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Original Article

Yolk sac tumor of the external auditory canal: a case report and literature review

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Abstract: We report one case of yolk sac tumor of the ear and review the literature. The patient was a 9-month boy who scratched his right ear repeatedly one month ago. Computed tomography scan showed an irregular elongated mass image measuring 42×16 mm was found in the right external auditory canal. The tumor was located underneath of the epidermis with ulceration. Mild or moderate atypical round or oval tumor cells were arranged in nest and reticular pattern around vesicular or cystic spaces. Tumor cells had abundant eosinophilic or clear cytoplasm and marked nucleoli. Mitotic figures were about 7/10HPF. Poorly formed Schiller-Duvall body was occasionally present. The stroma was loose and rich in capillaries. Hyaline globules could be found in the stroma. Immunohistochemistry staining showed that tumor cells were positive for cytokeratin, SALL4, glypican-3, focal positive for EMA, vimentin, CD10, and CD34, but negative for a-fetoprotein, HCG, PLAP. The serum α-fetoprotein was 664.60 ng/mL (normal, ≤25 ng/mL). Yolk sac tumor of the ear is extremely rare, especially α-fetoprotein negative expression in our case. The differential diagnosis includes embryonal rhabdomyosarcoma, paraganglioma, myoepithelioma, carcinoma of skin appendages, and metastatic renal cell carcinoma.

Keywords: Yolk sac tumor, ear

Introduction

Yolk sac tumor (endodermal sinus tumor) is one of the common malignant germ cell tumors, usually arises in the ovary and testis [1]. The tumor has been reported in extragonadal sites including mediatinum, retroperitoneum, head and neck [2]. Yolk sac tumor of the ear is extremely rare [3-7]. Herein, we present one case of yolk sac tumor of the external auditory canal with negative α-fetoprotein expression and reviewed the literature.

Materials and methods

Prior patient consent was obtained. Ethics approval was not required. Tumor specimens were fixed in 10% neutral buffered formalin and embedded in paraffin. Tissues were cut into 4-μm thick sections and stained with hematoxylin-eosin staining. Immunohistochemistry staining was carried out on formalin-fixed, paraffin-embedded tissue using an EnVision kit (Dako, Carpinteria, CA). The following primary antibodies purchased from Dako Corporation were used: cytokeratin, EMA, vimentin, placental alkaline phosphatase (PLAP), α-fetoprotein (AFP), GCDFP-15, renal cell carcinoma (RCC), human chorionic gonadotropin (HCG), androgen receptor, glypican-3, SALL4, CD10, CD31, CD34, CD30, CD56, p63, p53, smooth muscle actin (SMA), S-100 protein, synaptophysin, chromogranin A, and Ki-67. Positive and negative control slides were employed.

Results

Clinical findings

A 9-month boy scratched his right ear repeatedly one month ago. The parents found a mass measuring approximately 5×3 mm in his external acoustic foramen and smeared the mass with soybean oil. However, the mass increased gradually with 30 mm in greatest diameter and had a little bleeding prior to presentation. Physical examination showed that a soft dark-red mass measuring 30×20 mm was found in

