Yolk sac tumor of upper lip: A case report

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Abstract. Yolk sac tumors (YSTs) are a type of malignant germ cell tumor that usually grow in the gonads. They are difficult to recognize at other sites outside the gonads, and no case has been reported involving the upper lip. The present study reported the case of a 13-month-old girl exhibiting an isolated YST occurring in the upper lip. The histology and elevation of α-fetoprotein were typical for a YST. The patient was cured following effective chemotherapy and surgery resection. After 36 months of follow-up, there was no sign of recurrence or metastasis. A total of 20 cases of primary YSTs of the head and neck extracranial region since 1997 were reviewed. The present study aims to inform the scientific community of the clinical and pathologic features of this patient.

Introduction

Yolk sac tumors (YSTs), also referred to as endodermal sinus tumors, are a type of malignant germ cell tumor that usually grow in the gonads (1). In 1959, the tumor was identified in the ovaries and testes of young patients, and defined as a specific form of malignant germ cell neoplasm by Telium (2). YSTs are difficult to identify in other sites outside the gonads. However, between 10 and 15% of YST occur in the midline structures of the mediastinum, retroperitoneum and sacrococcygeal areas (3). Certain cases have been reported in other location such as in the pineal region and head and neck (4,5). No case has been reported involving the upper lip. The present study reports the case of a child with an isolated YST occurring in the upper lip, and reviews 20 cases of primary YST of the head and neck region, not including the intracranial and orbit regions, from the literature since 1997.

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Case report

A 13-month-old female damaged her upper lip upon falling and the hematoma formed 2 months prior to admission to hospital. The patient underwent a hematoma puncture drainage at Juxian People's Hospital (Rizhao, Cina), but the mass recurred quickly. Upon examination, an exogenous reddish mass measuring 4x5 cm in diameter was revealed at the midline of the upper lip. The surface of the tumor was bleeding and scabby, as demonstrated in Fig. 1. Magnetic resonance imaging demonstrated a strong signal mass on the fat suppression imaging T2 weighted image in the upper lip with a clear border, as illustrated in Fig. 2. A biopsy sample was obtained from the fleshy mass under general anesthesia and the results confirmed the diagnosis of a YST. The biopsy sample was cut into pathological sections (4 μm thick). Certain pathological sections underwent hematoxylin-eosin staining (stained with hematoxylin-eosin at 60˚C for 60 sec) and others underwent immunohistochemical staining with α-fetoprotein (incubated with anti-α-fetoprotein at 37˚C for 2 h). Subsequently, the tissue sections were observed using a biological microscope at a magnification of x400. Microscopic analysis revealed the characteristic reticular pattern and eosinophilic ball, as demonstrated in Fig. 3, Schiller-Duval bodies, as illustrated in Fig. 4, and immunohistochemical staining positive for α-fetoprotein (AFP), as demonstrated in Fig. 5. Laboratory screening revealed an AFP level >1,308 μg/l, with 1-30 μg/l being the normal range. Computerized tomography scans of the head, neck and thoracic regions and ultrasonography of the abdominal and pelvic areas demonstrated no signs of metastasis. Initial treatment comprised two cycles of Adriamycin (30 mg/m^2, day 2,9), vincristine (1.5 mg/m^2, day 1,8), cyclophosphamide (300 mg/m^2, day 1-3) and cisplatin (90 mg/m^2, day 1) (AVCP) chemotherapy and 1 cycle of ifosfamide (1.5 g/m^2, day 1-5), etoposide (100 mg/m^2, day 1-5) and vincristine (1.5 mg/m^2, day 1,8) (IEV) chemotherapy. Subsequent to this regimen, the mass in the upper lip reduced to ~1x2 cm in diameter. The patient then underwent surgical resection. The biopsies of the resected area revealed only fibrosis, without any residual tumor tissue. The AFP level was measured subsequent to chemotherapy and resection, and exhibited a decline to within the normal range. After 36 months, there were no signs of recurrence or metastasis at follow-up examination.

