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Extrarenal Malignant Rhabdoid Tumour of the Heel - A Case Report

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Abstract. *Malignant rhabdoid tumour is a rare soft-tissue neoplasm that occurs in children and young adults. Cases have involved numerous extrarenal sites, including the thymus, liver, paravertebral region, central nervous system, heart, prostate, pelvis, chest wall, extremities, as well as soft tissues. Given their highly aggressive nature, early diagnosis of rhabdoid tumours is essential; indeed, survival times after initial presentation are typically in the range of months rather than years. The low incidence of rhabdoid tumours and confusion between this type of tumour and other tumours has precluded the collection of adequate data on its clinical presentation and there is no specific therapeutic protocol. Owing to the rarity of this condition and the difficulties encountered in its diagnosis and treatment, we report the case of a malignant tumour with rhabdoid-like features in the foot that confirms the local aggressiveness and the high metastatic potential of this type of tumour.*

Malignant rhabdoid tumour is a rare soft-tissue neoplasm that occurs in children and young adults. It was first described as a variant of nephroblastoma (1). Subsequent studies have suggested that this tumour is more likely to be a distinct clinic pathological entity of unknown histogenesis (2-4).

Although rhabdoid tumour was originally described as a primary renal neoplasm, examples of a morphologically similar neoplasm have since been identified in many other sites, particularly in soft tissues. Cases have involved numerous extrarenal sites, including the thymus, liver, paravertebral region, central nervous system, heart, prostate, pelvis, chest wall, extremities, as well as soft tissues. Most patients are infants or children, though it can also occur in adults; the median patient age in one large series was 20 months, though the age range was from 3 weeks to 50 years. These tumours are more frequent in males than in females, the ratio being 1.5:1 (5-7).

Given their highly aggressive nature, early diagnosis of rhabdoid tumours is essential; indeed, survival times after initial presentation are typically in the range of months rather than years, with death occurring on average 6 months after diagnosis; survival times of between 72 and 156 months have, however, also been reported. Data concerning the 5-year survival rate are not available (8-11). The low incidence of rhabdoid tumours and confusion between this type of tumour and other tumours has precluded the collection of adequate data on its clinical presentation, anatomic location, prognostic factors, incidence and the anatomic distribution of metastases.

Microscopically, rhabdoid tumour is a monomorphous neoplasm composed of a fairly uniform population of round-to-oval cells growing in a diffuse, non-cohesive pattern. The cytological hallmarks of this tumour include large hyaline, globular cytoplasmic inclusions in a variable number of cells and a prominent nucleolus. Ultrastructurally, whorls of intermediate filaments correlate with cytoplasmic inclusions seen by light microscopy. There is immunohistological evidence of mesenchymal differentiation (12-15).

Owing to the rarity of this condition and the difficulties encountered in its diagnosis and treatment, we report the case of a malignant tumour with rhabdoid-like features in the foot, observed in the Department of Plastic Surgery of the University "La Sapienza", Rome, Italy, that confirms the local aggressiveness and the high metastatic potential of this type of tumour.

Case Report

A 29-year-old man presented, in November 2004, with a rapidly enlarging, soft, red-coloured, friable mass on the left heel; this mass had first appeared approximately two years

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earlier, when the patient had noticed the development of a subcutaneous node with a diameter of about 0.2 cm, which was solid and painful on palpation. The lesion grew rapidly and the patient had the node removed, without histological examination, one year previously.

On admission, he presented a large, oval, sprouting, bleeding mass measuring of 8 x 5 cm. The overlying skin had distended veins, was necrotic and ulcerated, and presented reddish nodular lesions on the surface (Figure 1a-1b). The lesion was painful, thus preventing normal walking. Physical examination revealed two hard, though painless, palpable masses in the left groin. Examination of the other organs revealed another palpable mass in the left inguinal region. The ultrasound examination revealed three lymphadenopathies, two of which were lumped together and had a combined diameter of 15 mm; all three were hypoechoic, heterogeneous and their hilus was not visible. A standard chest X-ray examination revealed a roundish, opaque area of tenuous density in the anterior mediastinal part on the anterior edge of the right ventricle and multiple nodular lesions (Figure 2). A CT total body examination performed shortly after the X-ray, using the multislice spiral technique after intravenous administration of iodized non-ionic contrast medium, revealed the presence of multiple nodular lesions (at least 22 on the right and 20 on the left), spread throughout the lungs, particularly in the medium-basal segments, all of which had repetitive features (Figure 3). The pleural cavities appeared to be effusion-free, and there were no significant mediastinal or axillary lymphoadenopathies. The CT body examination did not reveal any lesions in the other parenchymas, such as the brain, liver, spleen, kidney and surrenals, nor any abdominal or pelvic lymphonodal masses.

Given these clinical conditions, it was decided to remove the most extensive portion of the mass without amputating the foot, so as to restore correct, painless deambulation, and to perform a biopsy of the palpable mass in the left inguinal region. During surgery a large portion, though not all, of the mass was removed because the deeper tissues were found to be invaded. The area was reconstructed using a dermo-epidermal graft taken from the front of the thigh. A lymph node from the left groin was also removed.

