

# Unusual presentation of sacrococcygeal teratomas and associated malformations in children.

## Clinical experience and review of the literature



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### Unusual presentation of sacrococcygeal teratomas and associated malformations in children. Clinical experience and review of the literature

**BACKGROUND:** *Sacrococcygeal teratomas are the most common and best known extragonadal teratomas in neonates and infants, but they sometimes present unique, distinctive features unlike those commonly described, that can be considered exceptional and noteworthy.*

**MATERIAL AND METHODS:** *The Authors reviewed the most significant (Table I, II) clinical, laboratory, radiological and pathologic findings, surgical procedure, and early and long-term results in 5 children, 2 males and 3 females, suffering from sacrococcygeal teratomas. Four of 5 patients were observed and managed in the neonatal age. A prenatal diagnosis had already been made in 2 of them between the 2nd and 3rd trimester of pregnancy. Two patients were also suffering from the Currarino syndrome associated with Hirschsprung's disease and other, multiple malformations and a cloacal anomaly with anal imperforation, respectively. This last developmental anomaly had been prenatally suspected at US scanning, which had demonstrated a severe sacral anomaly and a large abdominal mass with perineal extension and dilated bowel loops. All the infants were born by scheduled caesarean section in a tertiary care hospital and were then referred to the N.I.C.U.s. because of a mostly acute clinical presentation, except for case N°4, who was referred at the age of 3.3 years. Laboratory and radiologic investigations confirmed the clinical diagnosis of teratoma on the basis of elevated AFP values and imaging findings. All patients underwent emergency surgical management, in accordance with recommended practice, consisting of complete exeresis of the tumor, including coccygectomy, in 3 of the 5 children.*

**RESULTS:** *Of the 5 patients, the female newborn affected by the Currarino syndrome, associated with persistence of the common cloacal canal and anal imperforation, died two days after surgery, of cardiovascular and respiratory complications. All the other patients had an uneventful postoperative course. Two years after the first exeresis at birth, relapse was observed in case N° 3, with a malignant component, YST, anticipated by elevated AFP values but negative physical signs and a benign cystic imaging pattern. After adjuvant chemotherapy she underwent a second complete exeresis. So far, 3 years after the second surgery and 5 years after the diagnosis and first treatment, no local recurrence or distant metastases have occurred. The other 3 patients are also all alive, disease-free and with no signs of relapse or distant metastasis, after a follow-up ranging from 2 years to 28 years. None of the 3 cases treated for sacrococcygeal teratoma, operated in 1985, 1984 and 2006, have ever developed functional sequelae such as ano-rectal and/or bladder dysfunction or hypotonia of the lower limbs.*

**CONCLUSIONS:** *From this review of our selected cases and in the light of literature reports, we can draw the following conclusions. Some sacrococcygeal teratomas may have unique characteristics distinguishing them from more common cases, especially those included in the Currarino Syndrome, with or without an association with other malformations such*

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as Hirschsprung's Disease and Cloacal anomalies. Being congenital tumors, prenatal diagnosis by US scan is extremely important in order to decide either for an anticipated delivery or to perform, in critical fetuses, prenatal treatment within highly specialized facilities, or to organize proper perinatal care, always in appropriate facilities where it is possible to define the diagnosis and carry out emergency surgery. An emergency procedure is frequently dictated both by complications related to the mass effect, and by the need to define the histology of the whole mass rather than just small biopsy specimens. Some sacrococcygeal teratomas can hide more or less extensive islands of immaturity or signs of malignant transformation that are clinically evident. The prognosis is generally benign, although AIEOP (Associazione Italiana Ematologia Oncologica Pediatrica) 2004 guidelines pointed out that high levels of circulating markers, including AFP, in children affected by mature or immature teratomas would indicate the presence of micro-foci of YST, marking them out as at high risk. The UKCCSG II (Children UK Cancer Study Group) and the SFOP (Société Française d'Oncologie Pédiatrique) indicated AFP values exceeding 10,000 ng / ml as the threshold identifying a group of patients with severe prognosis. The treatment indicated is early, complete exeresis, followed by a careful, extensive microscopic examination associated, if necessary, with adjuvant chemotherapy, that is indicated before surgery only in infiltrating primary malignant teratomas. Sacrococcygeal teratomas are commonly considered as lesions at particular risk, in which the coccyx must always be removed together with the mass and overlying skin, taking particular care of the deep pelvic fascia to prevent functional disorders of the bladder and anal canal, as well as any motor alterations of the lower limbs, usually due to iatrogenic lesions of the subfascial nerve structures. There is a unanimous consensus that to improve the prognosis, close, long-term clinical, laboratory and imaging surveillance is essential at shorter intervals during the first 5 years after the exeresis and annually thereafter. In newborns or infants suffering from congenital malformations associated with teratomas, definitive surgical correction, if indicated, must obviously be postponed to a proper time, especially in patients with multiple malformations or needing adjuvant chemotherapy, unless a complication arises or the repair cannot be delayed.

KEY WORDS: Extragenital tumors, Germ cell tumor, Sacrococcygeal teratomas.

## Introduction

Sacrococcygeal teratomas are the most common and best known extragenital teratomas in neonates and infants and can sometimes show unusual distinctive features unlike those commonly described. These characteristic features include: 1) a clinical, sometimes acute, presentation 2) an unusual phenotypic appearance of the mass. 3) primary multinodularity and biological behaviour. 4) a "fetiform" histotype of the lesion and/or 5) an association with other multiple or complex malformations such as Currarino Syndrome, Hirschsprung's Disease, or a cloacal abnormality. These elements may be isolated or associated within the same patient. We have extrapolated from our entire experience of teratomas, 5 unusual cases of sacrococcygeal teratomas, all operated as emergencies; 4 of them were treated just after birth. Aim of this paper is to report the clinical and pathologic findings, to evaluate the surgical approach and the long-term biological behavior in these cases, in the light of survival and current insights reported in the literature.

## Materials and methods

We reviewed the most significant (Tables I, II) clinical, laboratory, radiological and pathologic findings, surgical procedure, and early and long-term results in 5 children, 2 males and 3 females, suffering from sacrococcygeal teratomas (case N° 1-5). Four of 5 patients were observed

and managed in the neonatal age (Figs. 1-5, 7). A prenatal diagnosis had already been made in 2 of them between the 2nd and 3rd trimester of pregnancy. One patient was also suffering from the Currarino syndrome associated with Hirschsprung's disease and other, multiple malformations (case N°4 - Fig. 6) and another from a cloacal anomaly with anal imperforation (case N°5 - Fig. 7). This last developmental anomaly had been prenatally suspected at US scanning, which had demonstrated a severe sacral anomaly and a large abdominal mass with a perineal extension and dilated bowel loops. All the infants were born by scheduled caesarean section in a tertiary care hospital and were then referred to the N.I.C.U.s. because of a mostly acute clinical presentation, except for case N°4, who was referred at the age of 3.3 years.

The initial clinical presentation (Table II) was consistent with the site of the mass and/or its side-effects or associated developmental abnormalities. Case n°4, a child aged 3.3 years, had a history of chronic constipation since birth, complicated by an acute intestinal obstruction. The patient was also suffering from a multiple malformation syndrome characterized by: hypoplasia of the corpus callosum, a patent atrial septum secundum, occipital plagiocephaly, a bilateral leukoma, sternocleidomastoid muscle hypertonia and epilepsy, as well as low height-weight for age. In addition, a slight perineal swelling was evident, associated with a sacral anomaly, clinically supporting the diagnosis of the Currarino Syndrome. In case N° 5 there were also signs of intesti-

TABLE I

Cases	Age	Sex	Site	Pre-nat. Us.	Afp	Date	Procedure	Pathology	Results
1	G.F. 10 days	M	sacro-coccygeal region terat.	-	H	1985	Complete exeresis + coccygectomy	cystic triphyllic t. with immature gland. structures	Alive 27 y
2	G.A. 4 days	F	teratoma on back of the sacrum absence of coccyx	-	H	1984	complete exeresis	biphyllic ectomesoderm "fetiform" terat. + complete anlage of lower limb	Alive 28 y.
3	P.C. 2 days	F	sacro-coccygeal teratoma with satellite nodules	YES	H	2006	complete exeresis of mass + satellite nodules	mature solid-cystic triphyllic "fetiform" terat. *	Alive 6 y
4	T.A. 3,3 y.	M	hirschsprung's disease + t. s .c currarino syndr	-	N	2010	complete exeresis + coccygectomy + rectal biopsy	triphyllic malignant with somatic component (epitelial) terat.	Alive 2 y**
5	M.T. 1 days	F	+ persistence of cloacal canal	YES	N	2000	partial exeresis of abdominal lesion + vesicostomy vaginostomy colostomy	triphyllic malignantterat. with somatic (epitelial) component terat.	Dead 2nd post.op. day

\* Recurrence with malignant component (YST) 2 years after primary exeresis. Adjuvant chemotherapy prior to 2<sup>nd</sup> procedure.

