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A Long-Term Outcome of the Patients with Sacrococcygeal Teratoma: A Bosnian Cohort

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What is already known on this topic?

- *Sacrococcygeal teratoma is an extragonadal germ cell tumor that develops during fetal and neonatal periods and is associated with significant perinatal morbidity and even mortality.*

What this study adds on this topic?

- *Our study confirms the rarity and frequent postoperative complications of patients with Sacrococcygeal teratoma in the low-volume pediatric surgery service from a developing country.*
- *Immature, high-grade teratomas may locally recur or metastasize.*

ABSTRACT

Objective: Sacrococcygeal teratoma is an extragonadal germ cell tumor that develops during fetal and neonatal periods and is associated with significant perinatal morbidity and even mortality. This study aimed to determine the clinicopathologic characteristics, the clinical outcomes, and postoperative complications of sacrococcygeal teratoma cases in the low-volume pediatric surgery service in a developing country.

Materials and Methods: The study included data from all sacrococcygeal teratoma cases diagnosed from 2011 to 2020. All the relevant clinicopathologic data were recorded and analyzed.

Results: A total of 7 pediatric (5 females and 2 males) patients with sacrococcygeal teratoma were identified, ranging in age from 3 to 222 days. A prenatal diagnosis was made in 57.1% of cases. The mean gestational age for all cases was 37.1 weeks (34–38 weeks), and the mean birth weight was 3285 g (range, 2300–4700 g). Preoperative alpha-fetoprotein levels had a mean value of 24.327 ng/mL (range, 649.7–110.600 ng/mL). The surgery involved resection of the primary tumor and coccygectomy in all cases. Three (42.9%) tumors were classified as Altman type II lesions, 2 (28.6%) tumors were type IV, and 2 remaining cases were types I and III, respectively. Histology was benign in 4 (57.1%) and immature in 3 patients (42.9%). The mean follow-up time was 101.4 months (30–146 months), with 2 recurrences of high-grade immature teratomas at 11 and 30 months following the surgery. Three patients had postoperative bladder and rectal dysfunctions.

Conclusion: Sacrococcygeal teratomas are rare tumors associated with frequent postoperative dysfunctions. Recurrences may also be seen, particularly in immature, high-grade forms of sacrococcygeal teratomas.

Keywords: Clinical characteristics, outcome, sacrococcygeal teratoma, surgery

INTRODUCTION

Sacrococcygeal teratoma (SCT) is an extragonadal germ cell tumor (GCT) with an incidence of 1 in 35 000–40 000 live births.[1] Despite its rarity, it is the most common tumor in the neonatal period, with a reported female-to-male predominance of 4:1.[2,3] Sacrococcygeal teratomas originate from the totipotent cells of the Hensen's node and contain tissue derived from more than 1 germ layer.[4] Four anatomical types of SCT are distinguished according to the Altman classification (AC), which describes the intra- and extra-pelvic extension of the tumor mass.[5] Associated congenital anomalies are found in 15%–30% of patients with SCT.[3] Some anomalies are related to the extension of the tumor or as a consequence of the surgical intervention (i.e., hydronephrosis, hip dysplasia, or ventrally positioned anus). In contrast, others may be related to the presence of hydramnios or the occurring hydrops (i.e., infantile respiratory distress syndrome or bronchopulmonary dysplasia).[3] However, the sporadic

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occurrence of other true congenital anomalies without their direct relation to the tumor, including esophageal atresia, renal agenesis, Tetralogy of Fallot, congenital hyperthyroidism, and omphalocele, is also possible.[3]

The standard treatment to prevent the relapse of SCTs is early and complete resection with the coccyx en bloc.[6,7] Surgery can cure most cases, but recurrence and metastases are possible.[8]

No systemic study on SCT has been conducted in Bosnia and Herzegovina until now. Therefore, the present study explored the clinicopathologic characteristics, postoperative complications, and outcomes of SCT patients in the low-volume pediatric surgery service in a developing country.

MATERIALS AND METHODS

All medical records were pseudo-anonymized for the current study. Ethical approval was waived as the local institutional review board has a policy not to review case series/case reports. The study was carried out according to the Declaration of Helsinki.

Patient Selection

All cases of SCT diagnosed at the Clinic of Pediatric Surgery, Clinical Center University of Sarajevo, Bosnia, and Herzegovina, during 2011-2020 were retrospectively reviewed. Data collected include antenatal diagnosis, mode of delivery, gender, age at diagnosis, age at surgery, levels of alpha-fetoprotein (AFP), clinical presentation, associated anomalies, concomitant medical conditions, imaging, type of SCT (AC),[5] tumor size at postnatal diagnosis, operative management, histopathology, clinical outcome, recurrence, and postoperative complications.

