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Incidence of metachronous contralateral mature ovarian teratoma in childhood and adolescence—a single-centre 20-year experience

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Abstract

Background: Despite complete resection of mature ovarian teratoma, there remains a risk of metachronous contralateral disease with implications for further surgery and fertility. Current estimates of this risk are wide and practice regarding surveillance varies. We aimed to identify the incidence of metachronous contralateral disease in girls presenting with unilateral mature ovarian teratoma and to describe current follow-up.

Methods: Retrospective case note review was performed for all girls (< 17 years) undergoing surgery for histologically confirmed mature ovarian teratoma between 1998 and 2018. Data concerning initial hospital episode, follow-up, and further intervention were collected.

Results: Forty-five girls were identified with a median age of 10 years (range 1–16). Salpingo-oophorectomy (47%) and oophorectomy (36%) were the commonest operations. Median follow-up was 2 years (range 0–16 years) with surveillance ultrasonography performed in 49%. One case of metachronous contralateral teratoma (2%) was detected at 1 year, requiring oophorectomy and ovarian tissue cryopreservation.

Conclusions: This series has demonstrated a lower incidence of metachronous contralateral mature ovarian teratoma compared to previously published data. Postoperative surveillance is variable, and the true natural history of this condition remains incompletely understood. Prospective, multicentre investigation at national or international level is required to improve the evidence upon which to base safe standards of care.

Keywords: Mature ovarian teratoma, Dermoid cyst, Paediatric oncology, Paediatric surgery

Background

Mature teratoma is the most common benign ovarian neoplasm of childhood and adolescence [1]. Classified in the germ cell group, these tumours originate in multiple germinal layers and are characterised by the presence of ectopic tissue on histopathological examination [2]. Surgical excision, either as an ovarian sparing procedure or by oophorectomy, is the mainstay of treatment and typically confers an excellent prognosis [3]. Despite complete resection, data are emerging that suggest there remains a risk of metachronous contralateral disease in the remaining ovary. This would clearly have implications for future fertility and also for surveillance following resection of the index tumour. The precise incidence of metachronous contralateral tumour in childhood and adolescence is unclear but has been reported variably at 4–23% in several European studies [4–6]. In light of these concerns, the UK Children's Cancer and Leukaemia Group (CCLG) updated their guidance in 2018 to optimise detection of

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metachronous disease by routine follow up comprising annual ultrasonography for 10 years in cases with normal pre-operative tumour markers [3]. Given the range in incidence of metachronous tumours reported to date, the benefit of such a surveillance program is unclear and recent study has identified variation in the postoperative management of girls with mature ovarian teratoma in the United Kingdom (UK), likely due to a scarcity of evidence guiding practice [4]. We aimed to contribute to the existing limited literature on this topic and report the incidence of metachronous contralateral disease in our centre over a 20-year period.

Methods

A retrospective observational study was performed of all cases of mature ovarian teratoma treated at our centre between October 1998 and October 2018. Eligibility criteria were female patients aged 0–16 years undergoing surgery to remove a histologically proven unilateral mature ovarian teratoma. Cases of synchronous bilateral mature teratoma were excluded, as were ovarian neoplasms of other histopathological classification. The study sample was identified by cross-referencing the trust's clinical coding records with databases from the Departments of Paediatric Surgery, Paediatric Oncology, and Pathology. Data were collected from electronic records and patient case notes. The study was approved by our institution as a service evaluation.

The primary outcome was the incidence of metachronous contralateral mature teratoma. This was calculated as a percentage with the number of cases of metachronous contralateral disease divided by the total sample size and the resultant figure multiplied by 100. The secondary outcomes were a description of the follow-up time and of the investigations utilised to assess for disease recurrence (blood tests and imaging modalities). Data recorded included patient demographics, family history, clinical features, preoperative imaging and tumour markers, operative details, pathology report, frequency and duration of postoperative follow-up and details of any contralateral metachronous tumour identified. During this period, follow-up was typically at individual surgeon/oncologist discretion, although since the guidelines were introduced in 2018 follow-up has been in accordance with those.

