Germ Cell Tumors of the Head and Neck

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19.1 Introduction

The general aspects of germ cell tumors, common to all tumors, occurring at different sites, are discussed in the introduction chapter of germ cell tumors and genitourinary cancers (Chap. 39). Germ cell tumors of the head and neck region constitute rare, but characteristic extragonadal germ cell tumors of childhood (Jordan and Gauderer 1988). They most commonly present in the neonatal period or during infancy (Bernbeck et al. 2009). In this age group, virtually all tumors are mature or immature teratomas. A significant proportion of tumors are already diagnosed during prenatal ultrasound (Berge et al. 2004; Dunn et al. 1992).

In the perspective of the overall favorable prognosis, the diagnosis of a large, mostly cystic cervical tumor must not evoke therapeutic nihilism and lead to the recommendation of termination of pregnancy, but should rather lead to a close follow-up during pregnancy and optimal planning of the perinatal management (Langer et al. 1992; Backer et al. 2004; Bernbeck et al. 2009; Kerner et al. 1998).

Some tumors may include malignant yolk sac tumor components, sometimes only as microscopic foci. The risk of clinically relevant malignant yolk sac tumor components that are also associated with significant AFP secretion rises with age. Thus, among the rare head and neck germ cell tumors diagnosed beyond the first year of life, the majority show malignant yolk sac tumor as leading histology (Bernbeck et al. 2009). Other histologic subtypes of germ cell tumors only rarely develop at this site, and to the authors' knowledge, no seminoma has yet been reported in the head and neck region. No genetic survey of these tumors has been reported so far. Rare single reports indicate for

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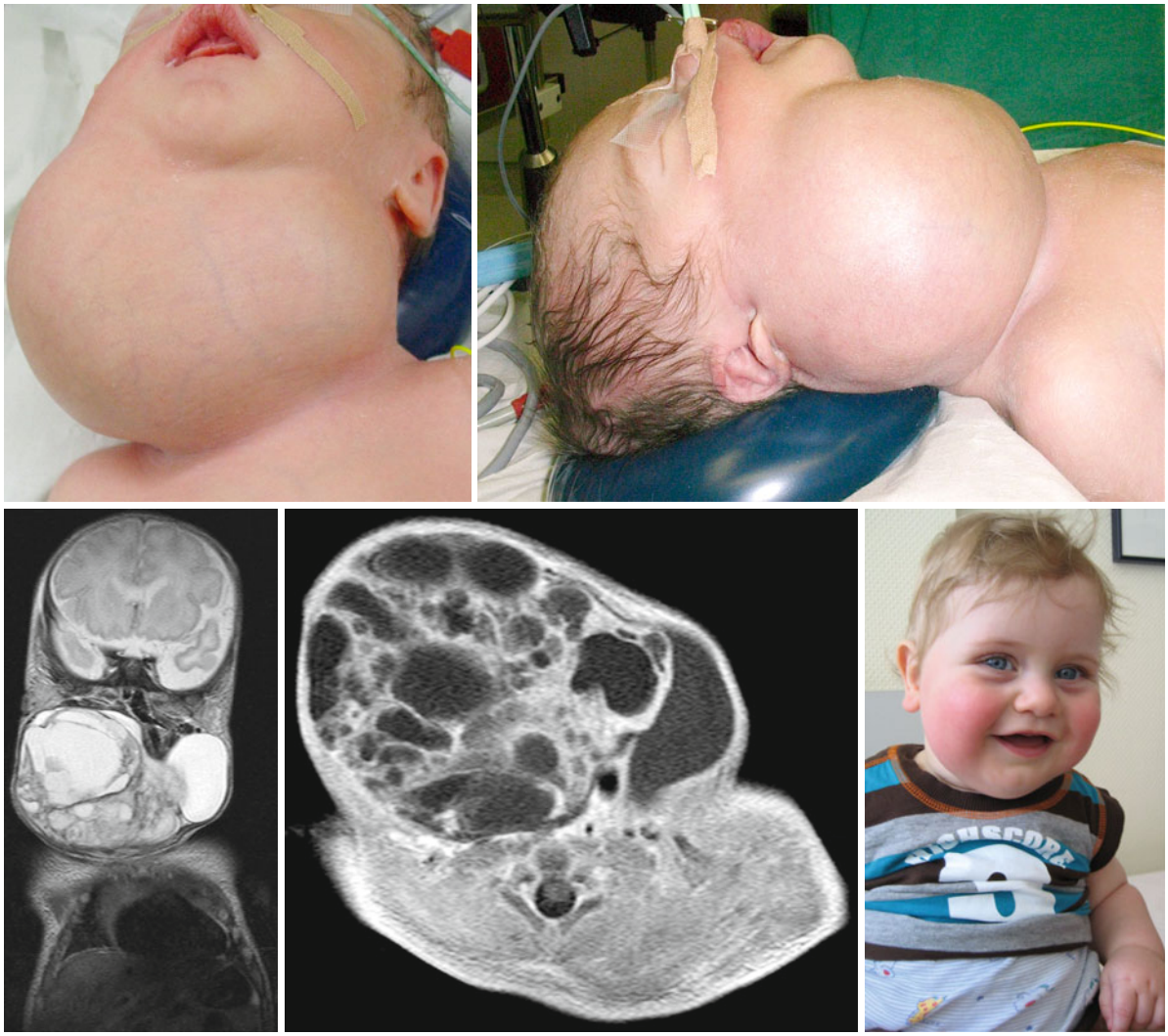

