CASE REPORT

Synchronous bifocal alveolar rhabdomyosarcoma

A CASE REPORT

We report a case of bifocal rhabdomyosarcoma involving the hand and thigh in an 11-year-old female. We highlight the importance of a thorough clinical examination and an aggressive surgical approach in which each lesion is treated as a separate primary.

Rhabdomyosarcoma is a highly malignant tumour of striated muscle cells and is the most common sarcoma in childhood. It accounts for nearly 65% of all sarcomas in patients of 15 years of age and younger, and approximately 7% of all childhood malignant solid tumours. In the United States, the incidence in African-American females is half that for Caucasian females, while the incidence in males is similar for both groups. The most common sites are the head and neck, and the genitourinary tract; approximately 20% occur in the extremities.

A rhabdomyosarcoma in the extremity most frequently presents in adolescence and spreads to the lymph nodes in approximately 20% of patients. The two major subtypes of rhabdomyosarcoma seen in the extremity are embryonal and alveolar, and both present with distinct histopathological appearances. The alveolar variant is seen in approximately 20% of rhabdomyosarcomas and is characterised by specific genetic changes, t(2;13) or t(1;13) chromosome rearrangements.

More than one-third of patients with the embryonal variant show chromosomal translocation breakpoints in the 1p11-q11 region and variable gains of chromosomes 2, 8, 12 and 13. Involvement of the hand is extremely rare, and its occurrence had not been recognised in the literature until the work of Potenza and Winslow in 1961.

We describe a patient presenting with concurrent masses in the soft tissue of the extremities, with no evidence of lymph node involvement or distant metastasis. These tumours, although histopathologically identical (alveolar rhabdomyosarcoma), responded differently to chemotherapy. We are unaware of a published report in the English literature of synchronous rhabdomyosarcoma involving the soft tissues of the extremities without concurrent pulmonary, lymphatic, or bone marrow involvement. Our patient and her family gave informed consent for publication.

Case report

An 11-year-old African-American female presented with a two-month history of an enlarging painless mass on the dorsum of her non-dominant hand. There was no history of injury, fever, chills, or weight loss, and no past or family history of malignancy. Examination revealed a 5 cm x 3 cm soft-tissue mass on the dorsum of her left hand between the index and middle metacarpals. The mass was firm, nontender, and fixed to the adjacent tissue. The overlying skin was intact and not inflamed. The range of movement of the index and middle fingers was within normal limits, and her ability to feel light touch was normal. There was no antecubital or axillary lymphadenopathy. Further examination revealed a 4 cm x 4 cm firm, painless, fixed mass on the front of her right thigh. There was no neuromuscular disturbance of the right lower extremity and no lymph nodes were palpable.

Radiographs of her hand showed a soft-tissue shadow in the intermetacarpal space between the index and middle fingers without involvement of bone. MRI showed a lobulated mass measuring 2.5 cm x 5 cm x 3 cm between the index and middle metacarpals (Fig. 1) which extended from the dorsal subcutaneous tissues to the deep surface of the flexor tendon sheaths. It enhanced with contrast. Radiographs of the thigh were unremarkable. An MR scan of the thigh showed a large lobulated mass, which did not obviously involve bone and which also enhanced with contrast. The thigh mass was adjacent to, but did not invade, the femoral neurovascular structures (Fig. 2). Incisional biopsies were performed of both masses. Microscopic examination of each mass...
revealed an infiltrative malignant lesion consisting primarily of sheets of small round blue cells with a focal alveolar growth pattern (Fig 3a). The lesions showed immunoreactivity with antibodies to desmin, myogenin and CD99 (Fig. 3b). Antibodies to cytokeratin, leucocyte common antigen, CD31, CD34, and Factor VIII-related antigen showed no reactivity. The cellular characteristics were consistent with rhabdomyosarcoma with spindle cell and alveolar differentiation. Reverse transcriptase-polymerase chain reaction (RT-PCR) analysis performed on each tumour showed PAX3/PAX7 fusion transcripts, characteristic of alveolar rhabdomyosarcoma. More specific testing revealed the PAX3-FKHR fusion product, consistent with a t(2;13) chromosomal re-arrangement. Assays for EWS-FL11 and EWS-ERG gene fusion products (associated with Ewing sarcoma/primitive peripheral neuroectodermal tumour) and SYS-SSX1 and SYT-SSX2 gene fusion products (associated with synovial sarcoma) were negative. All staging studies, including bone scan, CT of the chest, abdomen and pelvis, lymph node sampling and bone marrow biopsy, were negative.
Neoadjuvant chemotherapy was started according to protocol COG D9803, which consists of 12 weeks of treatment with vincristine, actinomycin and cyclophosphamide. An MR scan was performed after this which showed that the thigh mass had disappeared although the hand mass was only slightly smaller. The hand mass and the thigh tumour-bed were widely resected. The hand resection consisted of hemimetacarpal resection of the middle and index fingers with autogenous tricortical iliac crest grafting (Fig. 4). The thigh resection required partial resection of the vas-tus medialis.