\*\* Rectal nursing (daily irrigation) for coexisting Hirschsprung's

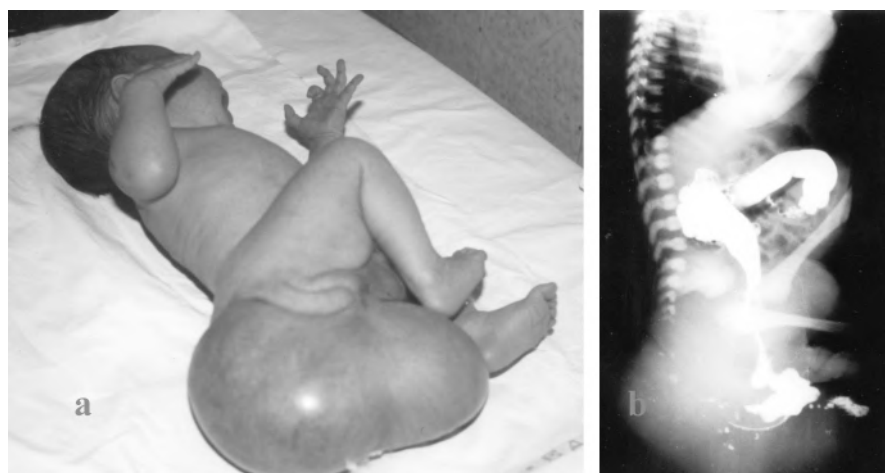


Fig. 1: CASE N° 1 Age: 10-day-old male newborn 1985.

Triphyllic Sacrococcygeal Teratoma with immature glandular components

a) Clinical feature: Sacro-perineal region deformed by voluminous, predominantly cystic mass. b) Colo-rectal visualization by c.m.: evident displacement of the rectum.

nal obstruction, related to the associated cloacal abnormality and anal imperforation. The remaining 3 infants (cases N°1-3), already displayed at birth a mass with a tendency to further growth, complicated in Case N° 1 by gradually worsening cardiovascular failure.

PHYSICAL EXAMINATION (Table II)

The general conditions were good in all patients, except for Case N°1, complicated by cardio-vascular failure. The physical features (Case N°1 - Fig. 1; case N°2 - Fig. 2 a,b; Case N° 3-Fig. 4b; Case N° 5- Fig. 7 a, b) are reported in Table II.

LABORATORY

Blood tests showed normal values in all patients, but serum AFP values (Table I) were elevated. In cases N° 4 and 5, biomolecular analysis of DNA samples revealed

a mutation of exon 1 of gene HLXB9, confirming the clinical suspicion of the Currarino Syndrome.

IMAGING STUDIES

The selection of imaging studies was dependent on the clinical presentation and time of hospitalization. In fact, 2 cases (N°1,2) were referred and managed many decades ago. Plain abdomino-pelvic radiography in duplicated view with visualization of the recto-colon using contrast medium was performed in all cases, associated in 3 patients with CT (cases N° 1, 2, 4) and MRI in cases N°3 and 4. The imaging findings are illustrated in TAB 2. In accordance with the classification system developed by Altmann, 4 of the 5 sacro-coccygeal teratomas can be classified as follows: Type I in cases N° 1 and 3; Type III in case N°5; Type IV in case N°4. Case N°2 cannot be included in Altaman's typing system because

TABLE II - *Clinical and imaging findings*

Case	Symptoms	Physical signs		Radiology
<b>10 days M (1985)</b>	<b>Extended lobulated cystic protrusion from the sacro-coccygeal region, with a tendency to further growth</b>	<b>Voluminous lobulated multicystic sacro-coccygeal mass deforming the perineum and forward displacement of anus - Cardio-vascular failure</b>	<b>Plain pelvic X-ray Visualization of the rectum by c.m.</b>	<b>Heterogeneous, predominantly cystic, calcified, perineal opacity protruding from sacro-coccygeal region and displacing the rectum – Minimal presacral extension</b>
<b>4 days F (1984)</b>	<b>Hard sacral mass with an anlage of a complete lower limb</b>	<b>Very hard mass on the back of the sacrum with protruding anlage of a lower limb – Coccyx absent Perineal region normal</b>	<b>Plain X-ray of pelvic region+ Visualization of the rectum by c.m.</b>	<b>A complete anlage of a lower limb, with a regular foot and pseudo-ilio-femoral junction, protruding from a homogeneous solid mass located on the back of the sacrum</b>
<b>2 days F (2006)</b>	<b>Protrusion from the sacro-coccygeal region; rapid growth immediately after birth</b>	<b>Large mostly solid mass with cystic component, slightly displacing the anus forward and to the right</b>	<b>MRI</b>	<b>Highly heterogeneous, predominantly solid, lobulated mass septated by adipose tissue, protruding from the sacro-coccygeal region and displacing the rectum – Minimal presacral extension</b>
<b>3.3 y. M (2010)</b>	<b>Symptoms of intestinal obstruction - associated multiple malformations – Mass located in the lower abdomen – Sacral anomaly</b>	<b>Hypogastric hard mass with minimal perineal protrusion, adherent to the overlying erythematous telangiectatic skin and deep structures – Ano-rectal narrowing with hypertonic rectal smooth sphincter - Abdominal distension and fecal plugs scattered along the left colon - Various associated malformations</b>	<b>Abdominal and vertebral spine MRI Visualization of Rectum by c.m.</b>	<b>- “S” thoraco-lumbar Scoliosis; D10-L5 Schisis with lipoma.- Large, heterogeneous, predominantly presacral opacity extending to the buttocks. Pelvic muscles dismembered -Narrowing of the ano-rectum, 8 cm. in height (Hirschsprung’s Disease)</b>
<b>1 day F (2000)</b>	<b>Symptoms of intestinal obstruction. Slight perineal swelling –Anus imperforatus – Cloacal anomaly – Extrarotation of the right lower limb</b>	<b>Hard mass occupying almost the entire abdominal cavity with a slight perineal protrusion – Persistence of cloacal canal and imperforated anus – Vulvar anomaly (fibrous umbilical cord-like structure protruding from the interlabial region just below the cloacal meatus, ending in a small reddish, swelling)</b>	<b>MRI</b>	<b>Sacral anomaly - Voluminous heterogeneous predominantly abdominal- pelvic opacity with minimal external manifestation, displacing and compressing the bowel, bladder and vagina (hydrocolpos). Bilateral Hydroureteronephrosis.</b>

it involved an exclusively exophytic lesion arising from the back of the sacrum.

#### TREATMENT

Emergency surgical management was advisable in all the patients, either because of a sudden volumetric increase or because of intestinal obstruction related to the coexisting anomalies such as Hirschsprung’s Disease (case N°4) and persistence of the common cloacal canal with anal imperforation (case N°5), as well as because of the general risk of finding immature tissue or actual malignant transformation from the usually benign type, more frequent in patients affected by sacrococcygeal teratomas.