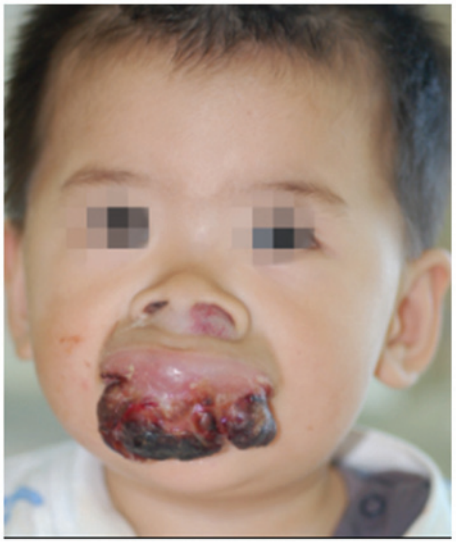

Figure 1. Yolk sac tumor in the upper lip of the patient.

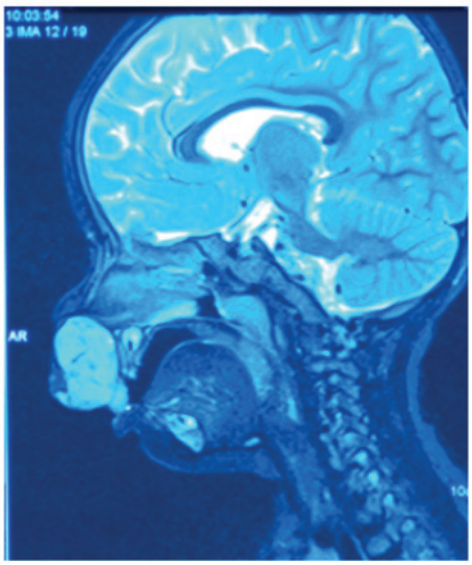

Figure 2. Magnetic resonance imaging demonstrated a strong signal mass on the sagittal section of the fat suppression T2 image in the upper lip with a clear border.

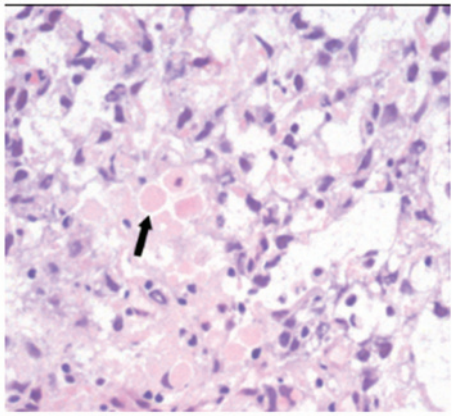

Figure 3. Characteristic reticular pattern and arrow highlights the eosinophilic balls of the hematoxylin-eosin stained tumor cells, at magnification, x400 using an Olympus CX23 microscope.

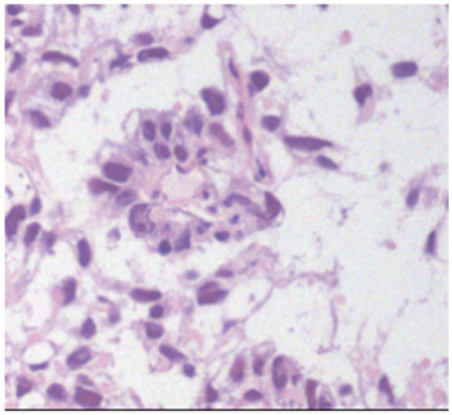

Figure 4. Cuboidal or low columnar-shaped tumor cells around the blood vessels forming characteristic Schiller-Duval body. Hematoxylin-eosin staining, at magnification, x400 using an Olympus CX23 microscope.