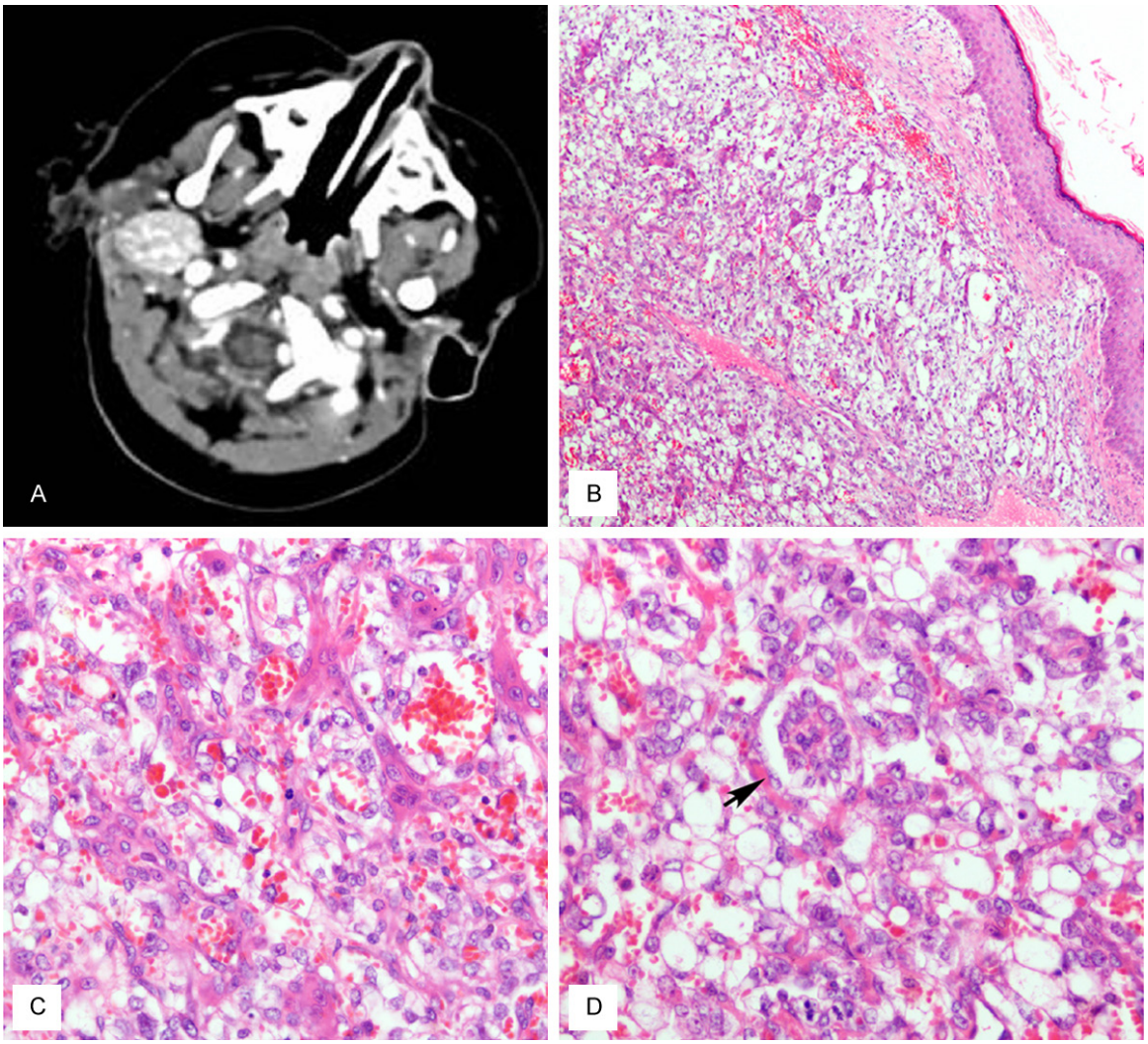

Figure 1. (A) Temporal bone enhancement CT scan showed an irregular elongated mass image measuring 42×16 mm in the right external auditory canal, the right middle ear tympanic cavity, the right mastoid process, and the right back parapharyngeal space with unclear border and hyperdense; (B) Histologically, the tumor was located underneath of the epidermis; (C) Tumor cells which had abundant eosinophilic or clear cytoplasm and marked nucleoli were arranged in nest or reticular pattern. Mitotic figures could be found; (D) Poorly formed Schiller-Duvall body was occasionally present (arrow indicated). HE, (B) ×100, (C, D) ×400.

