CASE REPORT

Histopathological And Immunohistochemical Appearance Of Pleomorphic Dermal Sarcoma

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Abstract

Pleomorphic dermal sarcoma is a rare and aggressive entity that originates in the skin's dermis. This poorly defined tumor usually appears on the sun exposed skin of the elderly and involves the male gender more often. We describe the case of a 54 year old male patient who presented to the Surgery Department with a tumor located on the scalp. Surgery was performed and the sample was sent to the Pathology Department of Mures Clinical County Hospital for further analysis. Histological analysis showed a tumor with solid architecture and nesting phenomenon, composed of pleomorphic epithelioid cells with high atypia. Typical and atypical mitoses were observed. Immunohistochemistry showed positivity for the following markers: vimentin, CD68 and ki67- proliferation value of 90%. The cells were negative to CK AE1/AE3, S100, SOX10, HMB45, MelanA, CD31, Desmin and SMA. In conclusion, pleomorphic dermal sarcoma represents a challenging diagnosis. The case highlights the histological and immunohistochemistry appearance of the neoplasm. Due to the local aggressivity, difficulty in providing negative resection margins and uncertain prognosis, it's important to take this entity into consideration each time we encounter a cutaneous pleomorphic tumor.

Keywords: pleomorphic dermal sarcoma, scalp, immunohistochemistry, rare, cutaneous.

Rezumat

Sarcomul dermal pleomorf este o tumoră rară și agresivă, cu originea la nivelul dermului. Această tumoră este imprecis delimitată și apare mai frecvent la vârstnici de sex masculin, la nivelul pielii expuse la soare. Relatăm cazul unui pacient în vârsă de 54 de ani care s-a prezentat în Secția de Chirurgie cu o tumoră localizată la nivelul scalpului, pentru care s-a intervenit chirurgical. Piesa excizată a fost trimisă la Serviciul de Anatomie Patologică din cadrul Spitalului Clinic Județean Mureș pentru analiză. Din punct de vedere histologic, tumora a prezentat arhitectură solidă, cu celule organizate în cuiburi și placarde, celulele tumorale având aspect epiteloid, pleomorfe, cu atipii cito-nucleare marcate. Au fost identificate mitoze tipice și atipice. Reacțiile imunohistochimice au fost pozitive pentru markerii vimentină, CD68 și ki67- indicele de proliferare având valori de 90%. Tumora a fost negativă pentru imunomarcajul cu CK AE1/AE3, S100, SOX10, HMB45, MelanA, CD31, Desmină și SMA. În concluzie, sarcomul dermal pleomorf reprezintă o provocare din punct de vedere al diagnosticului în principal datorită asemănării cu alte tumori maligne ale pielii. Cazul de față își propune evidențierea aspectului histologic și imunohistochimic al neoplaziei. Din cauza agresivității locale, a dificultății de a oferi margini de rezecție negative și a prognosticului incert, este important să avem în vedere posibilitatea acestui diagnostic de fiecare data când ne confruntăm cu o tumoră cutanată pleomorfă.

Cuvinte cheie: sarcom dermal pleomorf, scalp, imunohistochimie, cutanat, rar.

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INTRODUCTION

Pleomorphic dermal sarcoma is a very rare entity which originates in the skin. In the past, this neoplasm was referred to as malignant fibrous histiocytoma, but today it is considered to be an entirely different entity. This type of sarcoma is located in the dermis and is poorly defined. The population at risk is considered to be the male gender, the increasing age and the sun-exposed skin. Clinically, this type of tumor presents an exophytic appearance and rapid growth. Many of the cases described in the literature reported ulceration and also bleeding episodes[1-3].

The histological appearance of the tumor is highly challenging. It is known to be composed of pleomorphic tumor cells, some of them epithelioid, and some with spindle shaped. The cytoplasm is usually abundant. The nuclei are highly pleomorphic, hyperchromatic and one or multiple eosinophilic nucleoli are present. Invasion of the subcutis, vascular invasion, perineural invasion and necrosis might help in raising the suspicion of this diagnosis. However, because the tumor has an appearance similar to other malignant lesions such as melanoma and poorly differentiated carcinomas, the diagnosis is established largely with the help of immunohistochemistry[4-7].

