



Case Report

Metastatic Epithelioid Sarcoma Concomitant with Florid Alveolar Type II Cell Hyperplasia Resembling Primary Papillary Adenocarcinoma of Lung

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Abstract

Epithelioid sarcoma (ES) is a rare and aggressive malignant parenchymal tumour with an uncertain differentiation. Histopathologically, two clinicopathological subtypes are recognized: classical (or distal) and proximal forms. The classical ES is characterized by its predilection for acral sites and a pseudogranulomatous growth pattern. The proximal ES occurs mainly in truncal regions and shows nests and sheets of large epithelioid cells. Herein, we reported a 38 year-old man who had a proximal-subtype ES with lung metastases that displayed metastatic ES concomitant with florid alveolar type II cell (ATII) hyperplasia. Initially, this pathologic feature was tentatively diagnosed a primary papillary adenocarcinoma of lung in frozen sections. Metastatic ES was confirmed by its immunophenotype showing immune reactivity for vimentin and cytokeratin markers but not TTF1 and INI1. The ATII hyperplasia expressed TTF1 and cytokeratin markers. Both metastatic ES and ATII expressed epidermal growth factor receptor proteins. To our comprehensive review, this finding regarding metastatic ES induced florid ATII hyperplasia is the firstly reported. It would be a pitfall for tumour diagnosis when a small tissue sampled by routine lung biopsy or during frozen section examination. This possible relationship between metastatic ES and ATII hyperplasia is discussed.

Keywords: Epithelioid Sarcoma; Alveolar Type II Cells; Epidermal Growth Factor Receptor.

Introduction

Epithelioid sarcoma (ES) is a rare and aggressive malignant parenchymal tumour with an uncertain of etiology. The incidence is less than 0.05 per 100000 people and the prevalent rate is less than 1% of all soft tissue sarcomas in adults [1]. ES shows an aggressive behaviour due to high recurrent rates and metastases to the lymph nodes and visceral organs, including bone, liver and lungs. The five-year overall survival rate of patients with primary localized disease is approximately 60%, whereas survival rate

drops to 24% in patients with metastatic ES [1].

ES tumorigenesis was associated mainly with almost complete loss of SMARCB1/INI1 (SWI/SNF-related matrix-associated actin-dependent regulator of chromatin subfamily B member 1)/INI1 (Integrase Interactor 1), which biologically involved cell cycle regulation and maintenance of genomic stability [2]. The INI-related alternative mechanisms played a role in negatively regulating the cell-cycle genes or epidermal growth factor receptor (EGFR) signals [2-4].

Histopathologically, clinicopathological subtypes are composed of both classical and proximal ES. The classical

ES is characterized by its predilection for acral sites and pseudogranulomatous growth pattern. The proximal ES occurs mainly in truncal regions and shows nests and sheets of large epithelioid cells. Despite of ES classical and proximal subtypes, a typical immunophenotype displays immune reactivity for CK8 and CK19, focally expression for CK5/6, and total loss of INI1 nuclear expression and most cases show CD34 proteins [5].

Herein, case reported a 38 year-old man having a proximal-type ES with bilateral lung metastases, which showed a rare histopathology that florid alveolar type II cell (ATII) hyperplasia was always concomitant with metastatic ES. This would be a pitfall that pathologic feature resembled a primary papillary adenocarcinoma of lung. This possible relationship between metastatic ES and ATII will be discussed in this case report.

Case report

A 38-year-old male was a farmer, who had a cutaneous ES, measuring 2.5x1.1x1.1 cm and underwent a wide excision in 2015. Next year, tumour recurrence and metastasis of left pelvic bone occurred and he took medicine tazemetostat (EZH2 inhibitor) from November 2017 to November 2018. Due to disease progression, the anticancer drug was changed to oral endoxan, then, pazopanib on 14 Mar 2019. After a period of stable disease, this patient had unspecified multiple nodules of bilateral lung parenchyma and mediastinal lymph node metastasis identified on the computed tomography. He accepted a wedge resection of lung nodules for tissue diagnosis on 9 Aug 2019. The tentative diagnosis in frozen section showed a primary papillary adenocarcinoma of lung (Figure 1A). After routine tissue processing, tumour histopathology showed multiple nodular masses composed of large epithelioid tumour cells with two growth patterns. One growth pattern exhibited nesting epithelioid tumour cells with hyperchromatic nuclei and prominent nucleoli in a fibrous stroma (Figure 1B). Another growth pattern disclosed cuboidal to columnar epithelioid cells with florid papillary hyperplasia along the alveolar walls (Figure 1C), where nesting epithelioid tumours were present in the interstitium, sub pleura or lymphatic channels (Figure 1D).