the right cavity of auricular concha and blocked the right external auditory canal. The mass had a clear boundary. The results of urinalysis and serum chemistry, liver function, and coagulation were normal. Temporal bone computed tomography (CT) scan showed an irregular elongated mass image measuring 42×16 mm was found in the right external auditory canal, the right middle ear tympanic cavity, the right mastoid process, and the right back parapharyngeal space with unclear border and isodense. A few spotted hyperdense images were demonstrated in the mass, especially remarkable in the enhancement CT scan. Multiple enlarged lymph nodes were also found in the bilateral neck II region. The largest lymph node measuring 12×8 mm was located in the right neck II region with a clear border. The boy was suspicious of rhabdomyosarcoma of the ear by clinical doctor. No abnormal findings were found in other sites by CT scanning. So the partial excision biopsy of the mass was performed.

Pathological findings

Grossly, the specimen was grayish yellow and red, measuring 25×20×10 mm in size. Microscopically, the tumor was located underneath

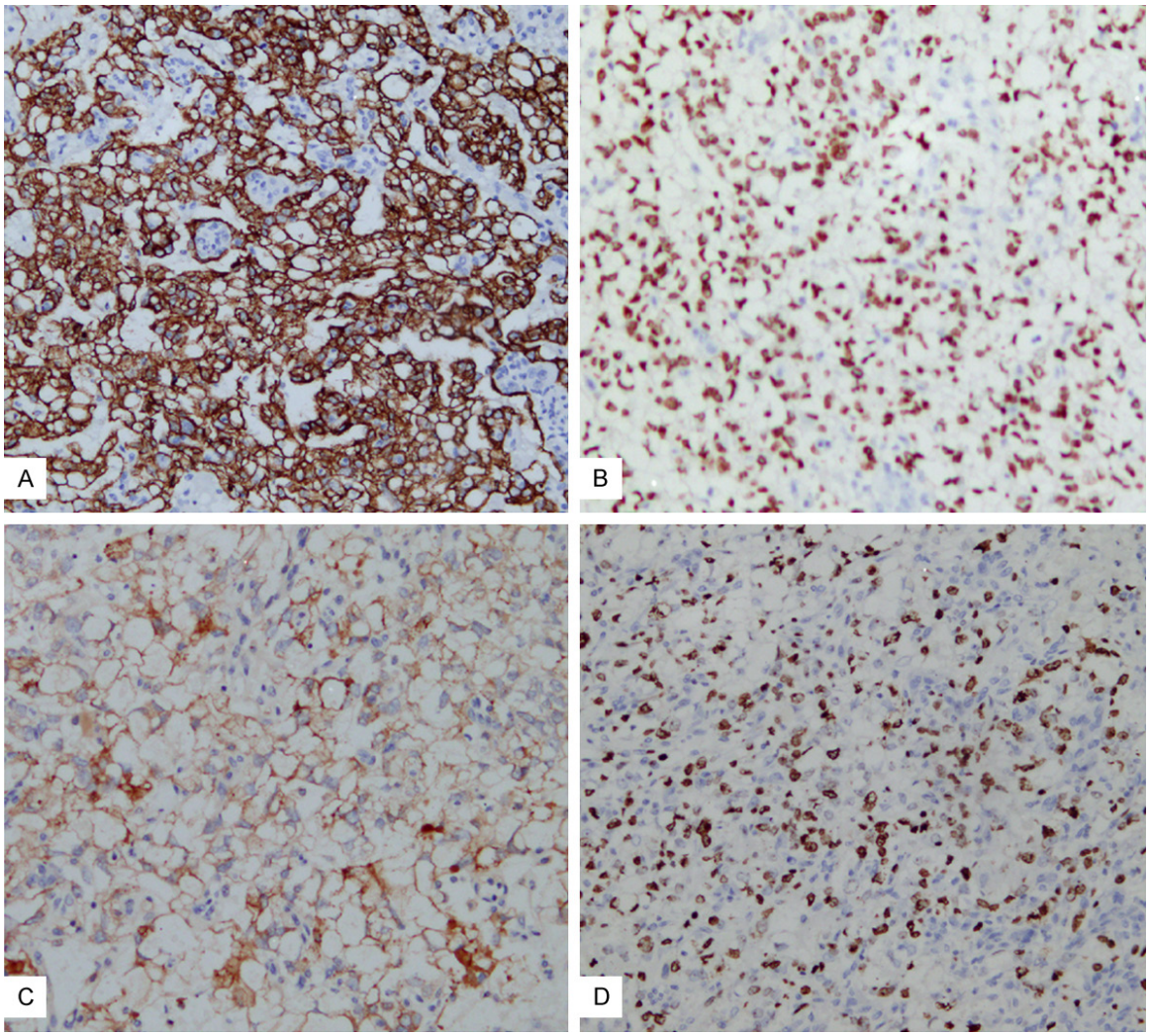

Figure 2. Tumor cells were immunoreactive for cytokeratin (A), SALL4 (B), and glypican-3 (C). Ki-67 positive expression was found in about 40% of tumor cells (D). Immunohistochemistry staining ×200.

of the epidermis with ulceration. Mild or moderate atypical round or oval tumor cells were arranged in nest and reticular pattern around vesicular or cystic spaces. Tumor cells had abundant eosinophilic or clear cytoplasm and marked nucleoli. Mitotic figures were about 7/10HPF. Poorly formed Schiller-Duvall body which was papillary fibrovascular structures in which a central blood vessel was mantled by the tumor cells and projected into a space lined by tumor cells was occasionally present (**Figure 1**). The stroma was loose and rich in capillaries. Hyaline globules could be found in the stroma.