The pathology of the hand specimen revealed a viable tumour with a 50% response to chemotherapy, while the thigh resection was negative for tumour. Both tumour margins were clear. Post-operatively the patient received external beam radiation to her hand, as well as chemotherapy. At the 30-month follow-up, the patient had normal function of her hand apart from the inability to adduct her middle or index fingers. This has not resulted in any significant disability. There is decreased feeling on the radial border of her middle finger and the ulnar border of her index finger. She has normal quadriceps strength with no neurological deficit in the lower extremity. Imaging studies, including bone scan, MRI of the thigh and hand, and chest CT, show no evidence of disease.

Discussion

We report an adolescent patient who presented with concurrent alveolar rhabdomyosarcomas of the left hand and right thigh. Formal staging revealed no other areas of involvement. Staging for rhabdomyosarcoma included CT of the chest, abdomen and pelvis, bone scan, MRI, bone marrow biopsy and lymph node sampling. When all these studies are negative, the Intergroup Rhabdomyosarcoma Study (IRS) classifies the lesion as group I (localised disease). Although nearly 20% of all extremity rhabdomyosarcomas present with lymph node involvement, the most common site for metastasis is the lungs, followed by the bone marrow. We are uncertain whether the tumours in this patient were both primaries, or whether one was metastatic from the other. The patient is alive and disease-free 30 months after surgery; this would be unusual for a patient presenting with a metastasis. A rhabdomyosarcoma involving the hand is extremely rare, and although an isolated soft-tissue metastasis of a rhabdomyosarcoma to other extremities is quite unusual, it is known that rhabdomyosarcomas of the hands and feet can metastasise to unusual sites (such as breast, ovary, testis, pancreas, and kidney).

Each tumour was treated as a primary with wide local excision. The mainstay of chemotherapy for rhabdomyosarcoma throughout most of the IRS studies has been combinations of vincristine, actinomycin, and cyclophosphamide. Radiotherapy has been used selectively in order to enhance local tumour control.

The most consistent chromosomal re-arrangements in alveolar rhabdomyosarcoma are t(2;13)(q35;q14) in 55% and t(1;13)(p36;q14) in about 22% of cases. The remaining 23% of patients did not have either translocation, however other genetic markers are under investigation including MYCN, MDM2 and CD4. The translocations involve two PAX genes, PAX3 and PAX7 located on chromosomes 2 and 1, respectively. These two genes are thought to be important in muscle development during embryogenesis, when the somites, from which skeletal muscle will develop, are formed. Disruption of these genes can result in abnormal muscle development. Both translocations result in fusion genes between the undisrupted PAX3 and PAX7 DNA-binding domains, and the transactivation domain of the FKHR gene on chromosome 13. These translocations cause an alteration of biological activity at the protein level and are thought to influence tumour development by impacting on the control of tumour cell growth, apoptosis, differentiation and motility. Each fusion gene is a specific diagnostic marker for alveolar rhabdomyosarcoma and can be used as an adjunct to classical histological diagnosis.

The outcome for children with extremity rhabdomyosarcoma is not as good as that for children with rhabdomyosarcoma in more favourable locations. Limb sparing by wide local excision of the tumour is the treatment of choice, but amputation may occasionally be necessary. A thorough history and physical examination is essential in patients with a sarcoma in order to exclude or identify other soft-tissue masses. Chromosomal studies are recommended at the time of biopsy, particularly in cases of rhabdomyosarcoma, as the response to chemotherapy may be predicted.
by the re-arrangement identified.\textsuperscript{3} In cases of rhabdomyosarcoma, the presence of one or the other of these gene fusions has been shown to have prognostic significance, because they can distinguish between a very high-risk subgroup (PAX3-FKHR) and a favourable outcome subgroup (PAX7-FKHR).\textsuperscript{13}

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No benefits in any form have been received or will be received from a commercial party related directly or indirectly to the subject of this article.

References


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