Fig. 19.1 Clinical images and magnetic resonance imaging of a neonate with a huge mature cervical teratoma involving the thyroids. The tumor was diagnosed with prenatal ultrasound. The patient was delivered with cesarean section and immediately intubated and ventilated after birth. At the second day of life, the tumor was completely resected including the thyroid gland which presented as the presumed site of tumor origin. After surgery, the patient showed intercurrent palsy of the vocal cords and hypocalcemia. Both resolved within weeks. The patient is on support of thyroid hormones. The boy is nicely developing without signs of neurocognitive deficits. (The pictures are kindly provided by Dr. M. Albrecht and Dr. Schmitz-Stolbrink, Westphalian Children's Centre, Dortmund)

genetic aberrations characteristic of germ cell tumors of infancy and childhood.

19.2 Clinical Diagnosis

Most tumors are diagnosed during the perinatal period. In countries which promote prenatal ultrasound assessment of the fetus, the majority of tumors are diagnosed with fetal ultrasound (Dunn et al. 1992). Tumors, in particular teratomas, present as partially solid and cystic lesions in the head and neck region, often in close association to the pharynx (Fig. 19.1). Vascular malformations and tumors such as lymphangioma constitute the most problematic differential diagnosis. Fetal MRI may assist in assessing the nature of the tumor and in evaluating the organ of origin of the tumor. Some tumors may develop within or in close anatomical proximity to the

thyroid gland. If a head and neck tumor is diagnosed prenatally, a close follow-up schedule is mandatory in order to compare the growth kinetics of the tumor and the fetus, respectively. In addition, significant hemodynamic distress caused by increased blood flow through the tumor should be excluded. These parameters may assist in planning of the time of delivery.

At birth, head and neck teratomas commonly present as large tumors, covered by skin. Due to airway compression, neonates may have asphyxia, and severe respiratory distress may occur. In these patients, primary tracheal intubation and ventilatory support are mandatory.

During infancy and childhood, head and neck germ cell tumors present as circumscribed tumors, mostly arising in the pharyngeal region or the nasal sinuses. The majority of tumors are malignant yolk sac tumors. Nevertheless, metastases rarely occur and mostly involve the cervical lymph nodes or the lungs.

In order to exclude malignant yolk sac tumor or choriocarcinoma, the measurement of AFP and β-HCG is recommended (Table 19.1). AFP levels must be compared to the age-related reference values (Blohm et al. 1998). In addition, the general considerations with regard to the diagnostic impact of tumor markers in germ cell tumors also apply to the head and neck germ cell tumors (see Chap. 39).

Prior to surgery, clinical assessment should include an endocrinologic work-up, specifically focusing on the thyroid and parathyroid function.

19.3 Therapy

In contrast to other teratomas and malignant germ cell tumors, the prognosis of head and neck germ cell tumors is primarily determined by the optimal management of local complications, which are primarily related to airway obstruction. Therefore, despite their benign histology, teratomas of the head and neck region constitute a life-threatening and potentially fatal disease. In a situation of suboptimal perinatal care, asphyxia may result in life-long neurological impairment. Therefore, careful planning of the perinatal management is absolutely mandatory, and treatment should be reserved to experienced neonatologic and pediatric surgical teams.

In the most comprehensive reviews by Jordan and Gauderer in 1988 and by Kerner et al. in 1998, a decrease in mortality from 37% to 25% has been described (Kerner et al. 1998; Jordan and Gauderer 1988). In most instances, patients died during the neonatal period as a result of respiratory failure caused by external airway obstruction. Different measures have been supposed to reduce perinatal risk, including intrapartum airway management (ex utero and intrapartum (EXIT) maneuver) or access to the airway in utero prior to delivery (Liechty et al. 1997; Hullett et al. 2006; Backer et al. 2004). However, the combined data of more-recent publications still report a high mortality in 5 of 16 cases (Martino et al. 2006) (Table 19.1).

In conclusion, optimal pre- and perinatal management is essential for successful management of head and neck germ cell tumors. The recommended clinical approach to prenatally detected teratomas includes repeated ultrasound, allowing for an optimized timing of delivery. Rapid tumor growth in utero may then necessitate a premature elective cesarean section. It is apparent that children with suspected large head and neck germ cell tumors should be referred to tertiary care centers that may provide optimal interdisciplinary management, including experienced neonatologists, pediatric anesthesiologists, pediatric oncologists, ear and nose and pediatric surgeons. Infants should be delivered through cesarean section, and in case of respiratory distress, immediate laryngotracheal intubation is required. To our knowledge cricotomy is required infrequently.