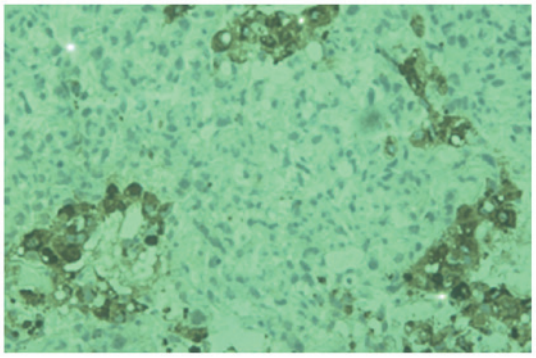

Figure 5. Immunohistochemical staining was positive for α-fetoprotein, at magnification, x400 using an Olympus CX23 microscope.

Discussion

YSTs are one of the most common types of malignant germ cell tumor exhibited within the pediatric age group, particularly in females (4,6). To the best of our knowledge, few cases of YST in the head and neck have been reported, whilst no cases have been reported involving the upper lip. Devaney and Ferlito (5) reviewed 27 patients with primary YSTs of the head and neck extracranial regions prior to 1997, and Kamal *et al* (7) reviewed 16 patients with primary orbital YST, yet there has been no review of those cases subsequent to 1997. Therefore, the present study reviewed 20 patients with primary YST of the head and neck region, not including intracranial and orbit region, occurring subsequent to 1997, and discussed the clinical and pathological features of YSTs, as summarized in Table I.

The mechanisms underlying primitive yolk sac cell migration to the upper lip remain unknown. There are two principal theories that have been put forward to explain the origin of extragonadal germ cell tumors (EGCTs) (8). The first hypothesizes that during embryonic development, those EGCTs arising from primordial germ cells are caused by defects in the cell migration pathways. In the 4-week-old embryo, primordial germ cells first appear in the wall of the yolk sac and migrate along the dorsal mesentery to the genital ridge during embryogenesis (9). Certain germ cells may not complete this

Table I. Clinical features of 20 patients with head and neck yolk sac tumors.

Study/year reported	Gender (M/F)	Age (y)	Primary site	Treatment	Follow-up period[a]	Outcome and survival	(Refs.)
Kusamakumari, *et al* 1997	M	1.5	Palate	Surgical excision, chemotherapy	Lost to follow-up	Unknown	(13)
Kusamakumari, *et al* 1997	F	1	Neck	Incisional biopsy, chemotherapy	Unknown	Died of infection	(13)
Choufani, *et al* 1998	F	26 mo	Ear	Surgical excision	3 months	Died of disease	(21)
Kutluhan, *et al* 1998	F	7 mo	Gingival	Incisional biopsy	17 days	Died of disease	(14)
Gangopadhyay, *et al* 1999	M	4	Maxillary sinus	Incisional biopsy, chemotherapy, radiotherapy	15 years	Alive, no evidence of disease	(22)
Frank, *et al* 2000	M	2.5	Temporal bone	Recurrence after surgical excision, chemotherapy	6 months	Alive, no evidence of disease	(23)
Gábris, *et al* 2001	F	3 y 9 mo	Nasal cavity	Incisional biopsy, surgical excision, chemotherapy, radiotherapy	7 years	Alive, no evidence of disease	(24)
Westerveld, *et al* 2001	F	3	Maxillary sinus	Incisional biopsy, surgical excision, chemotherapy	10 months	Died of disease	(17)
Sredni, *et al* 2004	F	16 mo	Parotid gland	Surgical excision, chemotherapy	2 years	Alive, no evidence of disease	(25)
Mishra, *et al* 2008	M	59	Paranasal sinuses	Incisional biopsy, chemotherapy, surgical excision, radiotherapy	1 year	Alive, no evidence of disease	(26)
Filho, *et al* 2008	M	48	Nasal cavity	Surgical excision, radiotherapy	7 years	Alive, no evidence of disease	(27)
Steinbacher, *et al* 2008	F	8 mo	Mandible	Incisional biopsy, chemotherapy, surgical excision	8 months	Alive, no evidence of disease	(20)
Pasricha, *et al* 2010	F	9 mo	Face	Incisional biopsy, chemotherapy	Lost to follow-up	Unknown	(28)
Furtado, *et al* 2011	F	10	Thyroid gland	Fine needle biopsy, surgical excision, chemotherapy	4 months	Alive, no evidence of disease	(19)
Jin, *et al* 2011	F	6	Floor of mouth	Surgical excision	2 months	Died of lung metastasis	(9)
Mamoon, *et al* 2011	M	4	Parapharyngeal space	Surgical excision, chemotherapy	1 year	Alive, no evidence of disease	(29)
Rozbahany, *et al* 2012	F	2	Postauricular	Incisional biopsy, surgical excision	9 months	Alive, no evidence of disease	(30)
Zhang, *et al* 2013	F	14 mo	Floor of mouth	Surgical excision	4 months	Died of disease	(15)
Chuang, *et al* 2014	F	1 y 3 mo	Sinonasal	Surgical excision, chemotherapy	13 months	Alive, no evidence of disease	(31)
Mei, *et al* 2015	F	58	Sinonasal	Incisional biopsy, surgical excision, chemotherapy	8 months	Alive, no evidence of disease	(32)

