Pathology – Research and Practice 213 (2017) 161–164

Contents lists available at ScienceDirect

Pathology – Research and Practice

journal homepage: www.elsevier.com/locate/prp

Case report

Primary pulmonary/pleural melanoma in a 13 year-old presenting as pleural effusion

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ARTICLE INFO

Article history:
Received 16 August 2016
Received in revised form 22 October 2016
Accepted 11 November 2016

Keywords:
Melanoma
Visceral
Pediatric
Cytology
Immunocytochemistry
Pulmonary/pleural

ABSTRACT

Melanoma in children, adolescents, and young adults is uncommon and reported almost exclusively as cutaneous melanoma. Melanoma presenting as a pleural effusion is very rare in adults and not reported in the pediatric population. Additionally, primary pulmonary melanoma is overall very rare and undocumented in pediatric patients. Furthermore, the distinction between a primary pulmonary/pleural melanoma versus a regressed cutaneous melanoma with pulmonary/pleural metastases remains extremely challenging. We discuss a case of a previously healthy 13-year-old girl that presented with a left-sided pleural effusion. Investigations revealed a large mediastinal mass, left-sided pleural and pulmonary nodules, a sacral mass, and bone marrow infiltration. The neoplasm was subsequently diagnosed by morphology and immunocytochemistry with histological correlation as malignant melanoma. As no mucosal, eye, or cutaneous lesions were identified, we deliberate the likelihood of a regressed cutaneous melanoma with metastases versus primary pulmonary/pleural melanoma with pleural effusion and discuss its diagnostic approach.

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1. Introduction

Worldwide, approximately 160,000 melanoma cases are diagnosed annually [1]. However, melanoma in children, adolescents, and young adults is rare, representing only 1.2% of malignancies in children under 15 [2] and 1–4% of melanomas [3], an incidence of roughly 5–6/million in patients younger than 20 years of age [4]. Children and adolescents (age 0–17 years) have accounted for only 1.3% of the cases of cutaneous melanoma in the United States during the past two decades [5]. However, there is no data in the literature regarding visceral melanoma in children. Metastatic melanoma with an unidentified primary represents 4% of all newly diagnosed cases of melanoma in adults [6]. However, little is known of about metastatic melanoma with an unidentified primary in the pediatric population [6,7]. One study reported that distant metastases were present in 0.99% (2/203) of melanomas in 10–14 year-olds while another study showed zero patients with distant metastases at diagnosis (0/36) in patients under 20 [7,8].

Pleural effusions are found in a variety of medical conditions including heart failure, infections, malignancies, and trauma [9]. Metastatic melanoma constitutes about 5% of all secondary malignancies of the lung [10], yet only 2% of patients with thoracic metastases have pleural effusions [11]. Primary melanoma of the lung/pleura is even more rare [12,13], and to date has not been reported in children.

We discuss a previously healthy 13-year-old girl presenting with pleural effusion diagnosed by morphology and immunocytochemistry with histological correlation as malignant melanoma representing the first case report of Primary pulmonary/pleural melanoma in the pediatric population.

2. Materials and methods

A literature review was conducted on Medline, with two search items exploded, 'melanoma' and 'neoplasm metastases/metastases', resulting in 98,233 and 268,314 items respectively. The term 'children' was focused, giving 792,563 papers. When all three terms were combined and limited to English, 108

Abbreviation: PEComa, perivascular epithelioid cell tumor.

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http://dx.doi.org/10.1016/j.prp.2016.11.013
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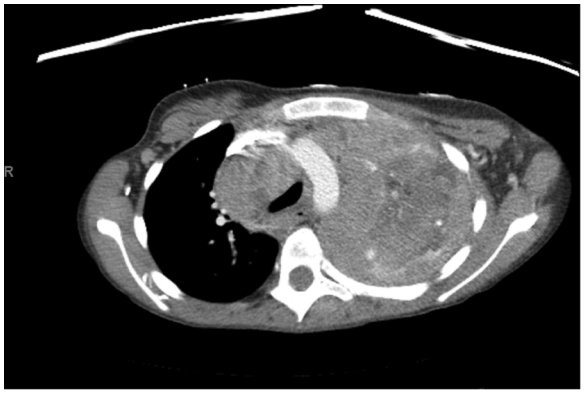

Fig. 1. CT scan image of a pleural based mass of the left lung that is markedly thickened and nodular and encompasses the entire pleura.

papers remained. The primary papers were analyzed with inclusion of all relevant secondary references

3. Results

The patient presented with a one-week history of nausea, fatigue, and progressive pain predominantly in her left shoulder and upper back. On physical exam, she was pale with no apparent distress and normal vitals except for an oxygen saturation of 96% on 3L. No increased work of breathing was observed, but there was no significant air entry in the bases and mid areas of the chest. On percussion, there was bilateral dullness, especially over the middle to bases of both lungs. Vocal fremitus and resonance were markedly decreased bilaterally. No skin lesions were identified.

Investigations showed an elevated white blood cell (14.1) and neutrophil (10.5) count. Chest x-ray showed a large left pleural effusion. Chest CT showed a large mediastinal mass predominantly in the right paratracheal region that was contiguous with right lower neck lymphadenopathy. Multiple pleural based masses on the left side with associated pleural fluid were noted. Nodules were also seen on the surface of the left lung (Fig. 1). In the pelvis, a mass was present involving the left side of the sacrum, extending from L5/S1 centrally to S2, about 4 cm in diameter with remodelling and expansion of the canal.