Immunohistochemistry staining showed that tumor cells were positive for cytokeratin, SALL4, glypican-3, focal positive for EMA, vimentin, CD10, and CD34, but negative for α-fetoprotein, HCG, PLAP, p63, SMA, CD30, CD31, CD56, S-100 protein, synaptophysin, chromogranin A, RCC, androgen receptor, and GCDFP-15, p53 and Ki-67 positive expression was found in about 50% and 40% of tumor cells, respectively (**Figure 2**).

To confirm our diagnosis, the blood analysis for tumor biomarkers was then performed. The values for β-HCG, carcinoembryonic antigen, CA125, CA15-3, CA19-9, CA211, CA72-4 were normal. However, the serum AFP value was 664.60 ng/mL (normal, ≤25 ng/mL) and the value for NSE was 28.3 ng/mL (normal, ≤16.3 ng/mL). Based on these histopathological findings and elevated serum AFP level, we made

Table 1. Summary of yolk sac tumor of the ear in English literature

Source	Male/ Female (No.)	Age (months)	Site	The greatest diameter (cm)	Serum α-fetoprotein level (normal: <15 IU/ mL or ≤25 ng/mL)	α-fetoprotein expression by immunohistochemistry staining	Treatment	Outcome
Stanley et al, 1987	0/1	11	Left external auditory canal	3.0	7850 IU/mL	+	Partial resection and chemotherapy	Alive and well at 15 months
Kebudi et al, 1993	0/1	21	Left temporal bone	5.0	Elevated	NA	Surgical resection and chemotherapy	Alive and well at 16 months
Fukunaga et al, 1995	0/1	8	Left external auditory canal	1.1	Elevated	+	Surgical resection and chemotherapy	Alive and well at 13 months
Choufani et al, 1998	0/1	26	Left external auditory canal	2.0	9750 IU/mL	+	Surgical removal	Relaspse and died at 3 months
Frank et al,2000	0/1	18	Left temporal bone	1.1	7020 ng/mL	Focal +	Partial resection and chemotherapy	Alive and well at 36 months
Kaveti et al,2010	1/0	60	Left external auditory canal	NA	>1000 ng/m:	+	Surgical resection and chemotherapy	NA
Rozbahany et al, 2012	0/1	24	Left postauricular region	NA	Elevated	+	Surgical resection	Alive and well at 9 months
Narula et al, 2014	1/0	30	Left temporal bone	10.0	Elevated	+	Surgical resection and chemotherapy	Alive and well at 9 months
This report case	1/0	9	Right external auditory canal	4.2	664.6 ng/mL	-	Partial resection	Alive with tumor at 3 months

