ENDODERMAL SINUS TUMOR: REPORT OF 12 CASES

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ABSTRACT

Twelve cases of endodermal sinus tumor were reviewed. There were 10 females and 2 males with a median age at presentation of 3 years. The primary site was sacrococcygeal in 4 patients, vaginal in 3, retroperitoneal in 2, and testicular, ovarian and left chest wall in one each. The diagnosis rested on histopathological examination and elevation of serum alfa feto protein levels (median 46,200 ng/ml). Two patients had Stage I disease, 9 had Stage III and one had Stage IV disease. Patients were managed by surgery and chemotherapy (BVP regime). All patients on BVP (even those lost at later stages), had achieved clinical remission with the first cycle of treatment.

Key words: Endodermal sinus tumor, Germ cell tumor, Vaginal tumor, Chemotherapy.

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Germ cell tumors are uncommon, with an incidence of approximately 3 per 100 person years(1). They may be benign or malignant(2). Endodermal sinus tumor (yolk sac carcinoma, yolk sac tumor) is the most common malignant germ cell tumor found in the pediatric age group(3). Sites for malignant tumors include the testis, ovary and sacrococcygeal region followed by less common mediastinum, retroperitoneum, pineal area, vagina and penis(4). We have reviewed 12 cases of pure or mixed endodermal sinus tumor diagnosed in the past five years at our centre.

Material and Methods

Twelve cases of Endodermal sinus tumor diagnosed between February 1987 and November 1992 were reviewed. All cases had a detailed work up at diagnosis including clinicial evaluation, complete blood counts, biochemical profiles, estimation of serum alfa fetoprotein, beta HCG (human chorionic gonadotropin), LDH, serum uric acid *X*-ray chest, liver scan, bone scan and ultrasonic examination of the mass. Whenever necessary, a CT evaluation of the presenting mass was done before attempting surgical excision or biopsy.

Results

The salient features with treatment and outcome is depicted in *Table I.*

Clinicial Features: There were 10 females and 2 male patients. Their ages ranged between 4 months and 11 years (median 3 years). The primary site was sacrococcygeal in 4 patients, vaginal in 3, retroperitoneal in 2 and testicular and ovarian in one each. All children had a mass. Three patients presented with vaginal bleeding alone, and had vaginal tumors extending beyond the pelvis in the abdomen. Two patients (Cases 2 and 8) had clinically detectable ascites. One male

TABLE I–*Salient Features of Cases with EST*

No.	Sex/Age (yr, mth)	Site	Clinicial Presentation mass (cm)	Stage	α-FP	β-HCG	Histopatho-logy	Treatment‡	Follow up (months)
1.	F,0,9	Vagina	Bleeding PV	III	ND	ND+	EST (Pure)	VAC × 4	Lost
2.	F,2,0	Retroperitoneum	Adbominal mass (8 × 8)	III	7,00,000	0	EST (Pure)	VAC × 2	Lost
3.	F,7,0	Retroperitoneum	Adbominal mass (6 × 7)	I	0 (*)	0	EST (Mixed)	BVP × 3	Died (CT)
4.	F,1,0	Vagina	Bleeding PV	III	17,000	0	EST (Pure)	VAC × 3, BVP × 3 + RT	Died (CT)
5.	F,3,6	Sacrococcygeal	Mass (8 × 6)	III	35,100	0	EST (Mixed)	-	Lost
6.	F,0,9	Sacrococcygeal	Mass (10 × 8)	III	5,00,000	47	EST (Mixed)	BVP × 6	Died (CT)
7.	F,3,0	Presacral	Constipation (6 × 5)	III	8,200	684	EST (Pure)	BVP × 6	10+ (Relapse)
8.	F,11,0	Ovary	Adbominal mass (11 × 10)	III	45,200	0	EST (Pure)	BVP × 3	Lost
9.	M,9,6	Chest wall and retroperitoneum	Mass (17 × 14), UMN, Paraplegia.	IV	3,000(+)	0	EST (Pure)	BVP × 5 + RT	Lost
10.	F,0,11	Vagina	Bleeding PV	III	-	0	EST (Pure)	-	Lost
11.	M,0,4	Testis	Mass (5 × 4)	I	-	0	EST (Pure)	S	4+
12.	M,1,2	Sacrococcygeal	Mass (6 × 6)	III	-	0	EST (Mixed)	BVP	1+