The histopathological investigation confirmed that the tumour was composed totally of rhabdoid cells; the tumour cells were highly cellular, consisting of monomorphic round or polygonal cells arranged in solid sheets or in alveolar, trabecular or non-cohesive patterns, multilobed eccentric vesicular nuclei, with one to multiple prominent nucleoli, and a large amount of eosinophilic cytoplasm containing globular hyaline-like inclusions (PAS+). Numerous atypical mitoses and large areas of superficial necrosis were observed (Figure 4).

The neoplastic cells tested positive for vimentin, for epithelial membrane antigen and negative for cytokeratins, smooth muscle actin, myoglobin, desmin, melanoma markers, lymphocyte common antigen, CD31, CD34 and neuroendocrine markers.

The histological examination of the biopsy of the inguinal lymph node revealed metastases of the extrarenal rhabdoid tumour.

The patient underwent chemotherapy and radiotherapy. To date, six months after surgery, the patient has undergone five cycles of chemotherapy (vincristine, actinomycin-D and cyclophosphamide) and his general condition is quite satisfactory, even if the metastases do not appear to have markedly regressed.

Discussion and Conclusion

External malignant rhabdoid tumours present two problems: diagnosis and treatment. Whether or not external malignant rhabdoid tumours exist has been a matter of debate, partly because of the broad spectrum of primary sites, including the extremities, brain and heart; however, an increasing body of evidence supporting the existence of this tumour has been provided by the growing number of case reports, which have led to it being widely accepted as a discrete entity. The two largest series of extrarenal soft tissue tumours with a rhabdoid phenotype were reported by Parham *et al*. and Kodet *et al*. (8-10).

It is crucial that the histological and cytological diagnoses of external malignant rhabdoid tumour be made with extreme caution and that these diagnoses be supported by appropriate immunohistochemistry. Microscopic analysis shows the presence of a monotonous population of large round polygonal cells with an abundant eosinophilic cytoplasm, vesicular eccentric nuclei and prominent nucleoli. Microscopically, solid sheets of cells are present with areas of compartmentalization. The most striking morphological feature is the deeply, homogeneously acidophilic cytoplasm of the tumour cells (the result of packing by intermediate filaments), with occasional lateral displacement of the nucleus. Myxoid, pseudoalveolar and hyalinized areas may be present. Immunohistochemically, there is positivity for vimentin and often for keratin and EMA, though generally not for skeletal muscle markers or S-100 protein. However, considerable phenotypical diversity has been recorded in these lesions, including the common expression of neural/neuroendocrine markers (16).

Metastases occur early in the lungs, liver and lymph nodes, as observed in our case. Response to therapy is poor and the clinical course extremely aggressive. Most evidence suggests that soft tissue rhabdoid tumour is not a specific tumour entity, but rather the expression of a "rhabdoid" phenotype that can develop in a wide variety of tumour types, including epithelioid sarcoma, synovial sarcoma, intra-abdominal desmoplastic small cell tumour,

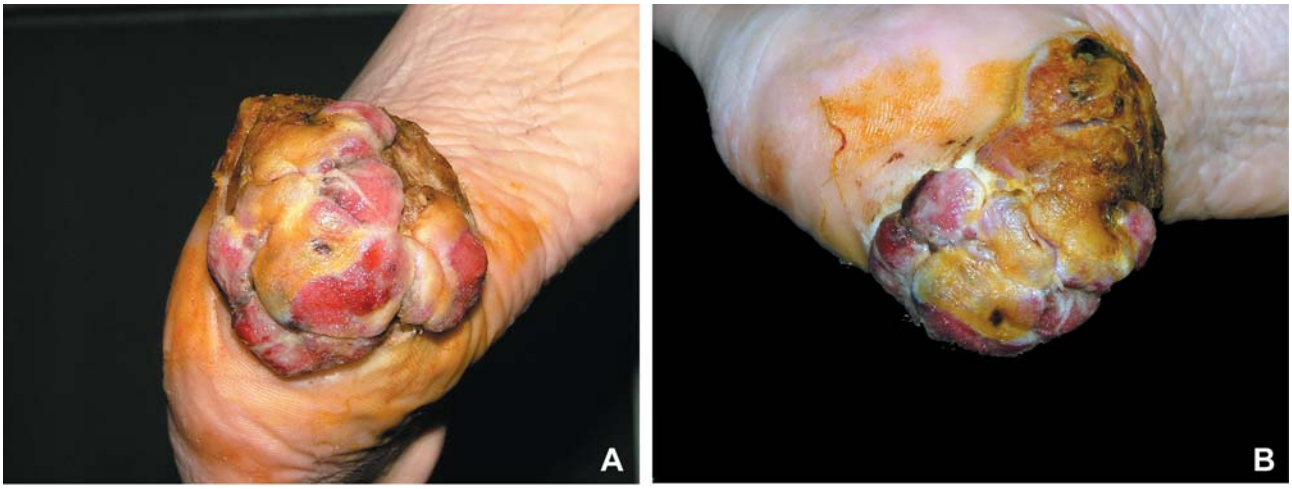

Figure 1. *a-b. Presence of an oval, soft, sprouting, bleeding mass measuring 8 x 5 cm, on the left heel.*