The location and extent of the expansile lesion dictated the surgical approach, which consisted of: a sacral approach in case N°1, and perineal alone in cases N°1,3,4. In 4 of the 5 patients, complete excision was the procedure carried out (Table II). In case N°5 with the Currarino syndrome associated with persistence of the cloacal canal and anal imperforation, only the abdominal portion of the mass, which was the most extensive, (Fig. 7 d) was removed and vesicostomy, vaginostomy and colostomy were also performed. The skin and areolar tissue overlying the lesion were always removed, as well as the coccyx in cases N°1,3,4, the coccyx being absent in case N°2. Rectal wall biopsy for his-



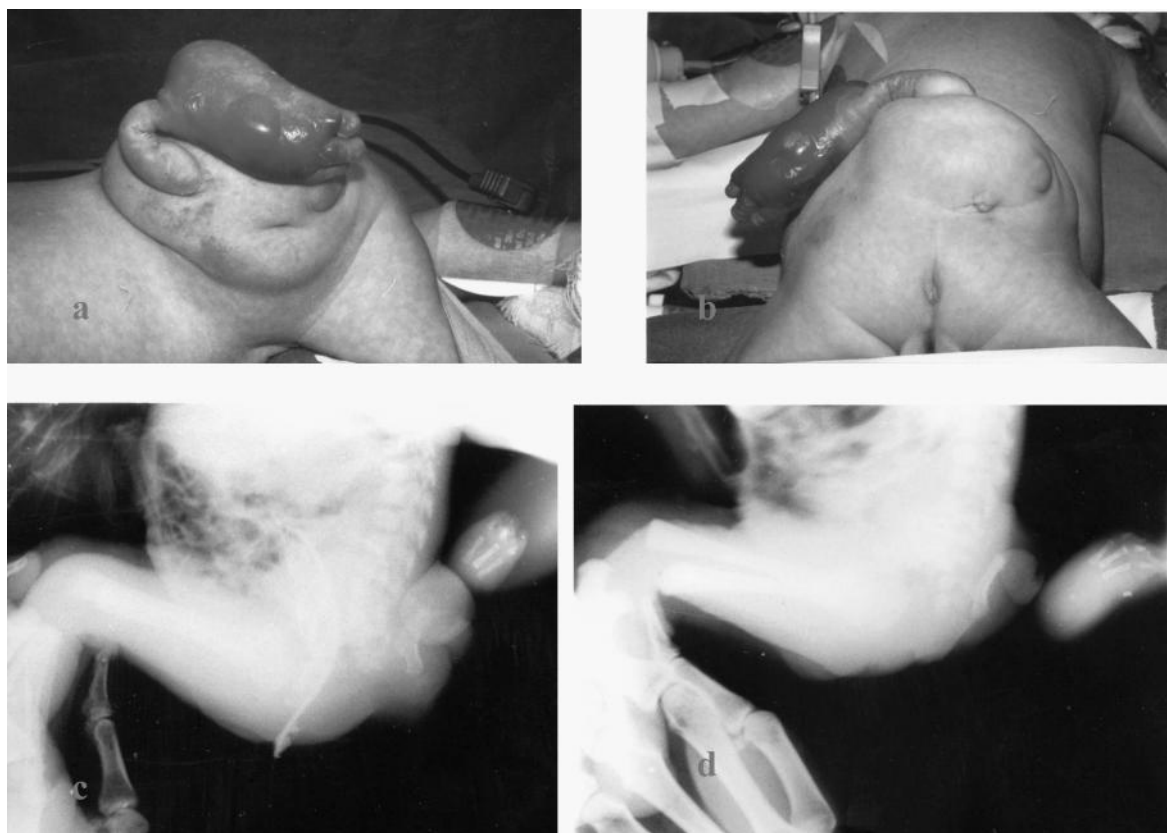


Fig. 2: CASE N° 2 Age: 4-day-old female newborn 1984. “Fetiform” biphyllic ecto-mesodermic sacral Teratoma with a regular anlage of the lower limb.  
 a) b) Clinical feature.  
 c) d) Plain X-ray of the sacro-pelvic-perineal region and visualization of the rectum by c.m.: sacral solid mass with anlages of skeletal segments of the lower limb with a pseudo-ilio-femoral joint. Absence of coccyx. Normal position of the rectum.

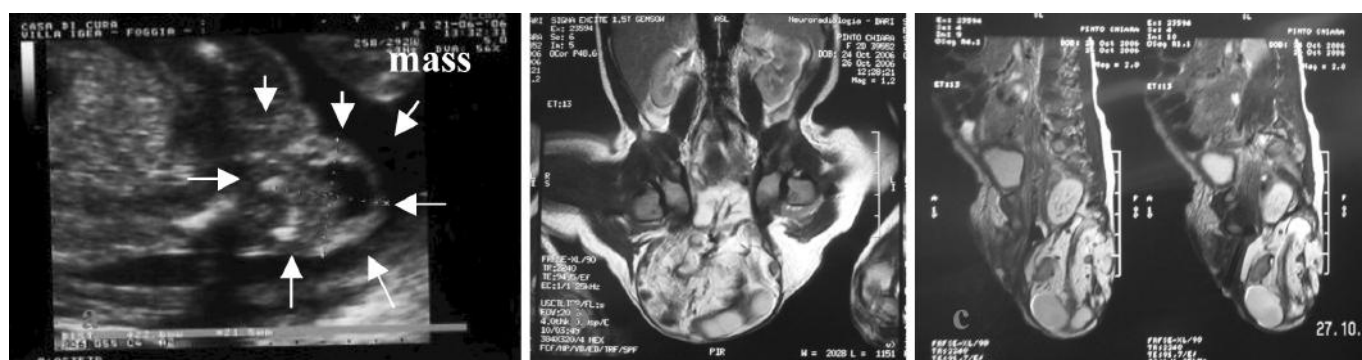


Fig. 3: CASE N° 3 Age: 2-day-old female newborn 2006 “Fetiform” triphyllic sacrococcygeal Teratoma.  
 a) Prenatal Ultrasonography at 2nd trimester of pregnancy.  
 b) c) MR: large heterogeneous sacro-coccygeal encapsulated mass with slight intrapelvic protrusion, septated by adipose tissue.

tochemical investigation was added in case N°4, affected by Hirschsprung’s Disease associated with the Currarino Syndrome. In case N°3, a female newborn, multiple, scattered lymph node-like nodules, of various sizes were excised with the help of loops after the tumor removal (Fig. 4d). The nodules, some partially confluent, were localized on the inner pelvic sheath (Fig. 4e).

#### PATHOLOGY

Most lesions showed mixed solid-cystic features with a prevalence of the cystic component in the male infant (case N°1, Fig. 1a). The mass appeared predominantly or almost entirely solid in cases N°2 (Sacral T. - Fig. 2), N°4 and N°5 (a mainly presacral abdominopelvic T. with the Currarino syndrome - Figs. 6 d,