The most important treatment for the pleomorphic dermal sarcoma is surgery, but unfortunately, since the tumor is poorly defined, clear resection margins are a goal hard to achieve. This type of neoplasm is very important especially because of the rapid growth and local aggresivity. In the past it was thought that pleomorphic dermal sarcoma is having a high local recurrence risk but it was considered a low-grade sarcoma for which the follow-up is important. Over the years, due to the large tumors for which the patients usually presented, vascular and perineural invasion, the mitotic activity and the aggresivity of the tumor remains a hot topic. Because the majority of the patients are elderly and have multiple illnesses associated, data about the mortality due to this tumor is limited[8-12].

MATERIAL AND METHODS

We describe the case of a 62 year old male patient who presented to the Plastic Surgery Department of Clinical County Hospital Târgu Mureș for a 45 mm tumor located on the scalp. Excision was performed and the specimen was sent to the hospital's Department of Pathology for further analysis. Tissue samples were collected and processed according to protocols: samples were fixed in 10% buffered formalin, paraffin embedding and staining with Hematoxylin–Eosin (HE). Immunohistochemistry analysis was performed on 4 µm-thick sections that were prepared from formalin-fixed paraffin- embedded tissue. We used an automated immunostainer (Bechmark GX, Ventana Medical Systems Inc., Tucson, AZ, USA). Immunohistochemistry assays were performed on Ventana Benchmark GX automated staining instrument according to the instructions of the manufacturer.

RESULTS

On the gross examination, we observed a cutaneous specimen of 85x80 mm with a thickness of 46 mm. The specimen presented a tumoral mass of 45x45 mm. The lesion was brown, poorly circumscribed, ulcerated, with a firm consistency. On the gross section, the tumor was yellow, with 45 mm thickness and appeared to extend and infiltrate the deep resection margin.

Microscopically, on the Hematoxilin&Eosin stain, we observed a cutis layered by keratinized stratified squamous epithelium with an underlying neoplastic proliferation which was poorly defined, with solid architecture. Areas of invasion and ulceration were visible. Tumoral cells were organized in nests and placards (Figure 1). The majority of these cells were epithelioid, but some of them were spindle shaped. We identified high atypia, abundant eosinophilic cytoplasm with enlarged, pleomorphic, irregular and hyperchromatic nuclei (Figures 2 and 3). Some tumoral cells presented multiple nuclei. Prominent eosinophilic nucleoli, necrosis and atypical mitoses were observed (Figure 4). Lymphovascular and perineural invasion were present and the lateral and deep resection margins were infiltrated (Figure 5).

In order to establish a proper diagnosis, a series of immunohistochemical reactions was performed. The tumoral cells showed intense positivity for vimentin-cytoplasmic stain (Figure 6), focal positivity for CD68-membranar stain (Figure 7) and a proliferation index ki67 of 90%- nuclear stain (Figure 8). The immunostaining with markers CK AE1/AE3 (Figure 9), S100, SOX10, HMB45, MelanA, CD31, Desmin and SMA were negative. The final diagnosis, after analyzing the histological appearance and immunohistochemistry profile, was pleomorphic dermal sarcoma.

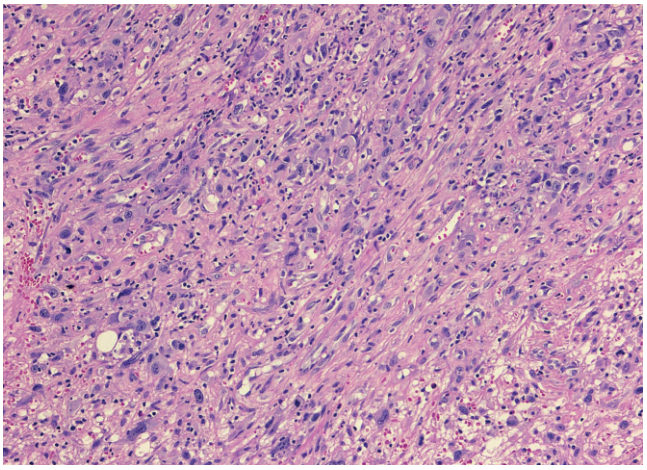

Figure 1. Solid architecture with nesting phenomenon. Epithelioid cells are observed. Hematoxilin&Eosin stain, 5x.