In a recent series reported from the German MAKEI study group, none of the patients received an ante- or intrapartum airway advice. Nevertheless, no newborn died perinatally, and significant asphyxia could also be avoided (Bernbeck et al. 2009). In 12 patients, repeated ultrasounds in short intervals demonstrated a marked enlargement of the tumor within a few days leading to preterm delivery during the 32nd to 37th week of pregnancy. Of note, the growth velocity after delivery was unpredictable. Six tumors showed dramatic tumor growth immediately after birth, while in others the growth velocity declined. As a consequence, three neonates were operated on soon after birth in an emergency situation. In tumors showing rapid growth, no beneficial short-time effects of chemotherapy have been reported, substantiating the central importance of timely planning and performance of tumor resection.

Notably, the tumor site has a significant impact on the therapeutic approach. Teratomas of the neck are usually better assessable to complete resection than pharyngeal tumors, in which microscopically complete tumor resection is often impossible (Bernbeck et al. 2009).

Table 19.1 Specific diagnostic strategy in head and neck tumors, suspicious of germ cell tumors

Procedure	Specific questions
Clinical assessment	
Physical examination	Signs of upper airway obstruction
Laboratory assessment	
AFP (β-HCG)	Malignant germ cell tumor with yolk sac tumor – consider age-related reference range (or choriocarcinoma)
Catecholamines	Exclusion of neuroblastoma
Thyroid hormones	Hypothyroidism – pre- and postsurgery
Calcium, phosphate	Hypoparathyroidism – pre- and postsurgery
Radiographic assessment	
Prenatal ultrasound	Site, organ of origin, cystic structures or calcification, observation of growth kinetics, timing of delivery
Head and neck MRI (+ angiography)	Site, size, organ of origin, cystic structures, calcification, involvement of larynx, pharynx, thyroid gland, proximity to large vessels and airways
Abdominal ultrasound	Liver metastases (if elevated AFP/YST)
Lung X-ray	Lung metastases (if elevated AFP/YST)
Histologic assessment	
H&E	Classification according to WHO
AFP	Yolk sac tumor (microfoci in teratoma)
(β-HCG)	Exclusion of choriocarcinoma
(CD-30)	Exclusion of embryonal carcinoma
(OCT3/4)	Exclusion of seminoma (embryonal carcinoma)

In the latter patients, it might be helpful to postpone surgery until the infant's weight has significantly increased in order to facilitate complete resection. However this is only possible if tumor size and growth velocity do not argue against a further delay. Moreover, a delayed tumor resection may bear the potential risk of malignant overgrowth. In this context, it should be noted that tumors of newborns may already include some small foci of yolk sac tumor. It should be considered that in teratomas of different sites in particular at the sacrococcygeal region, YST may be the leading histology at relapse. Therefore, preoperative chemotherapy aiming for the elimination of potential YST microfoci may be considered in selected patients with unresectable tumors in whom delayed tumor resection is reasonable. Nevertheless, these patients presumably constitute absolutely rare exceptions from the general rule that surgery is the mainstay of treatment.

During infancy, the risk of malignant germ cell tumors increases with age but may vary according to tumor site (Schneider et al. 2004). In a large series of teratomas registered to the German MAKEI studies, all children older than 1 year suffered from malignant germ cell tumors with yolk sac tumor as the leading histology (Göbel et al. 1998). This observation supports the meta-analysis of Kerner et al. that included children with malignant cervical germ cell tumors (Kerner et al. 1998). However, the biological switch from histologically benign teratomas to mixed malignant germ cell tumors with yolk sac tumor elements remains to be elucidated for this specific tumor site. In sacrococcygeal germ cell tumors, which contribute about 40% of all germ cell tumors in pediatric registries, the risk for malignant overgrowth rises after the second month of life. Prior to the age of 2 months, the incidence of malignant germ cell tumors was 10% in males and 7% in females, whereas at 6 months two thirds of the boys and about half of the girls had malignant tumors. In contrast, all germ cell tumors of the vagina registered in the MAKEI registry occurred in early childhood (<2 years), and the exclusive histology was yolk sac tumor (Mauz-Körholz et al. 2000). Again, these site-specific patterns illustrate the varying malignant potential of germ cell tumors depending on age, sex and primary site.

19.4 Prognosis

With a multidisciplinary approach, patients with germ cell tumors of the head and neck region have a favorable chance of survival and cure from their tumors.

The optimal perinatal and neonatal management, in particular postnatal life support in case of airway obstruction, strongly determines long-term outcome and presumably also neurological outcome if neonatal hypoxia can be avoided.

The oncologic prognosis is then determined by surgical experience and the ability to completely remove the tumor. Nevertheless, even with optimal management, patients may still suffer from late sequelae. These are predominantly related to local complications caused by the tumor or surgical therapy. Therefore, one important future issue will be to evaluate in how far early maybe even prenatal interventions or a centralization of the treatment to both neonatologic and pediatric oncologic centers will help to reduce or even avoid some of these handicaps.

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