NA = not available.

the pathological diagnosis of yolk sac tumor of the external auditory canal although tumor cells in our case were negative for AFP by immunohistochemistry staining. The family refused adjuvant chemotherapy because of poor economic condition. At the time of this writing, the child was alive with tumor without further therapy 5 months after diagnosis.

Discussion

Yolk sac tumor of the ear is extremely rare. To our knowledge, only 9 cases including our current case have been reported in English literature [3-10] (**Table 1**). There were 3 male and 6 female patients. The ratio of male to female was 1:2 with female patients was predominant. The patients' age ranged from 8 months to 5 years with a mean age of 23 months and median age of 21 months. The greatest diameter of tumor ranged from 1.1 cm to 10.0 cm with mean 3.7 cm and median 3.0 cm. Eight cases were located in the left ear, only our case was in the right ear.

Yolk sac tumor of the ear is very difficult to make a diagnosis especially tumor cells in our current case were not immunoreactive for AFP expression. So a panel of antibodies including cytokeratin, AFP, SALL4, glypican-3, and PLAP should be performed. Most importantly, serum elevated AFP level is great helpful to confirm the diagnosis. All patients with yolk sac tumor of the ear in the literature had dramatically elevated serum AFP level by laboratory studies. The differential diagnosis includes embryonal rhabdomyosarcoma, paraganglioma, myoepithelioma, carcinoma of skin appendages, and metastatic renal cell carcinoma. The patient was a 9-month boy and suspicious of rhabdomyosarcoma of the ear by clinical doctor. In addition, head and neck region is the common site for rhabdomyosarcoma. Some tumor cells in our case had abundant eosinophilic cytoplasm, which was easily confused with embryonal rhabdomyosarcoma. However, embryonal rhabdomyosarcoma is composed of round or short spindle cells with variable rhabdomyoblastic differentiation and immunoreactive for myogenin and MyoD1, negative for cytokeratin and SALL4. The stroma of Yolk sac tumor was loose and rich in capillaries and tumor cells were arranged in nest, which was similar to paraganglioma. However, tumor cells in paraganglioma are characteristic of organoid pattern and immunoreactive for synaptophysin, chromogranin A, NSE, and S-100 protein, but negative for cytokeratin and SALL4. Myoepithelioma of ear is very rare and tumor cells were spindle and immunoreactive for cytokeratin, p63, and SMA. Yolk sac tumor of the ear was mainly located underneath of epidermis, immunoreactive for cytokeratin. It was easily confused with carcinoma of skin appendages including syringocarcinoma and sebaceous carcinoma. However, carcinoma cells of skin appendages are arranged in adenoid structure and negative for SALL4 and glypican-3 by immunohistochemistry staining. Tumor cells of our case had abundant clear cytoplasm, were rich in capillary in the stroma and immunoreactive for cytokeratin, vimentin, and CD10, which were easily confused with metastatic renal cell carcinoma. However, the patient was only 9-month old. There were no abnormal findings in his kidneys. Furthermore, renal cell carcinoma is immunoreactive for RCC, negative for SALL4 and glypican-3.

The treatment for yolk sac tumor of the ear was mainly surgical resection followed by chemotherapy. Extragonadal yolk sac tumor is usually associated with a worse prognosis than the gonadal counterpart [1]. However, Frank et al. have reported a successful chemotherapeutic response in his case of the temporal bone [6]. Of 8 patients with yolk sac tumor of the ear with follow-up information reported in the literature, 7 patients were alive and well at 3 months to 36 months except one patient had tumor relapse and died at 3 months after treatment.

Disclosure of conflict of interest

None.

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