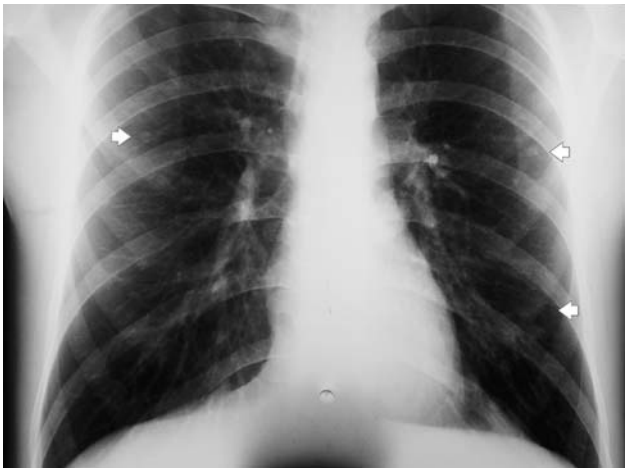

Figure 2. *Standard chest X-ray examination: presence of a roundish, opaque area of tenuous density in the anterior mediastinal part on the anterior edge of the right ventricle and multiple nodular lesions.*

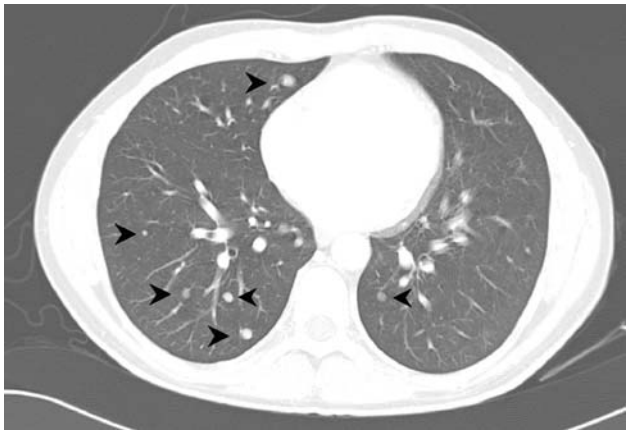

Figure 3. *CT total body examination using the multislice spiral technique after intravenous administration of iodized non-ionic contrast medium: presence of spread throughout the lungs, particularly in the medium-basal segments, all of which had repetitive-like features.*

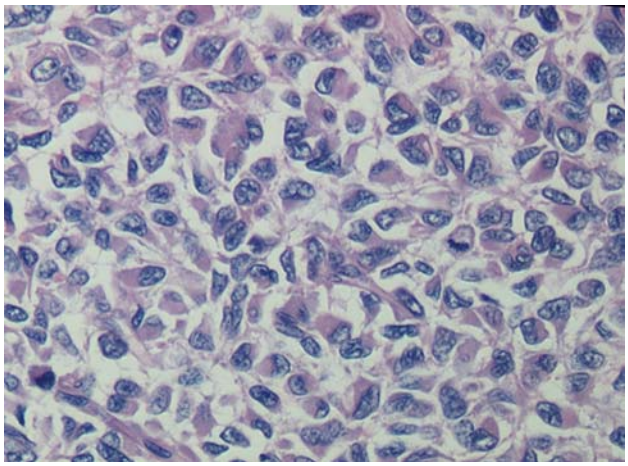

Figure 4. *Histopathological investigation: the tumour cells were highly cellular, consisting of monomorphic round or polygonal cells arranged in solid sheets or in alveolar, trabecular or non-cohesive patterns, multilobed eccentric vesicular nuclei, with one to multiple prominent nucleoli, and a large amount of eosinophilic cytoplasm containing globular hyaline-like inclusions. (Haematoxylin and eosin, original magnification x 40).*

rhabdomyosarcoma, malignant melanoma, and various types of carcinoma. Of practical importance is the fact that the emergence of the rhabdoid phenotype is invariably associated with an aggressive and almost always lethal clinical course (16-19).

The treatment of external malignant rhabdoid tumour is controversial and no specific therapeutic protocol has been set up because so few cases have been published. No centre has accumulated sufficient clinical experience to formulate a standard approach to the management of the disease. The primary tumour must be resected, and the surgical procedure should be followed by postoperative radiotherapy to the primary site and drainage of lymph nodes and chemotherapy. Some authors have suggested treatment with the same chemotherapeutic agents used to treat sarcoma of the soft tissues, such as cisplatin, adriamycin and cyclophosphamide, or those used for nephroblastoma, such as carboplatin, etoposide, doxorubicin and ifosfamide. There is, however, no documented benefit from either of these forms of chemotherapy in the long term, except in a few cases (20-24).

Recently, sentinel node imaging has become an adjunctive measure in the treatment of cancer, particularly in breast cancer and melanoma. Sentinel node biopsy may be a useful tool to diagnose early lymphatic spread and improve both local and regional control of this tumour.

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