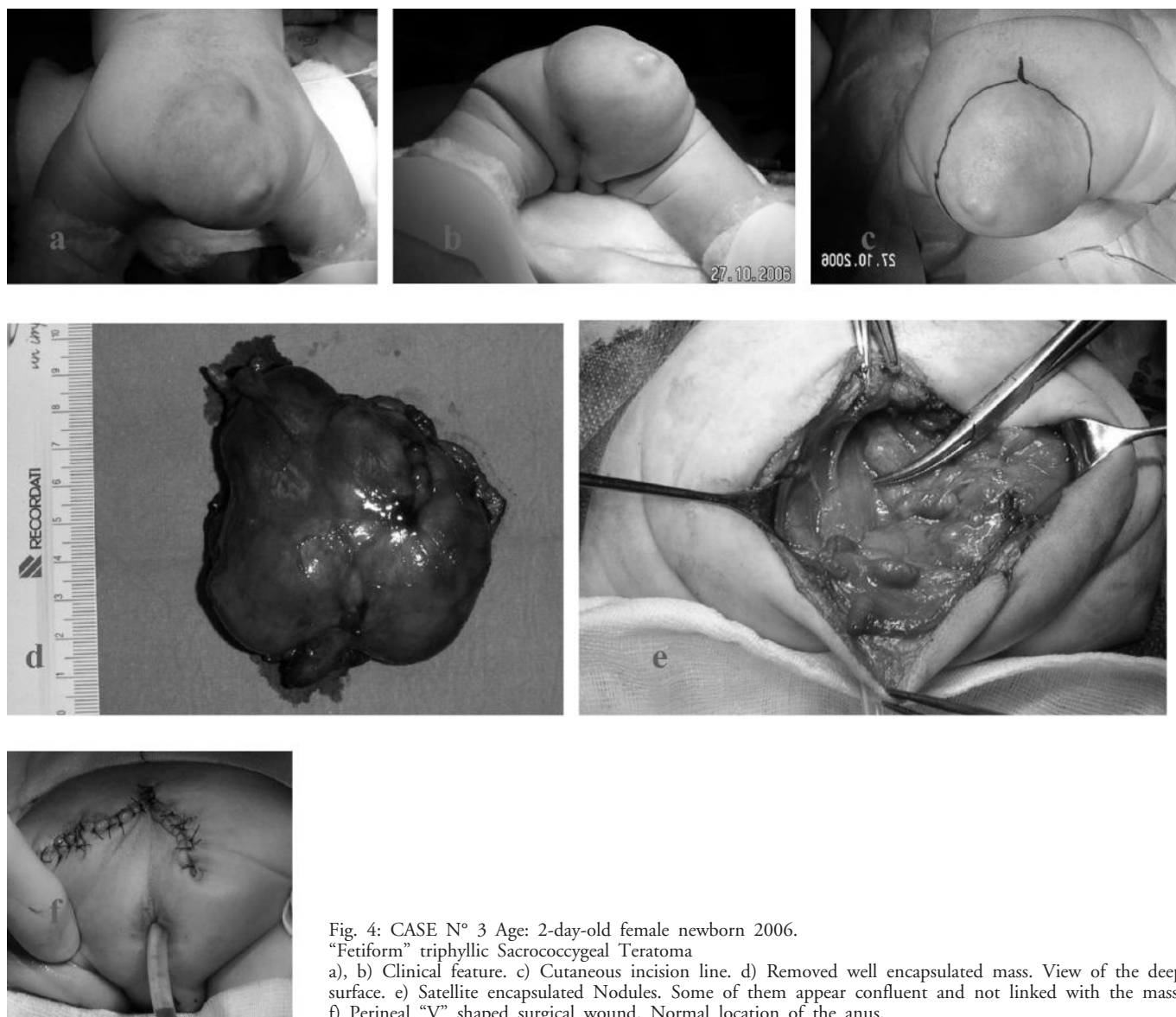


Fig. 4: CASE N° 3 Age: 2-day-old female newborn 2006.  
 “Fetiform” triphyillic Sacrococcygeal Teratoma  
 a), b) Clinical feature. c) Cutaneous incision line. d) Removed well encapsulated mass. View of the deep surface. e) Satellite encapsulated Nodules. Some of them appear confluent and not linked with the mass. f) Perineal “V” shaped surgical wound. Normal location of the anus.

7d). The final histologic diagnosis was: a biphyllic, ecto-mesodermic, “fetiform” teratoma in case N°2, displaying a complete anlage of a lower limb, with a regular foot and hip pseudo-joint; triphyillic teratomas in all the others. In these last cases elements of the 3 germ layers were present but with highly differentiated, normal adult-like structures (“fetiform teratomas”) in case N°3 (Fig. 5 a-i). Immature glandular structures, sporadically tough, were also detected in case N°1. In 2 patients, affected by the Currarino syndrome, histology revealed a moderate amount of immature neuroepithelial tissue with a predominance of malignant somatic-type components with a mostly epithelial differentiation. Poorly differentiated solid and cystic areas were intermingled with other areas with necrosis and spots of microcalcifications. Some mor-

phological details of case N° 3 (Fig. 5 a-i) are reported in Table III. Applying the classification system by Gonzalez-Crussy, widely followed in the literature, to the 5 cases, 2 (cases N°4 and N° 5 - sacrococcygeal teratomas with associated Currarino syndrome) were classified as Grade 3 because of malignant transformation characterized by a predominantly somatic epithelial component; 1 (case N°1 – triphyillic sacrococcygeal teratoma of cystic type associated with sporadically immature glandular structures) was classified as Grade 1, probably benign, and the 2 others as Grade 0, mature benign forms, cases N°2 and N° 3 being of “fetiform” type. As regards staging, all cases were Stage I, except for case N°5, in which partial exeresis was performed, only of the abdominal portion of the teratoma, the most voluminous.



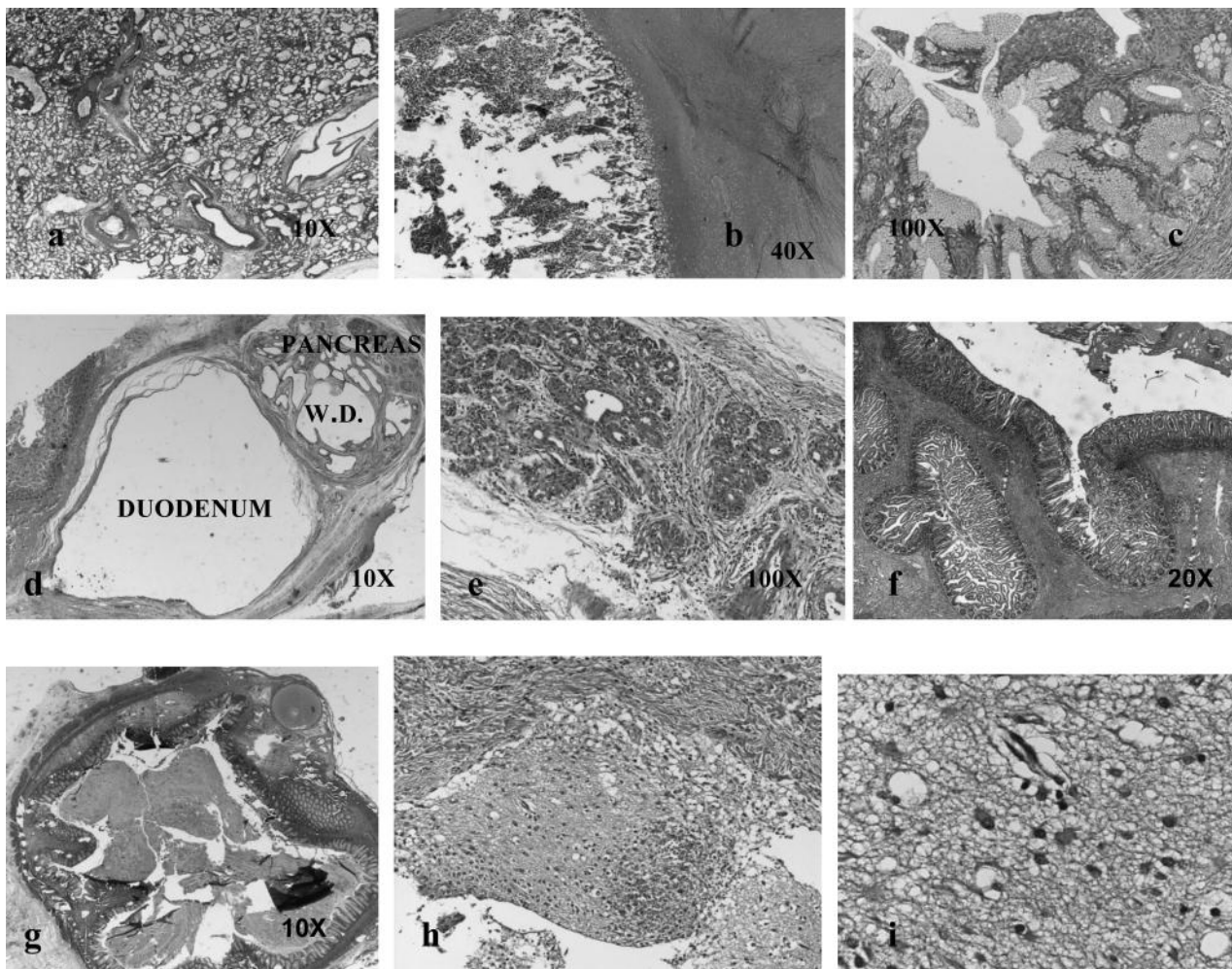


Fig. 5: CASE n° 3 Age: 2-day-old female newborn 2006 “Fetiform” triphyilic Sacrococcygeal Teratoma. HISTOLOGY - MAIN MASS: in addition to components of the 3 germ layers: a) Mature Lung Lobe. b) chondro-costal Junction. c) Esophago-gastric Junction. Cross-section of well differentiated tissue like normal intestinal tract: d) duodeno - pancreas with Wirsung duct. e) Pancreas: details of the glands. f) small bowel. g) vermiform appendix. h, i) cerebral parenchyma with white matter composed predominantly of astrocytes.