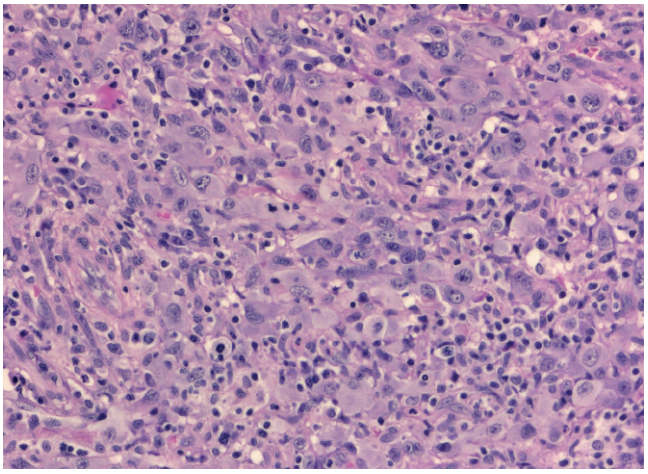

Figure 2. Epithelioid tumoral cells present a pale-eosinophilic cytoplasm with highly pleomorphic nuclei. Hyperchromasia is observed. Hematoxilin&Eosin stain, 10x.

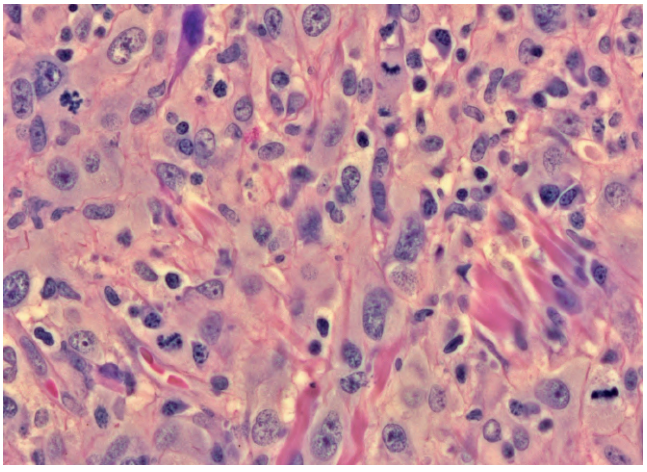

Figure 3. Highly atypical tumoral cells with hyperchromic nuclei and prominent, eosinophilic nuclei. Mitoses are observed. Hematoxilin&Eosin stain, 40x.

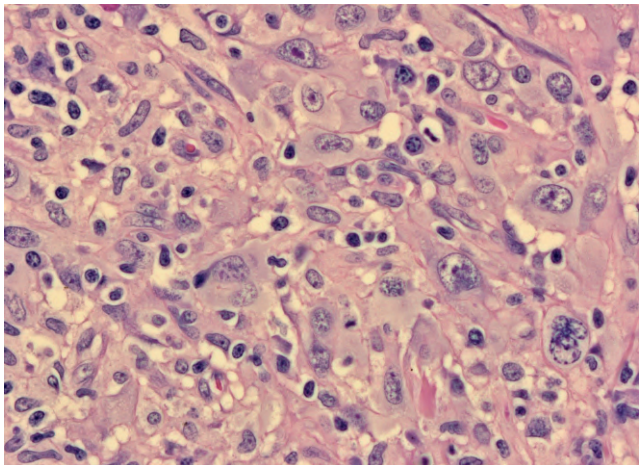

Figure 4. Multinucleated tumoral cells. Hematoxilin&Eosin stain, 40x.

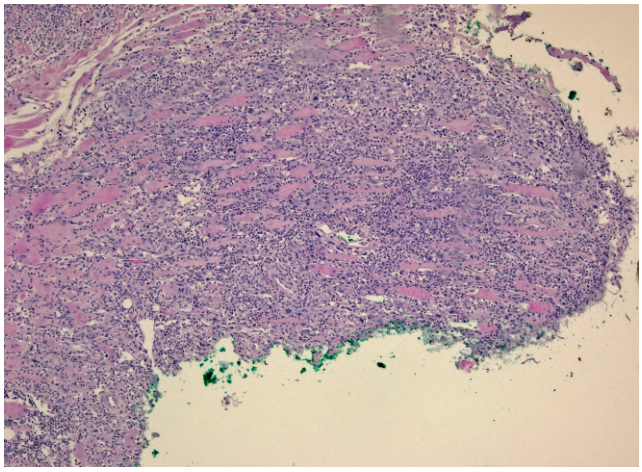

Figure 5. Surgical resection margin infiltrated by the tumoral cells. Hematoxilin&Eosin stain, 5x.

