Epidemiological, histological and immunohistochemical analysis of head and neck rhabdomyosarcoma in children

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Abstract

Introduction: Rhabdomyosarcoma is the most common soft-tissue malignancy in the pediatric head and neck tumors. The objectives of this study were to determine the epidemiological and pathological patterns of head and neck rhabdomyosarcoma in children in a Moroccan oto-neuro-ophtalmology pathological laboratory.
Material and methods: The study population consisted of patients who presented with head and neck tumors at the oto-neuro ophtalmology pathological laboratory of Rabat Morocco over a 10-year period (1999-2008).
Results: Twenty eight patients were identified for the study period among 364 head and neck tumors. The youngest case was 7 months old and the oldest was 14 years old; the median age was 5,39 years. 20 patients were male (71,42 %) with a male to female ratio of 5:2. The most affected areas were the orbit in 10 cases (35, 71 %), the cheek in 4 cases (14,28%), the maxilla and nasopharynx in 3 cases (10,71%) each. Histologically, 24 cases (85,71%) were embryonal and 4 cases (14,29%) were alveolar. Immunohistochemical findings highlighted positivity of desmin (64,28%), smooth muscle actin (57,89%) and myogenin (90%).
Conclusion: this large study about a single institution can pretend to reflect the real incidence of rhabdomyosarcoma of head and neck in children in Morocco. The results obtained in our study are similar to those related in the literature.

Keywords: Rhabdomyosarcoma, Head, Neck

Introduction

Rhabdomyosarcoma (RMS) is a malignant soft tissue neoplasm, with varying degrees of striated muscle cell differentiation. It is the most common soft tissue sarcoma, accounting for 5–10% of all childhood malignancies with a relative predilection for the head and neck region with a rate of about 40% [1-4]. Head and neck RMSs are classified according to their anatomical location and propensity for central nervous system invasion: Sites of origin include the parameningeal, and nonorbital non-parameningeal areas [1, 5]. Two general pathological types of RMS have been found in children: embryonal and alveolar. Two additional subtypes of embryonal rhabdomyosarcoma have also been documented to have a better prognosis: sarcoma botryoide and spindle cell rhabdomyosarcoma [1, 3]. Multimodal treatment with multiagent chemotherapy, radiation, and surgery confers the greatest chance for survival in the treatment of head and neck RMS [1, 5].
The objectives of this study were to determine the epidemiological and pathological patterns of RMS of head and neck in children in a Moroccan oto-neuro-ophtalmology pathological laboratory.

Material and methods

This retrospective study was carried out at the oto-neuro-ophtalmology pathological laboratory of Rabat, Morocco.

The study population consisted of children who presented with head and neck rhabdomyosarcoma among 364 head and neck tumors over a 10-year period (1999-2008). Formalin-fixed, paraffin embedded tissue sections were available on all 28 cases for routine (H&E)

Immunohistochemical staining was performed through the streptavidin-biotin technique using desmin (CloneD33, Labvision co., ph=7,4), smooth muscle actin (Clone 1A4, Thermoscientific co., ph=7,4) and myogenin monoclonal antibodies (Clone F5D, Labvision co., ph=7,4).

Results

Twenty eight patients were identified for the study period. The youngest case was 7 months old and the oldest was 14 years old; the median age was 5,39 years. 20 patients were male (71,42 %) with a male to female ratio of 5:2. The localisations affected were the orbit in 10 cases (35, 71 %), the cheek in 4 cases (14, 28%), the maxilla and nasopharynx in 3 cases (10, 71%) each. The parotid gland and neck presented 2 cases (7, 14%) each. There was 1 oral site (3, 75%), 1 nasal site (3, 75%) and one case in the external auditory canal (3, 75%). Histologically, 24 cases (85, 71%) were embryonal and 4 cases (14, 29%) were alveolar (Figure1). Immunohistochemical findings were positivity of desmin (64,28%), smooth muscle actin (57,89%) and myogenin (90%). 6 cases received a combination of chemotherapy, surgery and radiation. Chemotherapy and radiation were the main treatment in 3 cases. One case received chemotherapy and underwent surgery. The evolution was favourable for 4 cases with a standing back raging from 1 year to 4 years. 5 cases presented a recurrence after 3 months to 24 months. Metastases to the lung and to the cerebrum were seen in 2 cases. One patient died. We received no further information regarding the remaining cases.