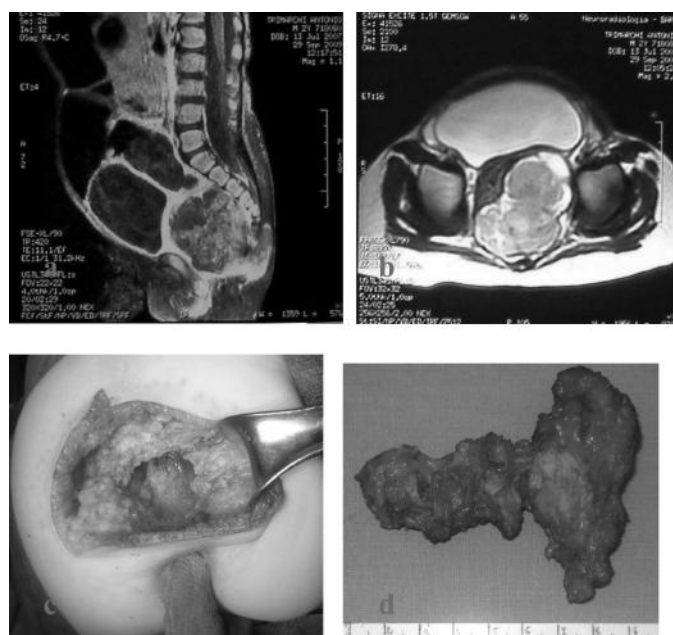


Fig. 6: CASE N° 4 Age: 3.3-year-old male child 2010 Triphyilic Sacrococcygeal Teratoma with malignant predominantly somatic component included in a Currarino Syndrome associated with Hirschsprung’s Disease. a), b) MR: Presacrale large lobulated high density opacity with gluteal extension. c) operativ field after the complete exeresis by a perineal approach. d) Removed mass.

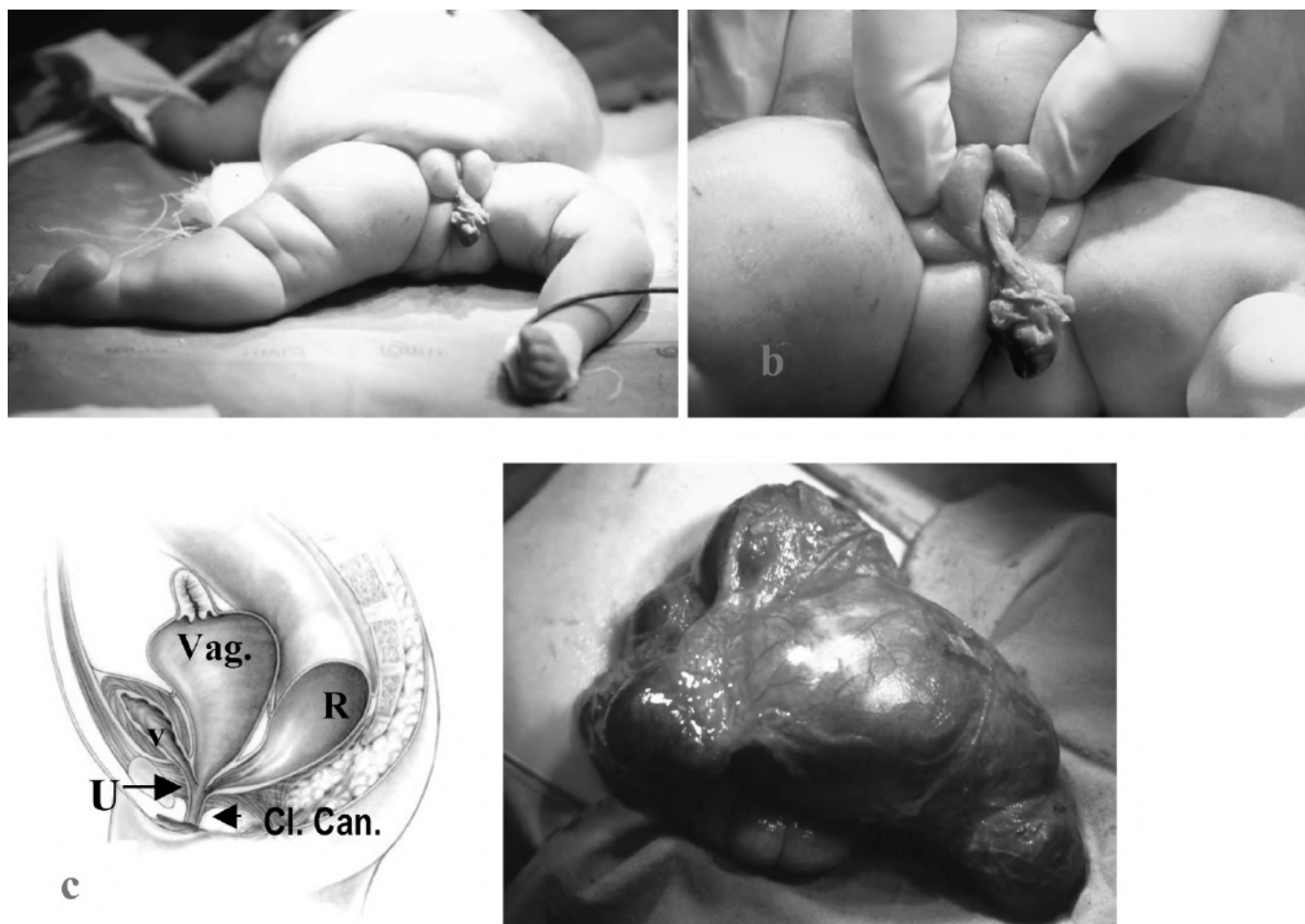


Fig. 7: CASE N° 5 Age: 1 day 2000 Triphyllic Sacrococcygeal Teratoma with malignant predominantly somatic component included in a Currarino Syndrome associated with persistence of cloacal canal and anal imperforation - a) b) Clinical feature. c) Drawing of cloacal malformation. d) Operative finding before the partial exeresis of the intrabdominal mass, which was the most voluminous portion of the neopalsia. R (rectum) Vag (vagina) U (urethra) Cl. Can. (persistent common cloacal canal).