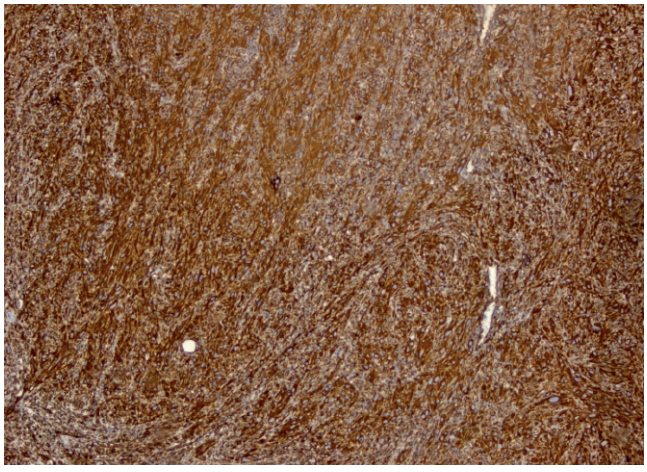

Figure 6. Immunohistochemistry staining with vimentin, 5x.

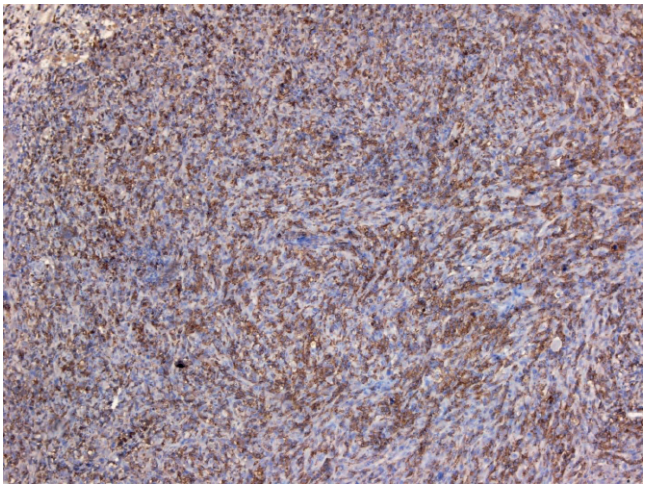

Figure 7. Immunohistochemistry staining with CD68, 5x.

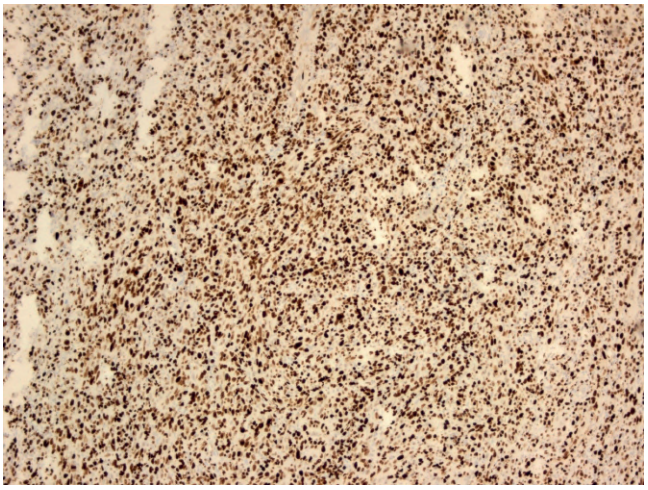

Figure 8. Immunohistochemistry staining with ki67, 5x.

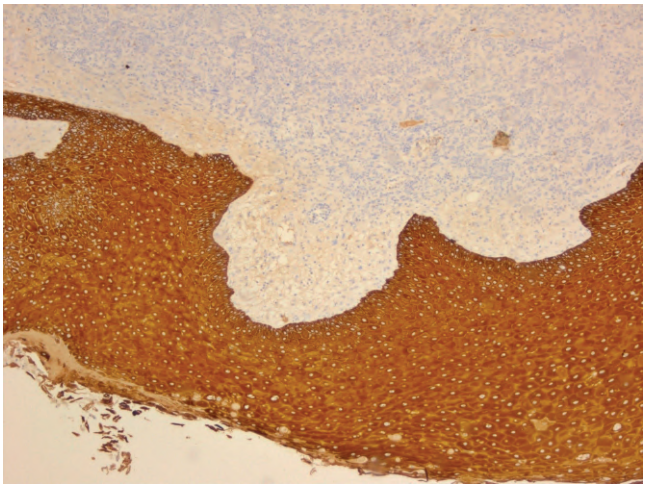

Figure 9. Immunohistochemistry staining with CTK AE1/AE3-positive reaction in the epidermis, negative in the tumoral cells, 5x.