Categorical data were summarised as number with percentage. Given the sample size, continuous data were summarised as median and range. Calculations were performed using Microsoft Excel (Microsoft Corporation, Redmond WA). Kaplan–Meier survival analysis was performed using R version 4.0.2 (R Foundation for Statistical Computing, Vienna, Austria) [7]. The outcome variable of interest was the detection of metachronous contralateral mature ovarian teratoma with the time to this event plotted on the Kaplan–Meier curve. Cases were censored if they were discharged from clinic or lost to follow-up prior to the end of the study period.

Table 1 Patient demographics

Total number	**45**
Age at diagnosis of index tumour (years)	
Median (range)	10 (1–16)
Family history of gonadal cancer	0
Presenting features *number* (*percentage*)	
Abdominal pain	29 (64%)
Abdominal mass	10 (22%)
Abdominal distension	5 (11%)
Incidental finding	
Number (*percentage*)	5 (11%)

Table 2 Operative factors

Salpingo-oophorectomy *number (percentage)*	**21 (47%)**
Oophorectomy *number (percentage)*	16 (36%)
Ovarian sparing resection *number (percentage)*	8 (18%)
Laparoscopic technique *number (percentage)*	7 (16%)
Intra-operative complications *number (percentage)*	1 (2%) Haemorrhage
Tumour size *median (range)*	8 (3–27) cm

Results

During the study period, forty-five patients meeting the inclusion criteria were identified and all were included. The median age at diagnosis of index tumours was 10 (1–16) years. Demographic and clinical data at presentation are summarised in Table 1. Diagnostic imaging was used in all cases preoperatively (ultrasound 91%, MRI 22%, CT 11%, plain abdominal X-ray 9%), and the majority (78%) had pre-excision tumour markers evaluated. CA125 was raised in 5 cases and AFP raised in 1 case. The patients with raised tumour markers all displayed mature ovarian teratoma on histological examination of resected specimens. The case with raised AFP preoperatively was lost to follow-up in the postoperative period. No patient had a biopsy performed prior to excision of primary tumour. Complications associated with the tumour were seen preoperatively in 44% of patients including ovarian torsion (31%), hydronephrosis (9%), urinary retention (2%), and tumour rupture (2%). Operative data are displayed in Table 2.

Overall, patients were formally followed up for a median of 7 (0–72) months following excision of their

index tumour. Four patients (9%) had no documented follow-up review, and two (4%) did not attend scheduled outpatient appointments. During follow-up, tumour markers were tested in 24% of children (all normal) and surveillance ultrasonography was performed in 49%. We identified that pelvic ultrasonography or cross-sectional imaging was performed for unrelated indications outside of the planned surveillance in 16 cases. Radiological follow-up across the entire cohort therefore ranged from 0 months to 16 years (median 2 years).

During this time, just one case of metachronous contralateral teratoma was detected one year following index tumour resection. This was identified on routine ultrasonography. Ovarian sparing surgery was not possible, so contralateral oophorectomy was performed with ovarian tissue cryopreservation. One further child (2%) had an ipsilateral tumour recurrence detected during surveillance by ultrasound scan, resulting in salpingo-oophorectomy. She had undergone ovarian cystectomy in her index procedure. Other complications identified during follow-up were adhesional bowel obstruction ($n=2$) and wound complications ($n=2$). Overall, the incidence of metachronous contralateral teratoma in this series was 2% (95% confidence interval 0–6%) and ipsilateral recurrence 2% (95% confidence interval 0–6%). Follow-up data for all 45 patients included in the sample have been plotted on the Kaplan–Meier survival curve (Fig. 1).

Discussion

This 20-year retrospective observational study has identified an incidence of metachronous contralateral mature ovarian teratoma during follow-up of just 2% (95% confidence interval 0–6%). This is a lower rate compared to similar retrospective European studies [a–6]. In the largest of these, Braungart et al. demonstrated an incidence of 4% (7/177) among patients treated in UK specialist centres [4]. Other single-centre studies which have featured smaller sample sizes than our own have reported higher rates of metachronous contralateral tumours including 13% (4/30) in a French series and 23% (5/22) in a series from Finland [5, 6]. Data from North America have also demonstrated a low incidence, though study design and clinical practice appear to differ from that in the UK. In Canada, Rogers et al. reported 66 children and adolescents undergoing ovarian cystectomy at a single centre and identified just one case (2%) of metachronous contralateral teratoma, which interestingly occurred in association with an ipsilateral recurrence [8]. In a single-centre study performed in the USA, Templeman et al. identified no cases of metachronous contralateral disease among their sample of 52 patients under 21 years of age [9]. It should be noted, however, that only six (12%) underwent elective ultrasonography postoperatively.