## Results (Table I)

Of the 5 patients, the newborn (case N°5) affected by the Currarino syndrome, associated with persistence of the common cloacal canal and anal imperforation, died two days after surgery, of cardiovascular and respiratory complications. All the other patients had an uneventful postoperative course. The laminar drain, used in some cases, was removed after 3-4 days. Clinical surveillance and tests of AFP and other markers were scheduled every 6 months for the first 5 years and annually thereafter. Two years after the exeresis at birth, case N°3, with a solid-cystic "fetiform" multinodular sacrococcygeal teratoma and extracapsular satellite nodules, displayed a slight elevation of  $\alpha$ -fetoprotein (40 IU/ml) and LDH, while local physical signs were lacking and chest radiography was negative. At the next control, scheduled for 7 months later, a sharp increase of  $\alpha$ -fetoprotein (40 to 855 IU / ml) was detected, while physical examination

of the buttocks was still negative. Abdomino-pelvic MRI showed a multichamber parasacral fluid collection, 4 cm.in diameter, located in the right buttock. That imaging finding was interpreted as either the outcome of the previous surgical procedure or a local recurrence. Biopsy of the new lesion performed elsewhere (March 2008) detected a recurrence with elements of malignancy YST (Yolk Sac Tumor). Therefore, adjuvant chemotherapy was firstly administered to the young child and then she underwent a new complete surgical procedure. So far, 3 years after the second surgery and 6 years after the first diagnosis and treatment, no local recurrence or distant metastases have occurred. The values of  $\alpha$ -fetoprotein are normal. The 3 other patients are also all alive, disease-free and have not suffered any recurrence, with a follow-up of: 28 years in case N°2; 27 years in case N°1; and 2 years in case N°4, as reported in Table I. More frequent monitoring was scheduled for the child with a primary malignant teratoma associated with the



Currarino Syndrome (case N°4), and for the little girl with tumor relapse. None of the 3 cases operated for sacrococcygeal teratoma, in 1985, 1984 and 2006, ever complained over the years of ano-rectal and/or bladder dysfunction or hypotony of the lower limbs. Nor did the child suffering from Hirschsprung's Disease associated with teratoma and the Currarino Syndrome (case N°4), ever suffer from any functional problem, but he does require rectal irrigation to prevent constipation and/or intestinal obstruction.

## Discussion

Teratomas are embryonal neoplasms of a considerable clinico-scientific and speculative interest. They arise from an abnormal development of the primordial germ cells and / or embryonal totipotential cells. Therefore, they may develop in both gonadal and extragonadal sites. The extragonadal lesions are rare, encapsulated tumors, which contain tissues from the three germinal layers; thus, histologically, they can be mono- bi- or triphyllic and show different patterns: mature, immature or primary malignant, sometimes intermingled in the same specimen.

Among *extragonadal teratomas*, sacrococcygeal lesions are the most common and best known in neonates and infants<sup>1,2</sup>, accounting for 40% of all teratomas<sup>3</sup>, with minor differences in the most recent series<sup>1</sup>: 27.92% - 98/351 patients; De Backer A et al.<sup>4</sup>: 36.27% - 70/193 patients). The recognized F: M ratio is 3:1-4:1<sup>5</sup>.

Generally, 2 different clinical presentations occur, related to age, location and probably malignant nature. Neonatal cases are characterized by a mass protruding from the sacrococcygeal region, with or without a variable extension upward into the pre-sacral space, as in Cases N°1 and N°3. The lesions observed in infants and / or in young children appear as a protruding mass inside the pelvic cavity (Cases N°4 and N°5), displacing the rectum and/or the bladder<sup>2,6-8</sup>. A rare, singular clinical feature was observed in Case N°2, due to the unusual tumor location on the posterior surface of the sacrum and a highly differentiated lesion, characterized by a complete anlage of a lower limb protruding from the tumor, with a well-differentiated foot and femur and an ischio-femoral pseudojoint located deep within the mass. The perineal region appeared normal while the coccyx was absent. A fairly similar feature has been reported in the literature<sup>9</sup>. Weiss et al.<sup>10</sup> also described a phenotypically similar case, but localized in the ovary of a young adult. Gopal et al.<sup>11</sup> reported a hereditary case and considered hereditary lesions separately from sporadic ones.

A wide range of congenital malformations is seen in association with sacrococcygeal teratomas. Single or combined malformations of the genito-urinary tract, rectum, anus, vertebrae and spinal cord, rarely cardiac, CNS, or ocular anomalies (Case N° 4), are found in

infants affected by these lesions, and, sometimes, in kindred, suggesting an autosomal dominant nature of the tumor<sup>2</sup>. Some, more rare sacro-coccygeal teratomas are included in the Currarino syndrome<sup>12-15</sup>, characterized by the triad: anorectal malformation, sacral dysplasia and a presacral mass, as in Cases N°4 and N°5. But the singularity of our 2 patients was the uncommon, further association with Hirschsprung's Disease (Case N°4) and a rare Cloacal anomaly (Case N°5 - Persistence of the cloacal canal and anal imperforation). The initial clinical presentation of sacrococcygeal teratomas may be further complicated by a mass effect due to compression on the surrounding pelvic structures (rectum, bladder, vagina) or secondary to the associated congenital malformations. Thus, a severe intestinal obstruction was observed in our 2 cases with the Currarino Syndrome, because of Hirschsprung's Disease (Case N°4) and a persistent common cloacal canal with anal imperforation (Case N°5), respectively. In this last patient, a 1-day-old female newborn, hydrocolpos and urinary retention were also present. Another critical post-natal presentation is a tendency to sudden volumetric growth of the tumor, especially when the cystic component is predominant (Case N° 1), inducing the well known "Growing Teratoma Syndrome". That is characterized by both significant enlargement of the mass and cardio-vascular failure of different degrees, mainly due to intralesional fluid and / or blood sequestration. Being congenital tumors, prenatal US scan, usually performed between the 2nd and 3rd trimester of pregnancy, can easily detect sacrococcygeal teratomas; this was available in Cases N°3 and N°5. It also allows the demonstration of lethal lesions associated with polyhydramnios, cardiomegaly and/or fetal non-immune hydrops<sup>16</sup>, which is usually the result of a vascular steal syndrome, leading to shunting of the blood from the placenta and causing high-output cardiac failure in the fetus. In such an event, the ultrasonographic findings can be a warning to anticipate delivery by emergency caesarian section, as in our Cases N°3 and N°5. Furthermore the US scan enables coexisting multiple malformations to be demonstrated, including the Currarino Syndrome or cloacal anomalies. In recent years, critical fetuses suffering from intrauterine complicated lesions, sometimes associated with the "mirror syndrome" in the mother, can be prenatally treated by Echo-guided or Endo-fetoscopic or open surgical treatment (E.X.I.T. i.e. ex-utero intrapartum treatment). Various procedures with successful results are reported in the literature, ranging from cyst drainage to facilitated delivery, laser vessel ablation, partial excision of the mass, all carried out in highly specialized structures<sup>17</sup>. In addition, prenatal assessment is essential to individuate the most logical, least invasive approach to the post-natal diagnostic work-up, for the purposes of organizing proper perinatal care in appropriate facilities where it is possible to define the diagnosis and carry

out emergency surgery, that is usually necessary. Post-natal diagnosis of a sacrococcygeal teratoma is easy on the basis of physical examination of the sacrococcygeal or sacral region (Cases N° 1-3), except in cases of a prevalently (Case N°5) or exclusively intrapelvic (Case N°4) location of the tumor. Thus, imaging studies, consisting mainly of plain abdominal and pelvic radiographs, CT and MRI, are essential tools to demonstrate typical calcifications or ossifications, the frequent spine anomalies and, especially, to define the location, extent and mass side effects on the surrounding structures, that are commonly dislocated, compressed or, rarely, infiltrated. The perineal muscles can sometimes be severely and extensively dissociated by the cystic component of the lesion, as in Case N°1, while the rectum is almost always involved. The imaging can confirm the tumor association with an intestinal obstruction, due to anal imperforation and cloacal anomalies or Hirschsprung's Disease, as in Cases N° 4 and N° 5, respectively. Retrograde injection of contrast medium, commonly used to display dislocation of the pelvic organs: rectum and/or bladder, can raise the preoperative suspicion of an associated aganglionosis, showing the typical imaging pattern that should subsequently be confirmed by histochemical studies. In any case, additional investigations are necessary, especially blood tests for detecting the pathognomonic elevated values of AFP and/or beta-HCG. AIEOP 2004 guidelines pointed out that high levels of circulating markers, including AFP, in affected children would indicate the presence of micro-foci of YST, marking them out as at high risk. The UKCCSG II and the SFOP indicated AFP values exceeding 10,000 ng / ml as the threshold identifying a group of patients with a severe prognosis. Moreover, these tumoral markers levels also help the oncologist to assess clinical recovery from the disease or the presence of recurrence and/or distant metastases, in the long term. In rare cases suffering from sacrococcygeal teratomas included in the Currarino Syndrome, the diagnostic work-up must also be extended to DNA analysis to detect gene mutations as in Cases N°4 and N°5<sup>12-15</sup>, in which biomolecular analysis of the DNA samples revealed a mutation of exon 1 of gene HLXB9, confirming the clinical suspicion. Mixed, cystic-solid, or predominantly solid or cystic, at gross examination sacrococcygeal teratomas are usually histologically graded (Grade 0-3) according to the Gonzales-Crussi classification, widely followed in the literature. This grading is based on the findings of mature, immature teratomas, with or without YST foci, or a primarily malignant component in the specimen. It is noteworthy that these neoplasms exhibit a biologically bizarre behavior. In fact, pure teratomas of grade 0, 1 and 2 have a malignant potential (grade 3)<sup>18-19</sup>. The rare form of teratomas with malignant transformation may not contain germinal malignant components but may be of somatic type, such as leukemia, cancer or sarcoma<sup>20,21</sup>. In addition, a teratoma may present elements of other