* = Postoperative; +ND = Not done; ‡BVP = Bleomycin, Vinblastine, Cis-platinum;
VAC = Vincristine, Actinomycin-D, Cyclophosphamide; CT = Chemotherapy; RT = Radiotherapy; S = Surgery.

child (Case 9) presented with an acute total upper motor neuron type paraplegia with a neurogenic bladder. He had a large left lower thoracic and abominal wall mass with intra-abdominal extension to the lumber paravertebral and retroperitoneal regions, epidural space and there was destruction of lower dorsal vertebrae. Case 7 presented with constipation and difficulty in micturition and had a presacral variety of sacrococcygeal mass.

Diagnosis: Surgical staging was performed in all cases using the criteria described in *Table II*. In 3 cases with vaginal tumors histopathological diagnosis was done on tissue obtained from vagina. Two patients had Stage I disease, 9 had Stage III and one had Stage IV.

Ultrasonography (USG) of abdomen was very helpful in evaluating the size and consistency of mass, involvement of lymph nodes and other organs and for follow up of these patients. Calcifications in the tumors were observed in 3 patients on USG. *X*-rays of chest and radionucleide liver and bone scans were normal in all patients except Case No. 9. He had a MRI scan of thorax and abdomen which revealed a left paravertebral mass affecting lower dorsal vertebrae with compression of spinal cord from D11 to L2. Alfa fetoprotein levels ranged from 8,200 to 7,00,000 ng/ml (median 45,000 ng/ml). In 3 cases it could not be done preoperatively.

TABLE II—*Staging for Germ Cell Tumors*

Stage I :	Disease limited to one organ or structure completely resected at the time of the initial surgical procedure using a single incision.
State II :	Disease extending to structure adjacent to the primary tumor but completely resected at the time of the initial surgical procedure.
	Tumors requiring more than one incision for removal but without tumor spillage during surgery.
State III :	(*a*) Tumors with microscopic residual following surgery, due to spillage or extension of tumor to resection margins.
	(*b*) Tumors incompletely resected at surgery.
Stage IV :	Disseminated disease.

Histopathology: Multipe sections of the excised tumor were examined. Eight had pure endodermal sinus tumor (EST), while 4 had a mixed pattern with predominant EST component (>50%). These 4 had teratomatous elements in addition. All cases classically had presence of Shiller-Duval bodies on microscopic sections.

Treatment, Complications and Outcome: Therapy consisted of surgery, chemotherapy and radiotherapy in different combinations depending on the stage of the disease (*Table I*). Surgery alone was performed in one of the Stage I patient. The Stage III candidates had surgery and received chemotheapy (BVP - Bleomycin 15 mg/m^2/wk×3, Vinblastine 0.15 mg/kg/d × 2, Cisplatinum 100 mg/m^2/d × 1) or (VAC - Vincristine 2.0 mg/m^2/wk × 3, actinomycin D 0.15 µg/kg/d × 5, Cytoxan 10 mg/kg/d × 3) and one child had radiotherapy as well. Stage IV was treated with BVP and radiotherapy.

Nine children were placed on chemotherapy. All were in clinical remission at the end of first chemotherapy cycle. Four of them took, chemotherapy for 2-4 cycles and then did not return to complete their therapy; one relapsed; and 3 died. These 3 were on BVP, 1 died of azotemia, one with metabolic acidosis, and one with electrolyte disturbances. Chemotherapy was complicated

with an absolute neutrophil count (ANC) of less than 100 per cumm on 9 occasions (26 courses of BVP were administered).

Generalized skin hyperpigmentation was noted in 2 cases and one had moderate pulmonary restrictive impairment after 3 BVP courses.