Of note, one patient had a raised preoperative AFP with benign histology on examination of the surgical specimen. She was unfortunately lost to follow-up, so no further biochemical testing was performed and her raised tumour marker remains unexplained. There was variation in formal postoperative follow-up in our series, with

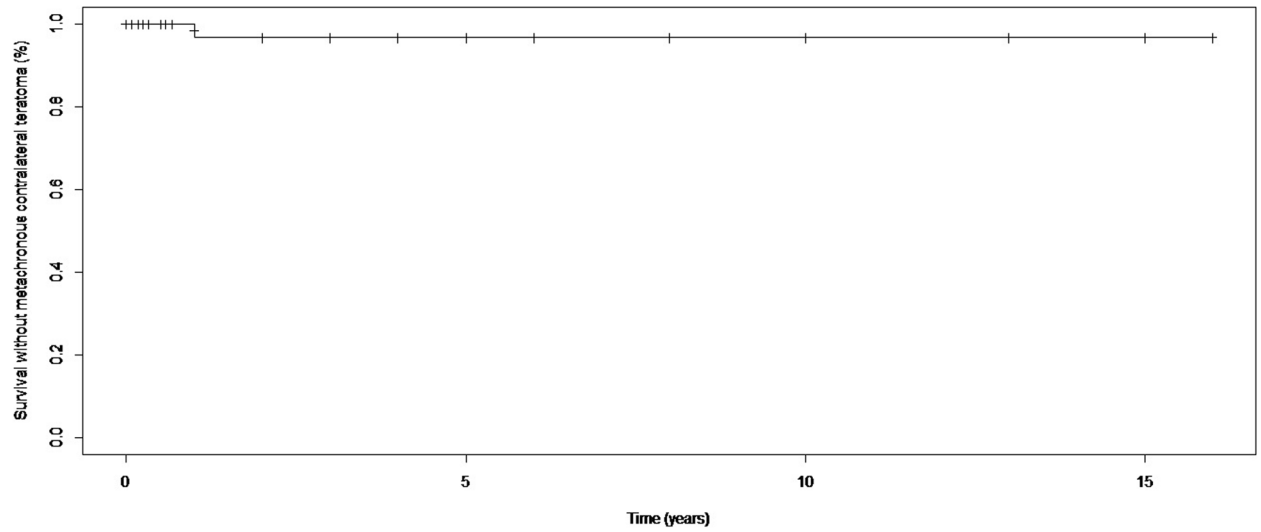

Fig. 1 Kaplan–Meier survival analysis. The percentage of patients identified as having no metachronous contralateral teratoma on follow-up imaging is plotted on the *y*-axis against follow-up time in years on the *x*-axis. Censored patients (no further follow-up) are demonstrated as perpendicular marks on the plotted line

a median surveillance period of 7 months and a minority of patients receiving no postoperative imaging. Similar variation has been identified in previous European and North American studies [4–6, 8, 9]. This variation in follow-up contributes to ongoing uncertainty regarding the actual incidence of metachronous contralateral tumours. However, appreciation that this is a clinically relevant phenomenon has resulted in development of surveillance protocols in some jurisdictions, including the UK since 2018 [3]. The importance of surveillance and early detection and treatment is twofold. It is hoped that early detection prior to the point at which a tumour becomes clinically evident will increase the possibility of complete resection prior to other complications developing (e.g., transformation to immature tumour, local mass effect). Secondly, it is anticipated that removal of a smaller tumour detected during surveillance may increase the possibility of ovarian sparing resection. Since many index tumours are large at the time of presentation and treated with oophorectomy, ovarian sparing surgery in the case of a metachronous contralateral tumour may be the only possibility of a girl maintaining her native fertility.