[a]Times given are post-diagnosis. Age: y, years; mo, months.

migration, resulting in retention at several sites along the dorsal wall of the embryo near the midline (9). This provides the basis for the midline propensity of the case reported in the present study, but does not explain the development of EGCTs in the out-of-midline regions. The second theory suggests that EGCTs arise from totipotential cells, which are scattered throughout numerous areas of the body during embryonic development and normally remain dormant. However, these cells possess the potential for additional growth and differentiation when suitably stimulated, leading to the formation of EGCTs (8).

In the rare case discussed in the present study the diagnosis was established by histological and immunohistochemical examinations. The major pathologic characteristics of YSTs include a reticular pattern, a solid pattern, a hepatoid pattern with hyaline globules, a festoon pattern, enteric differentiation, Schiller-Duval bodies, the presence of a granulomatous tissue reaction and a polyvesicular vitelline pattern (10,11). Schiller-Duval bodies have been reported as a common feature to extragonadal YSTs, as observed in large quantities in a previous study (12). Typical Schiller-Duval bodies comprise cuboidal or low columnar-shaped tumor cells surrounding the capillaries of a thin-walled sinus (13,14). Immunohistochemically, AFP is an important tumor biomarker for diagnosis (15). Immunofluorescent techniques have been developed to localize the site of AFP synthesis in YST samples (16). The serum level of AFP was elevated in the patient of the present study, and reduced subsequent to excision of the tumor. The serum levels of the protein may be used as a tumor biomarker during diagnosis, and in the follow-up of patients with YST (14,17).

Similar to testicular tumors, YSTs generally exhibit a poor prognosis as they tend to recur locally and demonstrate a high incidence of metastasis (18). Consequently, therapy includes extensive surgical resection, an intensive combination of chemotherapies and occasionally radiation therapy (19). Chemotherapy may improve the prognosis between 20-50% for YSTs (18). The combination of cisplatin, bleomycin and etoposide has been demonstrated to be effective, and is the most common type of chemotherapeutic regimen (4). The patient of the present study was administered AVCP chemotherapy. When the first cycle of AVCP chemotherapy was completed, the patient exhibited bone marrow suppression associated with an infection and high fever. Consequently, treatment was altered temporarily to IEV chemotherapy. Subsequent to 3 cycles of chemotherapy, the tumor mass of our case almost entirely disappeared and the patient was eligible for surgical resection All cases of YST should receive adjuvant chemotherapy except primary testicular tumors, which exhibit excellent responses to surgery alone (20).

The present study reported the first case of an isolated YST in the upper lip. The histology and AFP elevation were typical for this tumor. In the case of the present study, the YST was cured through effective chemotherapy and surgical resection. The patient remained asymptomatic after 36 months and exhibited no sign of recurrence or metastasis. According to data of previous studies, multimodal therapy including surgery, chemotherapy and radiotherapy may achieve a good prognosis.

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