Discussion

An extraembryonal malignant differentiation of the yolk sac gives rise to a yolk sac tumor (endodermal sinus tumor, orchioblastoma). These tumors occur mostly between 1-5 years of age. Three out of twelve (25%) of our cases were above 5 years old.

The sacrococcygeal area is the major site of involvement and the ovary is the chief location(6,7). Altman and colleagues have classified children presenting with sacrococcygeal germ cell tumors into 4 types(3). Type IV presents itself as a presacral mass, and with no external mass of pelvic extension, (as occurs in 10% of patients). Case No. 7 presented with an entire Type IV presacral mass.

Vaginal presentations are uncommon and occur in children younger than 3 years(8). In our group of 12 patients, 3 had vaginal tumors, and they were one year of age or younger. One presented with a bloody and blood-tinged vaginal discharge from a polypoid, friable vaginal mass.

Testicular tumors have 2 peaks of incidence, one in infancy and the other in adolescence. We had a 4 month-old male baby with a testicular EST mass.

The most spectular case was a 9½-year-old boy who presented with a massive tumor involving the chest and abdominal wall on the left side. This is unusual not only because of its tremendous size, but also because ESTs arise near the midline(10).

Elevations of AFP (as in all our cases) occur with yolk sac tumors, since the fetal yolk sac is the source of physiologic AFP in early embryogenesis(11). In full term newborns, children and adults, the half life of AFP is 5.5 days, whereas in low birth weight infants it is greater than 7.7 days; these values are important in determining whether a resected EST has been totally removed. In full term infants, LFP is 2×10^4 ng/ml, and adult levels of less than 20 ng/ml are reached by 6 months of age(12).

ESTs are chemosensitive, and successful treatment with a variety of different drug combinations has been reported(13-18). The United Kingdom Children's Cancer Study Group has reported results of treatment with Vincristine, actinomycin and cyclophosphemide (VAC), cisplatin, vinblastine and bleomycin (BVP) and bleomycin, cisplatinum and etoposide (BEP)(2). An overall survival of 84% was obtained. Treatment is given every 3 weeks until tumor markers return to normal followed by further two courses. The Children's Cancer Study Group (CCSG) in the U.S. has reported treatment with vinblastine, bleomycin, cisplatinum, cyclophosphemide, actinomycin D and doxorubicin with a progression free survival rate at 5 years of 47%, comparing unfavorably with other protocols(19). A series of patients at St. Jude's Children's Hospital were treated with VAC or BVP with cross over to the other regimen of response was incomplete and with surgery, if necessary. Overall survival was 71%, with a complete remission rate 46% for VAC and 35% for BVP(20).

Infants with vaginal endodermal sinus tumors have been successfully treated with surgery and various combinations of VAC(21) and recently by chemotherapy alone(22), as done with two of our cases. But the chemo-

therapy related morbidity and mortality has been high in our patients, although all the patients achieved a complete clinical remission initially.

These encouraging results from chemotherapy suggest that refinements are now needed to increase the efficacy of treatment for the small proportion of patients who currently fail treatment and additionally reducing the toxicity of treatment for those for whom cure can be reliably achieved.

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NOTES AND NEWS

FIRST NATIONAL SYMPOSIUM-CUM-WORKSHOP ON GLOMERULAR DISEASES IN CHILDREN

We are dedicating the First National Symposium-cum-Workshop on Glomerular diseases in children to the memory of our beloved Dr. S.M. Merchant who was our guiding force for this symposium. This Symposium-cum-Workshop is being organized under the auspices of IAP Chapter on Nephrology and Research and Pediatric Nephrology Department of Bai Jerbai Wadia Hospital for Children on *17th and 18th December, 1993* at Bai Jerbai Wadia Hospital for Children, Parel, Bombay 400 012.

The last date of registration-cum-Workshop is extended to 30th November, 1993. The registration fee for Symposium-cum-Workshop is Rs. 250/-, for Symposium alone is Rs. 200/-, for postgraduates Rs. 150/-.

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