Discussion

Rhabdomyosarcoma represents the most common soft-tissue neoplasm of the head and neck found in children [1-8]. The reported peak age for head and neck RMS in children is 2-6 years of age [1,3,9]. The mean age in our study population was 5,39 years which is similar to the previous reports. The literature had documented that males are affected more often than females [1, 8]. This study observed a similar trend. Head and neck RMS is anatomically divided in two categories: parameningeal (including nose, nasopharynx, paranasal sinuses, mastoid region, infra-temporal and pterygopalatine fossae and medium ear) and non-parameningeal (which include scalp, orbit, parotid gland, oral cavity, oropharynx and larynx) [1,5, 9]. Approximately 40% of head and neck tumors occur in parameningeal sites [3] but this study report 14,64%. In the literature, 30% of head and neck RMS are presenting in non-parameningeal non-orbital locations [4]. In our study, approximately 59,73% of the cases were non-parameningeal non-orbital sites. In the present study, the orbit is affected in 35,71% of the cases which support previous publications reporting that orbital tumors account for 30% of head and neck RMS [10].

Histologically, rhabdomyosarcoma is a highly malignant mesenchymal tumor thought to originate from immature striated muscle. It is one of the “small round blue cell tumors of childhood” like neuroblastoma, Ewing’s sarcoma, and lymphoma [3]. It is divided into several subtypes, including embryonal, alveolar, and undifferentiated types. Embryonal RMSs are characterized by primitive spindle cells, often with a myxoid background [3, 11] (figure 2).

This histologic type is associated with loss of heterozygosity at the 11p15 locus [3, 8]. In our study, 85,71% cases were embryonal. Alveolar RMS are characterized by loose, non cohesive, round or oval tumor cell aggregates, separated by a fibrous septal framework [3, 11]. Chromosomal analyses have demonstrated two translocations associated with the alveolar histology: t (2; 13) (q35; q14) and t(1;13)(p36;q14). The resulting gene fusions encode PAX3-FKHR and PAX7-FKHR proteins [3, 8]. With head and neck rhabdomyosarcomas, there is a slight increase in embryonal types with a somewhat lower proportion of alveolar rhabdomyosarcoma [8] as seen in the present study.

Immunohistochemical studies, including staining for desmin, smooth muscle actin and myogenin are additional studies which can support the diagnosis of rhabdomyosarcoma [2, 3, 8, 12]. The expression of desmin has been the reference for a long time but it lacks specificity (figure3). MyoD1 and myogenin, respectively the products of genes MYF3 and MYF4 are transcription factors that are physiologically expressed in the nuclei of striated muscular cells during embryonal and foetal development. Their expression in rhabdomyosarcoma is more specific and equally sensitive as desmin. Currently, anti-myogenin antibodies are much easier to use because they provide less interference and seems to be preferred (figure 4). Less than 50% of the tumoral cells express myogenin in the embryonal type meanwhile more than 50% of tumoral cells are positive for myogenin in the alveolar type which matches with our study [1].

Recommended treatment for RMS is a combination of surgery, multiagent chemotherapy and radiotherapy. The treatment of choice depends on the anatomical site affected. Localized or easily accessible non-orbital non-parameningeal head and neck tumours are most often amenable to surgery with low longterm surgical morbidity. Surgical resection can also be used in the salvage therapy of those who do not respond to chemotherapy and radiotherapy [1, 2, 4-6, 10,13]. Currently, the approach to orbit tumors has been to use chemotherapy and radiotherapy to preserve visual function [3, 10]. Both chemotherapy and radiotherapy may be required for parameningeal tumors. The role of surgery for these tumors is limited because of extent of disease and involvement of surrounding critical organs [3, 10].

Some favorable prognostic factors have been identified with pediatric rhabdomyosarcoma. Superficial head and neck sites and the orbit are associated with an improved prognosis. Other favorable factors include gross total tumor excision without distant disease, smaller tumor size (4-5cm), younger age (4-10 years), and embryonal histology. In our study, all the cases with favourable evolution are embryonal accuring in younger age. Prognosis for head and neck rhabdomyosarcoma is considered favorable partially due to the lower stage at presentation than at other body sites. In particular, orbital and periorbital tumors have an especially favorable 5-year survival (95%), with most failures occurring due to central nervous system infiltration [2, 4, 8].

In conclusion, rhabdomyosarcoma is the most common soft tissue sarcoma in children. We described epidemiological, histological and immunohistochemical aspects of head and neck RMS in children in a Moroccan oto-neuro-ophtalmic pathological laboratory. Survival for children with this malignancy has improved as a result of multiple factors, including better imaging and pathologic classification, use of multiagent chemotherapy, and use of appropriate radiotherapy especially in parameningeal primaries.

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Figures:

Figure 1: Epidemiological aspects of head and neck rhabdomyosarcomas in children
Figure 2: HEx200: embryonal rhabdomyosarcoma with rhabdomyoblasts
Figure 3: IHCx400: positivity of desmin
Figure 4: IHCx400: positivity of myogenin