Tumor Classification and Diagnostic Approach

Sacrococcygeal teratomas are classified according to AC into 4 types: type I SCTs are predominantly external with a minimal presacral component; type II SCTs are predominantly external but have a significant intrapelvic component; type III SCTs have an apparent but small external component with a significant pelvic mass extending into the abdominal cavity, and type IV SCTs occupy the presacral area with no external presentation.[5]

Based on the presence of immature neuroepithelial components, SCTs were histopathologically classified into mature and immature subtypes.[9] The tumor size at birth was evaluated by magnetic resonance imaging (MRI) or ultrasound (US) imaging, and the largest dimension measured was recorded (cm).

Immature teratomas were graded following the updated, 2-tiered grading system (low grade vs. high grade) based on the extent of the immature neuroepithelial component.[10]

Follow-up Information

The follow-up was calculated from the date of the surgery until the last check-up (November 15, 2022). Alpha-fetoprotein was assessed monthly in the first 6 months, every 2 months in the following 6 months, and every 3 months in the second and third years, respectively. Depending on the clinical presentation and AFP values, US and/or MRI imaging were utilized.

RESULTS

Clinicopathologic Characteristics of the Cohort

Clinicopathologic characteristics of the cohort are provided in Table 1.

Seven SCT cases (5 girls and 2 boys) were found from 2011 to 2020. The SCTs were identified prenatally by the US and later in infancy in 4 (57.1%) and 2 (28.6%) cases, respectively. Three (42.9%) patients presented after the neonatal period: one presented at the age of 3 months, the second at the age of 6 months, and the third at the age of 8 months. The mean gestational age (GA) for all cases was 37.1 weeks (range, 34-38 weeks), and the mean birth weight (BW) was 3285 g (range, 2300-4700 g) (Table 1).

The most common preoperative SCT-related complications were anterior displacement of the rectum (4 patients) and obstructive hydronephrosis (2 patients). Of the 3 patients diagnosed beyond the neonatal period, the presenting symptoms included bladder rupture in the youngest patient at the age of 3 months (tumor extirpation performed 7 days after emergency surgery), while the remaining 2 patients presented with constipation, dysuria, palpable suprapubic mass, and abdominal pain. In addition, a single patient had obstructive hydronephrosis, and another patient had a Currarino triad with type IV SCT, sacral bony defect, and anal stenosis as components of the Currarino syndrome (Table 1).

Alpha-fetoprotein levels were substantially elevated in all patients, with a mean value of 24.327 ng/mL (649.7-110.600 ng/mL) (Table 1). The mean patient age at the surgery was 98.7 days (range, 3-222 days).

Tumor histology included benign mature teratoma in 4 (57.1%) cases and immature teratoma in 3 (42.9%) patients. About 71% of the tumors were entirely or predominantly cystic (Table 1). Two out of 3 immature teratomas were high-grade tumors (Table 1). In our case series, all SCTs were diagnosed as pure teratomas without other germ cell components, but high AFP levels in some cases may indicate the mixed germ cell tumor morphology.

Treatment and Clinical Outcome of the Patients with Sacrococcygeal Teratoma

The surgery involved resection of the primary tumor and coccygectomy in all cases. A posterior sacral approach with early isolation and control of the median sacral vessels was used in 4 patients. In contrast, the remaining patients underwent a combined abdominosacral procedure to enable a complete tumor resection. Three (42.9%) tumors were classified as AC type II lesions, 2 (28.6%) tumors were type IV, and 2 remaining cases were types I and III (14.3%), respectively. The mean tumor size was 9.3 cm (4.5-16 cm). Postoperative morbidity included wound infection in a single patient (14.3%) and superficial wound dehiscence in another patient.

Follow-up information was available for all 7 patients. The mean follow-up time was 101.4 months (30-146 months). Two patients with immature SCT (high-grade tumors) had a recurrence 11 months and 30 months after resection, respectively

Table 1. Overview of the Pediatric Patients Diagnosed with Sacrococcygeal Teratoma During the 10 Years

