures. In addition, cystovaginoscopy and laparoscopy allow the response to treatment to be evaluated, during and after therapy, revealing the presence of active residual disease.

Riassunto

I Tumori del seno endodermico sono rare neoplasie maligne che originano dalle cellule germinali, che possono essere a sede sia gonadica che extragonadica: rara, 3- 8% circa di tutti i casi, è la localizzazione vaginale che si sviluppa quasi esclusivamente in bambine al di sotto dei tre anni di età. Questa neoplasia veniva trattata in un recente passato con terapia radiante e procedure chirurgiche altamente lesive con frequente compromissione delle funzionalità sessuali e riproduttive delle pazienti. Più recentemente, specie con l'affermarsi di protocolli chemioterapici basati sull'utilizzo del platino, si è osservato un deciso miglioramento della prognosi in termini di sopravvivenza e di funzionalità. In questo attuale contesto pertanto non sono più accettabili interventi chirurgici che comportino estese mutilazioni genitali; il ruolo della chirurgia rimane comunque fondamentale sia nella fase di inquadramento diagnostico sia nel follow-up dopo chemioterapia, e pertanto risulta ideale il ricorso a tecniche chirurgiche mini-invasive per operare in sedi anatomiche così delicate. Riportiamo il caso di una bambina di 9 mesi, giunta alla nostra osservazione perché affetta da neoplasia pelvica che si era manifestata con sanguinamento vaginale, sottoposta a vaginoscopia con prelievo biptico della massa per la definizione diagnostica della neoplasia. L'esame istologico confermava la diagnosi di Tumore del seno endodermico. Al termine del trattamento chemioterapico, persistendo in sede vaginale una lesione di non univoca interpretazione radiologica all'es. RMN di controllo, la paziente veniva sottoposta ad una seconda vaginoscopia ed alla completa escissione endoscopica delle lesione, dimostratasi istologicamente un esito cicatriziale. La ispezione laparoscopica della pelvi e della cavità peritoneale, consentiva infine di escludere la presenza di lesioni ripetitive e di eseguire prelievi biptici dell'utero. A due anni di distanza, i controlli ematici ed ecografici, non dimostrano alcuna ripresa della malattia.

Conclusione: il caso presentato evidenzia che l'evoluzione del trattamento medico chemioterapico, supportato da tecniche chirurgiche mini-invasive, consente di ottenere la remissione della neoplasie preservando la funzionalità degli organi sessuali. Fondamentale resta il ruolo della chirurgia anche nella fase di inquadramento diagnostico e nel follow-up dopo chemioterapia.

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