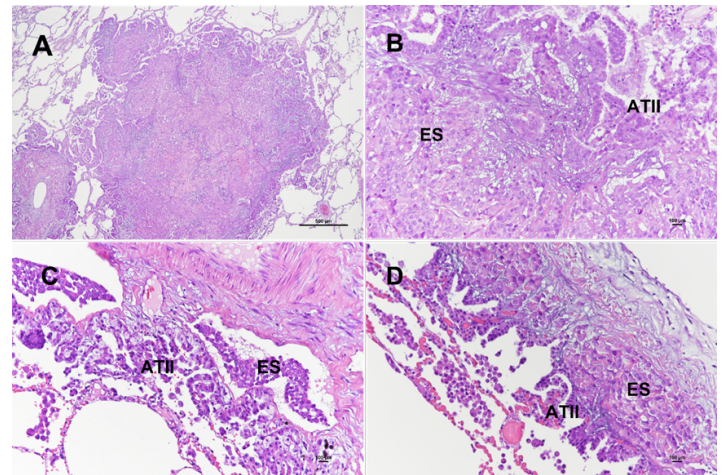


Figure 1: Metastatic epithelioid sarcoma (ES) concomitant with florid alveolar type II cell (ATII) hyperplasia resembling primary papillary lung adenocarcinoma in frozen section (A). Differential morphology between ES cells and ATII hyperplastic cells in high magnification (B). Concomitant ATII hyperplasia beneath lymphatic channels with ES emboli (C) or close to pleura metastasized by ES (D).

Immunohistochemical studies showed different phenotypes between nesting epithelioid tumor cells and papillary hyperplastic epithelioid cells. Papillary hyperplastic cells displayed diffusely positivity for CK, TTF1 (Figure 2A) and INI1 (Figure 2C) but not vimentin (Figure 2B), compatible with ATII hyperplasia. By contrast, nesting epithelioid tumour cells disclosed immune reactivity for CK and vimentin (Figure 2 B) but not TTF1 (Figure 2A); notably, total loss of INI1 nuclear expression (Figure 2C) was observed, compatible with an immunophenotype of ES. Metastatic ES and ATII both showed EGFR expressions (Figure 2D). Accordingly, the final pathology diagnosis was metastatic epithelioid sarcoma concomitant with ATII hyperplasia.

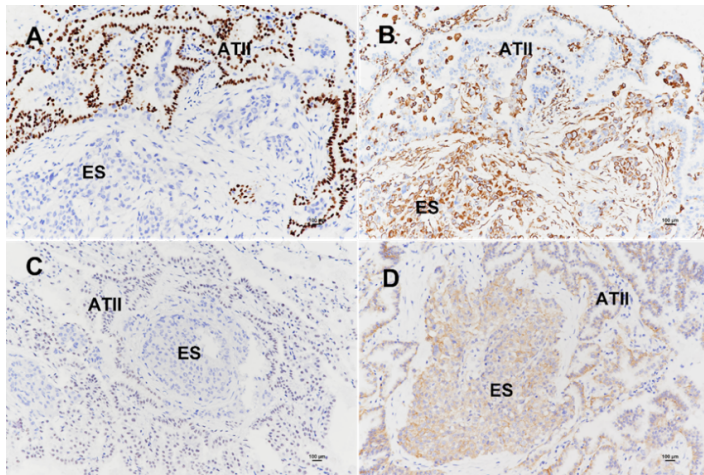


Figure 2: Immunophenotype between ES and ATII hyperplasia. A: TTF1 positivity for ATII but not ES cells. B: Vimentin positivity for ES but not ATII cells. C: INI1 lost nuclear expression for ES but not ATII cells. D: EGFR positivity for both ES and ATII cells. Immunohistochemistry, chromogen showing a brown colour.

This patient enrolled into a clinical trial of onivyde plus TAS-102 (Lon surf) since 11 Dec 2019. On 2 Dec 2019, the image survey demonstrated that his disease still progressed with multiple distant metastases of organs including bilateral kidneys, bones and liver in addition to bilateral lungs. Thus, he ended of treatment on 22 Jan 2020.

Discussion

To our review, the pathologic feature of florid ATII hyperplasia concomitant with metastatic ES was the firstly described. Lung is one of common metastatic sites of malignancies; however, the concomitant ATII hyperplasia is not often identified. Furthermore, this picture implied on metastatic ES cells secreting growth factors or cytokines, that directly or indirectly induced the ATII hyperplasia [2,6]. ES tumorigenesis is associated with loss of SMARCB1/INI1 protein expression [2]. INI1 negatively controls cyclin D1, E2F and AURKA expression, leading to tumour cell proliferation. Besides impaired chromatin metabolism, ES features alterations in several signalling pathways, including EGFR, c-MET and AKT/

mTOR. In this reported case, metastatic ES and ATII cells both showed the immune expression of EGFR. In one in-vitro study, Gerharz and colleagues found that ES cells could secrete TGF and PDGF showing autocrine or paracrine interactions to EGFR and PDGFR, leading to the ES cell proliferation [4]. Cascio et al. using immunohistochemistry also showed that high expression rate of epidermal growth factor (EGFR) in human ES samples [3]. EGF-induction contributed to cell-cycle progression partly through upregulation of cyclin D1 [7]. Therefore, metastatic ES cells in this case might secrete the EGF that induced the ATII hyperplasia.

Conclusively, this case report firstly shows metastatic ES inducing florid hyperplasia of alveolar type II cells. This pathologic feature might be a pitfall in a small tissue sampled by core needle biopsy or frozen section. Using a combination of tumour histology, immunophenotype and patient's medical history warrants making an accurate diagnosis.

Conflict of interest: None.

References

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