No	Delivery Mode GA (Weeks)	Sex (M/F) and BW (g)	Prenatal Diagnosis	Age at Time of Surgery (Days)	Tumor Type (AC)	Tumor Size at Postnatal Diagnosis (cm)	AFP Values at Diagnosis (ng/mL)	Associated Anomalies	Tumor Morphology	Histopathology Findings	Length of Stay (Days)	Outcome
1.	Vaginal 38	M 3600	Nil	195	4	4.5 × 4	1100	Currarino syndrome	Cystic	Mature teratoma	21	NOD
2.	Vaginal 37	F 2900	Nil	99	4	6 × 5	2880	Bladder rupture	Mixed, predominantly solid	Mature teratoma	18	NOD
3.	Vaginal 38	F 3450	Nil	222	3	10 × 6	870	Neurogenic bladder, hydronephrosis	Mixed, predominantly cystic	Mature teratoma	12	NOD
4.*	CS 38	F 4700	In the eighth month	12	1	15 × 13	27 800	Nil	Mixed, predominantly cystic (high-grade)	Immature teratoma	17	Recurrence, Live
5.	CS 38	F 3700	In the sixth month	116	2	5 × 4	649.7	Nil	Mixed, predominantly cystic (low grade)	Immature teratoma	12	NOD
6.	CS 37	F 2350	In the sixth month	62	2	9 × 6	26 400	Nil	Cystic	Mature teratoma	15	NOD
7.*	CS 34	M 2300	In the sixth month	3	2	16 × 15	110 600	PPROM, hydronephrosis cardiomegaly	Solid (high grade)	Immature teratoma	18	Local recurrence and liver metastases

*Both cases were high-grade tumors.
AC, Altman classification; BW, birth weight; CS, cesarean section; GA, gestational age; NOD, no evidence of disease; PPROM, preterm premature rupture of membranes.

(patients #4 and #7 in Table 1). The first patient was asymptomatic, but the elevated AFP values (278.4 ng/mL) indicated tumor recurrence. The patient underwent surgery, and the tumor was entirely removed. The histopathologic examination of the recurrent tumor revealed similar immature morphology as in the primary tumor. The patient was treated at another institution abroad with chemo- and radiotherapy and was alive with no evidence of disease after a 9-year follow-up. The second patient (Figure 1A-B) had a local recurrence and multiple liver metastases 30 months after the surgery (early November 2022). The patient is planned to be treated with chemotherapy.

The remaining 5 patients did not receive adjuvant chemotherapy. They are alive with no evidence of disease at the last follow-up.

We also assessed the postoperative bladder and rectal functions of all patients. Four patients (cases 2, 5, 6, and 7) had no urinary and rectal functional sequelae. Patient 1 (with mature teratoma and Currarino triad) and patient 4 (with immature SCT and with tumor recurrence) had chronic intractable constipation and were treated with laxatives and stimulant medications. Both patients also required cognitive behavior therapy and biofeedback. Patient 4 also had an unsightly scar and underwent buttock scar revision. Patient 3 had neurogenic bladder dysfunction characterized by areflexic low-pressure bladder and urinary incontinence with recurrent urinary infections. This patient also had fecal incontinence.

DISCUSSION

Studies on clinical features and management of SCT are not rare; however, its low incidence usually makes it difficult for pediatric surgeons to accumulate experience in this disease.[11] This is especially true for low-volume pediatric surgery centers in developing countries with low birth rates, such as Bosnia and Herzegovina. The clinical information on SCT from Bosnia and Herzegovina is very limited,[7] and the present analysis is the first systematic study with a long follow-up.

In our study, >50% of SCT cases were diagnosed prenatally, which aligns with the literature data.[12,13]

The tumor size and other associated complicating factors determine the recommended mode of delivery. In all our cases of prenatally diagnosed SCTs, a "classical" cesarean section (large incision in the uterus) was performed primarily due to the tumor size. This approach is consistent with other studies recommending cesarean delivery to avert tumor rupture and dystocia, especially in large SCTs (>10 cm).[14,15] There is also a recommendation that in cases complicated by fetal hydrops, cesarean delivery is advisable as soon as fetal lung maturity is established (>30 weeks).[16] However, cesarean delivery and open or minimally invasive fetal surgical interventions were not indicated in our series.

We confirm a female preponderance in SCT, although it was slighter lower (2.5:1) than previously reported (3:1-4:1 ratio),[17-19] probably due to the small sample size. The reason for the female predominance is still not clear. However, it might result from later sex-specific differentiation of the caudal mesenchymal tissue, including the embryo's vertebral column and pelvic skeleton.[20]

The age of onset of SCTs varies across studies. Numerous studies[12,18,21] reported the more-frequent presence of SCTs in the neonatal period, as confirmed in our study. However, the mean age at surgery was higher in other studies.[22]

According to the American Academy of Pediatrics Surgery Section Survey, SCT is classified into 4 types.[5] Although the most common type of SCTs is type I,[19] the most common type in our series was type II, followed by type IV. This difference might reflect the small sample size.