tumors with germinal cells, particularly YST, even in recurrent primary benign teratomas. These last lesions are considered mixed forms of teratomas; they behave like malignant teratomas and occur more frequently in infants and young children. Applying the above grading system to our 5 cases: 2 (cases N°4 and N° 5 - with associated Currarino syndrome) were classified as Grade 3 because of malignant transformation, characterized by a predominantly somatic epithelial component, as reported in the literature<sup>20,21</sup>; 1 (case N°1 - triphyllic teratoma of cystic type associated with sporadically immature glandular structures) was classified as Grade 1, probably benign, and the 2 others as Grade 0, mature benign forms, cases N°2 and 3 being of "fetiform" type, due to the high grade of differentiation (evidence of organoid-like normal structures). As reported in the literature, Case N°3, operated for a multinodular benign, triphyllic, highly differentiated, "fetiform" teratoma, presented YST foci within the local recurrence lesion, despite a benign cystic appearance at imaging. These relapses, to be considered as mixed form teratomas, with a predictably malignant behavior, are more frequently observed in infants and young children. Moreover, some unusual and singular characteristics are to be noted in our selected cases: the "fetiform" pattern of lesions in newborns N°2 and N°3 and a rare primary multinodularity in Case N°3. Generally, sacrococcygeal teratomas are considered lesions at high risk, because even mature forms can hide, at clinical examination, more or less extensive isles of YST (with a highly malignant potential) or signs of malignant transformation just evident at presentation (Cases N° 4 and N° 5)<sup>12-15</sup>. Commonly, mature and immature histotypes, associated to a mass protruding from the sacrococcygeal region, are prevalent in neonates, while the lesions observed in infants and / or in young children appear as a protruding mass inside the pelvic cavity, and are most likely to be malignant<sup>22-24</sup>. Thus, according to some Authors<sup>25-28</sup>, the pelvic location, sometimes included in the Currarino syndrome, as in Cases N°4 and 5<sup>12-15</sup>, is considered a poor prognostic factor because of the greater risk. A correlation of malignancy with sex and age at diagnosis has been reported<sup>3</sup>. Among patients over the age of 2 months, malignancy accounts for 48% in females and 67% in males, while among patients under 2 months the sex distribution is 7% in females and 10% in males. Malignancy appears to be predominant in males over 2 months of age. As regards the risk of recurrence of sacrococcygeal teratomas, it is well known that even benign lesions recur in 10-21% of cases, usually within 3 years from exeresis<sup>29-32</sup>. Malignant lesions are recurrent in 43-50% of children, so they require adjuvant chemotherapy. On the other hand, De Backer et al.<sup>3</sup> have also reported that 10 of 12 immature benign sacrococcygeal teratomas with microscopic residues of neoplastic tissue did not undergo long-term relapse. It should be noted that primary malignant sacrococcygeal teratomas may show malignant

TABLE III - Case N°3: Pathologic features

Case N°3

Age: 2 Days F (2006) Plurinodular Sacro-Coccygeal T.

#### GROSS PATHOLOGY

Encapsulated solid lesion with various consistency and polycyclic contour, cm 7x6,5x6 in diameter, covered by cm 6x4 large cutaneous coating. Numerous capsulated nodules with parenchymatous consistency close to but isolated from the mass capsule. Cut surface of the main mass: predominant adipose tissue mixed with cartilaginous tissue and cysts. At the periphery of the mass, a mixed solid-cystic pulmonary lobar-like structure delimited by adipose tissue was identified.

#### HISTOLOGY

Components of three embryonic layers. Adult high differentiation: skin with cutaneous appendage, well differentiated tissue like normal intestinal tracts such as gastro-esophageal junction, vermiform appendix, duodeno-pancreas with Wirsung duct, part of mature lung lobe, cerebral parenchyma with fetal white matter composed predominantly of astrocytes. Histology of satellite nodules displayed non organized elements of the 3 embryonic layers.

Microscopic Diagnosis: Solido-cystic adult mature "fetiform" Sacro-Coccygeal Teratoma.

features, even at an advanced stage, after their clinical detection; local infiltration is present in 2 / 3 of them and 50% show metastases<sup>5,34,35</sup>.

Given the clinical (risk of rupture, tendency to sudden enlargement, hemodynamic changes), histological (initially malignant pattern, as in Cases N°4 and N° 5, or hidden malignant spots in an otherwise mature lesion), and biological (malignant recurrence from mature lesions or malignant transformation) characteristics of sacrococcygeal teratomas and the related common complications, also due to associated congenital malformations, early, emergency surgical treatment is always mandatory in all cases. Therefore, an accurate, complete excision of the mass, together with the overlying skin, always associated with coccygectomy, appears to be the best, recommended procedure, except for contingent reasons as in our Case N° 5. The procedure is easy and usually accomplished by a perineal approach, except when a predominantly or exclusively intrapelvic lesion is evident. This requires a abdomino-perineal or abdominal approach (Cases N° 4 and N°5). Coccygectomy is essential because microscopic isles of neoplastic cells are commonly found in or immediately adjacent to the coccyx<sup>16</sup>. A Mercedes/inverted "Y" incision is usually made with mobilization of the skin flaps. Moreover, the surgeon must take particular care to preserve the ano-rectal muscular sling to ensure post-operative anal continence; sometimes additional rectoplasty is to be performed (Case N°1 and Case N° 4). The wound reconstruction commonly results in an aesthetically acceptable scar with reconfiguration of the buttocks. Sometimes a skin "Z" plastique, as in Case N° 2 (external sacral teratoma), is required. Generally the post-operative course is uneventful, as in our cases, except for Case N° 5 (pelvic teratoma with cloacal anomaly), that ended in death 2 days after partial removal of the mass, of cardio-respiratory complications not related to the surgery. Nevertheless,

minor early complications, such as wound infection or minimal dehiscences, are reported in the literature. In any case newborns, especially those suffering from huge tumors, are at higher risk of postoperative cardiac arrest due to hemodynamic events arising after the removal of a highly vascularized mass<sup>2</sup>. After excision, careful and extensive microscopic examination must be carried out on the entire mass to detect malignancy or any microscopic malignant foci within an otherwise apparently benign pattern of a mature or immature lesion. In such an event adjuvant chemotherapy must be administered. The association of complete removal of the lesion with chemotherapy has significantly improved the prognosis of both newborns and infants, even in cases affected by primary, infiltrating malignant forms. Thus, adjuvant chemotherapy should be administered to these patients before surgery, and results, as reported in the literature, in an EFS of 75-85% and an OS of 80-90%<sup>36,37</sup>. But after chemotherapy, complete exeresis is always necessary and appears to be a further, essential prognostic factor<sup>2,38,39</sup>. Indeed, if the resection margins are intact EFS (Event Free Survival) is more than 90%; instead, if there are microscopic residues EFS falls to 75-85%, while if there are macroscopic residues EFS is unfortunately less than 40%. The pelvic location is considered a poor prognostic factor because of the greater risk of incomplete exeresis<sup>3, 30-32</sup>. It is noteworthy that, as reported in the literature, the "Growing teratoma Syndrome" may also occur in newborns with mixed (mature/ or immature/malignant) histological forms after effective adjuvant chemotherapy. It is suspected that chemotherapy is able, in such instances, to destroy the malignant component of the tumor, but spares the pure teratoma, which paradoxically begins to grow very quickly.