Pathology specimens sent included pleural fluid for cytology, pleural nodule biopsy, and bone marrow aspirate and biopsy. Pleural cytology showed the presence of scattered, discohesive population of malignant cells with nuclear pleomorphism, binucleation, irregular outlines, central or eccentric hyperchromatic nuclei with coarse chromatin and prominent nucleoli in a background of mixed inflammatory cells including eosinophils (Fig. 2). Pigment was not identified. On cytomorphological features, a differential diagnosis of Hodgkin's versus melanoma was entertained. Immunocytochemistry on the cell block showed neoplastic cells to strongly overexpress S100, HMB-45 and Melan-A (Fig. 3) with no staining to calretinin, CD45, CD30, CD3, and CD20, confirming a melanocytic/neuroectodermal cell lineage (Fig. 4).

Histological examination confirmed a pleomorphic mitotically active epithelioid malignant neoplasm with focal prominent pigmentation (Fig. 5a) and diffuse positivity to S100, Melan A, and HMB45 (Fig. 5b) raising the differential diagnosis of clear cell sarcoma, PEComa (perivascular epithelioid cell tumor), and melanoma. PEComa usually have fewer mitotic figures, lack prominent pigmentation, and are usually negative to S-100. The degree of cytologic and nuclear atypia exceeded that usually seen in clear cell sarcoma. Clear cell sarcoma was excluded as the FISH analysis for EWSR1 gene rearrangement was negative. Malignant melanoma was thus the final definitive diagnosis. No primary lesion was found

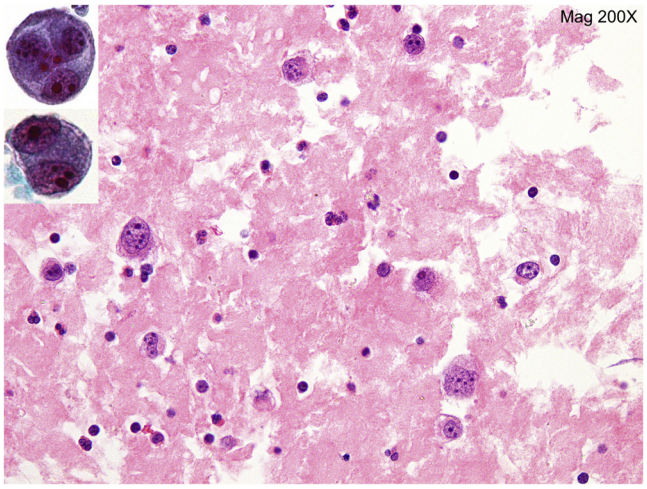

Fig. 2. Photomicrograph of the cytology specimen stained with hematoxylin and eosin (original magnification ×200) showing solitary markedly discohesive atypical cells scattered in a background of mixed inflammatory cells including lymphocytes and eosinophils. Inset shows enlarged single cells with binucleation and prominent nucleoli mimicking Reed Sternberg cells of Hodgkin's lymphoma.

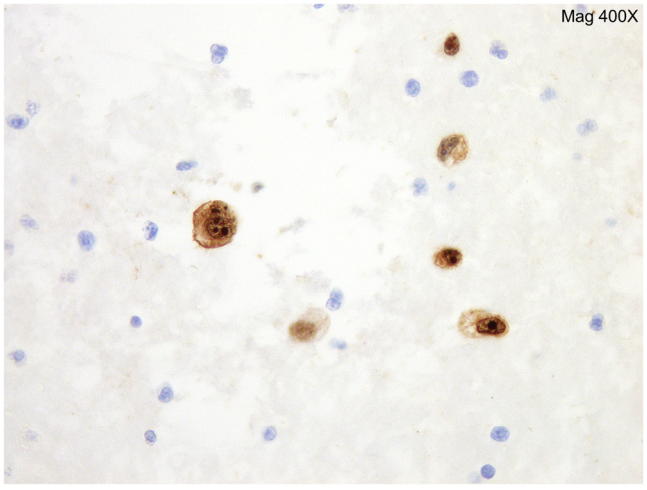

Fig. 3. Photomicrograph of the cytology specimen cell block with immunocytochemical staining with S100 antibodies (original magnification ×400) shows strong overexpression in the atypical malignant cells (similar staining pattern was seen with Melan A and HMB45).

despite a dedicated physical re-examination of the patient, including skin, ocular and mucosal locations. Her initial bone marrow showed infiltration by tumor cells. Despite immunomodulation therapy with Ipilimumab (an anti-CTL4 monoclonal antibody) and some initial improvement (repeat bone marrow showing no tumor cells) she died with progressive metastatic melanoma within 4 months of diagnosis.

4. Discussion

Melanomas can masquerade as poorly differentiated carcinomas, fibrosarcomas, liposarcomas and other histological types of tumor such that the pathologist must 'think melanoma' in order to diagnose melanoma [14]. In smear cytology preparations 'melanoma cells' present as singly scattered cells with a round central or eccentric nucleus, coarse chromatin, prominent nucleoli, and variable intracytoplasmic vacuolization. The background environment can be dirty, necrotic, hemorrhagic or inflammatory, as seen in the index case. Cytoplasmic melanin pigment, if present,

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