Since the fetal liver and yolk sac usually produce serum AFP, its level typically increases throughout the newborn period, and values normalize within months after birth.[23] However, AFP serum levels that exceed normal, age-related concentrations or increasing serum AFP levels help assess the likelihood of endodermal sinus tumors and the clinical differentiation between benign and malignant teratomas, as well as for the evaluation of the effectiveness of treatment.[24,25] In our case series, all patients had markedly elevated AFP values that gradually decreased during the postoperative period. Elevation of AFP in 1 patient 11 months after extirpation of tumor and coccygectomy indicated recurrence.[26,27] The recurrent tumor had a predominantly external growth pattern (AC type I) and exhibited histological features of immature teratoma. Data from the literature show that the recurrence rate is 10%

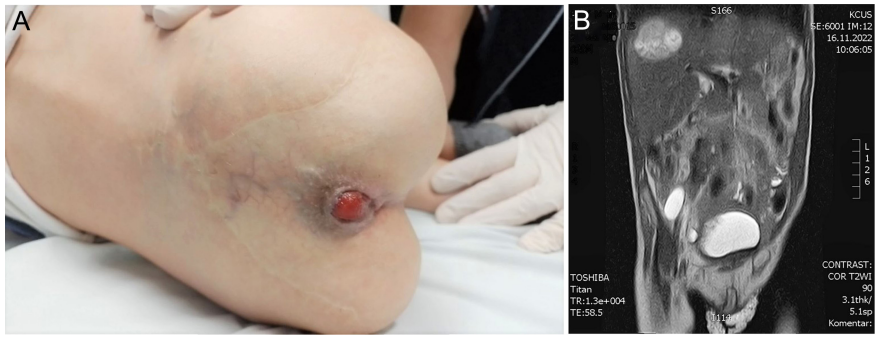

Figure 1. (A) A gross appearance of the immature teratoma recurrence (patient#7), 30 months following the surgery; (B) A pelvic and abdominal MRI scan (1.5 T) confirmed a 10×7×5 cm pelvic mass, infiltrating the surrounding structures, including the spinal canal, sacral, and vertebral-body structures. Extrapelvic propagation into soft tissue structures was also present. Multiple liver metastases, the largest measuring 4 cm, were also observed. MRI, magnetic resonance imaging.

for mature teratomas and 33% for immature teratomas.[28] Yao et al[29] found that the risk factors for SCT recurrence are tumor spillage, immature/malignant histology (yolk sac tumor and/or embryonal carcinoma), or incomplete resection. In our case series, all SCTs were diagnosed as pure teratomas without other germ cell components, but high AFP levels in some cases may indicate the mixed germ cell tumor morphology.[30]

Additionally, they found that immature elements in neonatal teratoma are not associated with malignant behavior. However, the presence of a non-teratomatous component is considered evidence of malignant potential.[29] The predominance of solid components is also suggestive of malignant SCTs.[31]

According to the data of this and other studies, SCT can be detected prenatally or have a late onset. Similar to other studies, the incidence of SCTs outside the neonatal period in our case series was not high (28.6%).

The risk of bladder and renal dysfunctions associated with SCT is determined by its location, anatomical anomalies in the tumor region, and surgical complications.[32] Although it is difficult to determine precisely whether the incidence of constipation of approximately 29% in our study is caused only by the mentioned factors related to the tumor and the surgical treatment itself or is partly related to the extreme frequency of constipation in the general pediatric population, its frequency is similar to findings reported in other studies.[33] The incidence of fecal incontinence of 14% also coincides with the results of other studies.[33]

Our study is limited by its retrospective design and a small number of recruited patients. Consequently, the treatment options and clinical outcome (e.g., tumor recurrence) should be cautiously interpreted. High AFP values in some cases may also indicate that some SCTs may not be pure teratomas but mixed germ cell tumors.[30]

CONCLUSIONS

We confirm the rarity and relatively good clinical outcomes of the patients with SCT in the low-volume pediatric surgery service from the developing country. However, recurrences are seen in immature teratomas, particularly high-grade variants. A significant degree of postoperative urinary and rectal dysfunctions in our cohort indicates that early and long-term multidisciplinary management is crucial to prevent or reduce sequelae.

Ethics Committee Approval: Ethical approval was waived as the local institutional review board has a policy not to review case series/case reports.

Informed Consent: The patient's family consented to publish the images in Figure 1.

Peer-review: Externally peer-reviewed.

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Declaration of Interests: The authors declare that they have no competing interest.

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