In newborns or infants suffering from malformations associated with teratomas, the definitive surgical correction of the maldevelopmental anomalies, if indicated,



must be obviously postponed to a proper time, especially in patients with multiple malformations or those needing adjuvant chemotherapy. Nevertheless, acute complications, such as intestinal obstruction or genito-urinary dilatation, may dictate interim but urgent measures. Thus, once the mass has been removed, two different strategies were judged necessary in Cases N°4 and N°5, affected by a pelvic, Grade 3, teratoma in the Currarino Syndrome, associated to Hirschsprung's Disease, and a cloacal anomaly with anal imperforation, respectively. Colostomy, vaginostomy and vesicostomy were added in Case N° 5, while a nursing program consisting of daily recto-colon irrigation, to prevent constipation or recurrent acute intestinal obstruction, was advisable in Case N°4, in which other severe malformations were present. Therefore, the definitive surgical treatment of aganglionosis (Hirschsprung's Disease) was postponed. This strategy is to be followed in all cases of sacrococcygeal teratomas associated with malformations, which should be surgically cured, if indicated, at the appropriate time, unless a complication arises or the repair cannot be delayed.

Generally, the long-term prognosis of sacrococcygeal teratomas is benign. but recurrence or malignant transformation, especially in newborns treated late or infants (Case N°4), can occur<sup>16</sup>. Our Case N°3, already remarkable for the primary multinodularity predisposing to relapse, underwent recurrence with malignant YST foci, 1,5 years after the initial surgery, despite an apparently complete exeresis of the lesion and a high histological differentiation, characterized by organoid-like normal "fetiform" structures,. But adjuvant chemotherapy and second surgery resulted in a stable and complete recovery. She is alive and disease free 3 years after the second surgery and 6 years after the first diagnosis and treatment. The other 3 patients (cases N°1,2,4), treated with extensive complete exeresis, are alive, disease-free and with no signs of relapse or distant metastasis, after a follow-up ranging from 2 years to 28 years. Therefore, it must be emphasized that early, careful, extensive excision of the tumor, always associated with coccygectomy, is commonly regarded as an essential prognostic element in the management of sacrococcygeal teratomas. But there is also a unanimous consensus that long-term clinical, imaging and laboratory surveillance, particularly monitoring levels of AFP and/or beta-HCG, must be scheduled at shorter intervals during the first 5 years after surgery and annually thereafter. Lahdenne<sup>40</sup> reported three cases of recurrence between 21-43 years in patients operated, when they were infants, for a benign lesion. Thus, more frequent monitoring was scheduled both in the little girl with tumor relapse and, particularly, in the child with a primary malignant teratoma associated with the Currarino Syndrome (Case N°4). Although alive and disease-free, we may expect a poor prognosis in this child because the diagnosis and surgical treatment were carried out late. Finally, some Authors

have reported post-operative functional complications, such as constipation, fecal soiling, vesico-urethral dysfunctions, as well as cosmetic changes<sup>2,32,38,39,41-43</sup>. These conditions, particularly frequent in children reoperated for recurrence, are thought to be due to coccygectomy<sup>44</sup> and/or an extensive procedure. Mann JR et al.<sup>2,32,38,39,41-48</sup> reported that 10 of 95 survivors complained of a neurological bladder and 2 of 95 of a lower limb hypotonia. Thus, the surgeon must pay particular attention, in dissecting the tumor from the deep pelvic fascia and ano-rectal muscular sling, to prevent functional disorders of the anal canal and bladder, as well as any motor alterations of the lower limbs, usually due to iatrogenic lesions of the subfascial nerve structures. In our selected cases, none of the 3 patients, operated in 1985, 1984, and 2006, ever complained of ano-rectal and/or bladder dysfunction nor hypotony of the lower limbs, over the years. This is particularly remarkable in Case N°1, operated long ago in 1985. Nor has there been any complaint of a functional problem in Case N°4, except for the need, because of the associated Hirschsprung's Disease, to resort to a nursing program consisting of rectal irrigation to prevent constipation and/or recurrent intestinal obstruction.

## Conclusions

From this review of our selected cases and in the light of literature reports, we can draw the following conclusions. Some sacrococcygeal teratomas may have unique characteristics distinguishing them from more common cases, especially those included in the Currarino Syndrome with or without an association with other malformations, such as Hirschsprung's Disease and cloacal anomalies. Being congenital tumors, prenatal diagnosis by US scan is extremely important in order to prevent prenatally lethal fetus/mother complications and also to decide on anticipated delivery or, in critical fetuses, prenatal treatment within highly specialized facilities, or the organization of proper perinatal care in appropriate facilities where it is possible to define the diagnosis and carry out emergency surgery. An emergency procedure is frequently dictated both by complications related to the mass effect and by the need to define the histology of the whole mass rather than just small biopsy specimens. Some sacrococcygeal teratomas can hide more or less extensive islands of immaturity or signs of malignant transformation that are clinically evident at the initial presentation. The prognosis is generally benign, although the AIEOP 2004 guidelines pointed out that high levels of circulating markers, including AFP, in children affected by mature or immature teratomas would indicate the presence of micro-foci of YST, marking them out as at high risk. The UKCCSG II and the SFOP indicated AFP values exceeding 10,000 ng / ml as the threshold identifying

a group of patients with a severe prognosis. The recommended treatment is early, complete exeresis, followed by a careful, extensive microscopic examination, associated, if necessary, with adjuvant chemotherapy, reserving preoperative chemotherapy to initial apparently infiltrating malignant forms.

Sacrococcygeal teratomas are commonly considered as lesions at particular risk, in which the coccyx must always be removed together with the mass and overlying skin, taking particular care of the deep pelvic fascia to prevent functional disorders of the bladder and anal canal, as well as any motor alterations of the lower limbs, usually due to iatrogenic lesions of the subfascial nerve structures. There is an unanimous consensus that to improve the prognosis, close, long-term clinical, laboratory and imaging surveillance is essential, at shorter intervals during the first 5 years after exeresis and annually thereafter. Finally, in newborns or infants suffering from malformations associated with teratomas, the definitive surgical correction, if indicated, must obviously be postponed to a proper time, especially in patients with multiple malformations or those needing adjuvant chemotherapy, unless a complication arises or the repair cannot be delayed.

### Riassunto

I teratomi sacrococcigei sono, fra i teratomi extragonadici, i più frequenti e meglio conosciuti nei neonati e nei bambini e possono talvolta presentare aspetti insoliti che li distinguono da quelli comunemente descritti. Queste caratteristiche comprendono: 1) una localizzazione insolita. 2) una presentazione clinica a volte acuta. 3) un insolito aspetto fenotipico della massa. 4) multinodularità primitiva della neoplasia con particolare comportamento biologico. 5) l'istotipo "fetiforme" della lesione e/o l'associazione con altre e multiple o complesse malformazioni come la Sindrome di Currarino, la Malattia di Hirschsprung o anomalie della cloaca. Gli Autori hanno estrapolato, dalla loro complessiva esperienza sui teratomi, 5 casi insoliti, tutti operati in urgenza, 4 di essi immediatamente dopo la nascita. Scopo di questo lavoro è quello di descrivere i dati clinici ed anatomopatologici, valutare l'approccio chirurgico ed il comportamento biologico a lungo termine di questi casi, alla luce della sopravvivenza e delle conoscenze riportate in letteratura.

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