We established the required differentiation score by using parameters specific for this type of sarcoma, according to FNCLCC criteria, AJCC 8th edition 2017: grade of tumoral differentiation- 3 points, necrosis below 50%-1 point, mitosis of 43/20 HPF- 3 points, with a total score of 7. The sarcoma was the 3rd grade of malignancy.

DISCUSSION

A study conducted by Miller showed that the majority of patients were males and the median age of presentation was 81, with a ratio between male and female patients of 7:1. The most frequently involved area of the body was the scalp, which was also the case for our patient. Other areas affected were the forehead, temple and the eyebrow. Most of the tumors were large, with a range from 7 mm up to 60 mm in dimension. In our case, the tumor's largest dimension was 45 mm [13].

Clinically, most cases reported ulceration and bleeding, along with rapid growth. In the case presented, ulceration was a feature of the lesion.

Histopathologically, in the same study conducted by Miller, 32 tumors were reported to be located in the dermis and presented irregular outlines, data in concordance with the description of our case. Tumors were extended towards the epidermis and the Grenz zone was not visible. In most of the tumors, ulceration was observed. In our case, the tumoral cells were distributed in the entire thickness of the dermis and extended towards the epidermis. In 19 of the cases, the tumoral cells infiltrated the subcutis. In our case, the tumor also extended in the subcutis, reaching the underlying muscle tissue[13-15].

In literature, the shape of the tumoral cells is described as epithelioid and spindle, while the cytoplasm of the cells is described as abundant and pale. The tumoral cells in our case showed the same characteristics. Most of them were epithelioid, only a few presented spindle shape[16-18].

Regarding the nucleus, it is known that they have a bizarre shape and prominent eosinophilic nucleoli, feature that makes the differential diagnosis with melanoma almost impossible in the usual stain. Multinucleated tumoral cells are also described. Our case presented enlarged, hyperchromic nuclei, with high pleomorphic and eosinophilic nucleoli. Atypical multinucleated cells were also observed. The mean mitotic activity examined on 10 HPF is described in many

cases to be around 20, while our case presented 43/20 HPF, in concordance with the data. Also, in majority of the cases, necrosis was reported, a feature which is very important for the differential diagnosis, especially with melanoma. Our case showed necrosis in less than 50% of the tumor[19-20].

Immunohistochemistry is extremely important for establishing a diagnosis. After analyzing the aspect on the usual stain, we took into consideration the following lesions: melanoma, poorly differentiated squamous cell carcinoma and sarcoma. We performed vimentin, CK AE1/AE3 and SOX10 to orientate the diagnosis. Pleomorphic dermal sarcoma is negative for all cytokeratin antibodies including the high molecular weight cytokeratin and the cytokeratin cocktail AE1/AE3. The tumor showed no positivity for AE1/AE3 for our patient either, excluding epithelial origin. SOX10 was also negative, which excluded melanocytic origin. Vimentin was positive for all tumoral cells, confirming the mesenchymal origin, and orientated our diagnosis towards a sarcoma[21-22].

Studies postulate that no staining reaction is observed for S100, HMB45, Desmin, CD34 and caldesmon. All this markers, along with SMA and CD31 were negative in our case. By comparison, the literature describes positivity in a large number of cases for SMA. A few cases that presented MelanA positivity were described, but for our case, this marker was also negative. In the light of these investigations and results, we established the diagnosis of pleomorphic dermal sarcoma[23-24].

The outcome of the tumor is uncertain. There are only a limited number of cases described so far and the perspective of the research changed over years. A study conducted by Tardio highlighted the problem that positive resection margins represent lead to recurrence in 20% of the cases. Another 20% presented distant metastases to other sites of the skin, in the lungs or regional lymph nodes. All the cases from the studies mentioned above were located in the head region, more precisely the scalp and the forehead. In our case, the surgical margins were positive and perineural and lymphovascular invasions were present. These parameters are negative prognostic factors for the patient[25-30].

CONCLUSION

The purpose of this case is to highlight the histological and immunohistochemistry aspect of pleomorphic dermal sarcoma. The tumor is a malignant mesenchymal neoplasm which requires a detailed analysis and it is very rare, with only few cases described so far. The known aggressivity and high risk of recurrence demands a fast and clear diagnosis, which is possible with the help of immunohistochemistry.

Compliance with ethics requirements: The authors declare no conflict of interest regarding this article. The authors declare that all the procedures and experiments of this study respect the ethical standards in the Helsinki Declaration of 1975, as revised in 2008(5), as well as the national law. Informed consent was obtained from all the patients included in the study.

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