The current challenge to those developing surveillance guidance however is the ongoing uncertainty regarding the natural history of this condition in terms of true incidence of contralateral metachronous disease and the timescale over which this may happen. Any surveillance program requires resources, has a cost implication and carries the possibility of introducing anxiety. Thus, surveillance must be justifiable and should be informed by adequate data. The current UK guidance is based on just one series with an incidence of 23%. The majority of other published series, including this one, report a lower incidence. Furthermore, the UK guidance recommends surveillance for a 10-year period after primary tumour resection but metachronous contralateral tumours have been detected up to 14 years later [4, 5]. Currently, the optimal design of a surveillance program is uncertain due to the lack of adequate data and, in particular, a lack of data with complete follow-up over a long time period [4–6, 8]. The principal limitation to this study is that there was variation in follow-up with a relatively short median period of 7 months. As such, it is possible that the true incidence of metachronous contralateral tumour may be higher than we have detected. However, we believe this is unlikely since we are the only centre in our region to whom cases of ovarian pathology are referred. It remains possible however that other cases exist. As with other single-centre studies, the small sample size limits the accuracy with which we can estimate the true incidence of metachronous contralateral teratoma. However, we report one of the largest single-centre series to date and include patients over a 20-year period.

Conclusions

This study has demonstrated a lower incidence of metachronous contralateral mature ovarian teratoma compared to previous series, albeit with limited follow-up. The true natural history of this condition remains incompletely understood and greater understanding is needed to guide clinical practice and, in particular, to inform surveillance programmes and consideration around fertility preservation. Given the rarity of this condition, prospective, multicentre investigation at national or international level is required to improve the evidence upon which to base future practice.

Abbreviations

UK: United Kingdom; CCLG: Children's Cancer and Leukaemia Group.

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Authors' contributions

TM: study design, data collection, data analysis, and manuscript preparation. SS: study design, data collection, data analysis, and manuscript preparation. CK: manuscript review. RW: manuscript review. JG: data analysis and manuscript review. NH: data analysis and manuscript review. The author(s) read and approved the final manuscript.

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Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

The study was approved by the University Hospital Southampton NHS Foundation Trust as a service evaluation (reference number SEV/0079). Further ethical approval and consent to participate was not required.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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References

1. Zhang M, Jiang W, Li G, Xu C. Case report ovarian masses in children and adolescents - an analysis of 521 clinical cases. J Pediatr Adolesc Gynaecol. 2014;27:e73–7.

2. Lala SV, Strubel N. Ovarian neoplasms of childhood. Pediatr Radiol. 2019;49:1463–75.
3. Children's Cancer and Leukaemia Group. Interim guidelines for the treatment of extracranial germ cell tumours in children and adolescents. Leicester: CCLG; 2018.
4. Braungart S, CCLG Surgeons Collaborators, Craigie R, Farrelly P, Losty P. Ovarian tumors in children: how common are lesion recurrence and metachronous disease? A UK CCLG Surgeons Cancer Group. J Pediatr Surg. 2019;S0022–3468(19):30794–8.
5. Chabaud-Williamson M, Netchine I, Fasola S, Larroquet M, Lenoir M, Patte C, et al. Ovarian-sparing surgery for ovarian teratoma in children. Pediatr Blood Cancer. 2011;57:429–34.
6. Taskinen S, Urtane A, Fagerholm R, Lohi J, Taskinen M. Metachronous benign ovarian tumors are not uncommon in children. J Pediatr Surg. 2014;49(4):543–5. https://doi.org/10.1016/j.jpedsurg.2013.09.019a.
7. R Foundation for Statistical Computing. R: a language and environment for statistical computing. 2020. Available from: https://www.r-project.org/. [Cited 7 Jul 2020].
8. Rogers EM, Allen L, Kives S. The recurrence rate of ovarian dermoid cysts in pediatric and adolescent girls. J Pediatr Adolesc Gynecol. 2014;27:222–6.
9. Templeman CL, Hertweck SP, Scheetz JP, Perlman SE, Fallat ME. The management of mature cystic teratomas in children and adolescents: a retrospective analysis. Hum Reprod. 2000;15(12):2669–72.

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