

Cutaneous Metastases from Thymic Carcinoma Primary Tumor: A Rare Case

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Abstract: Cutaneous metastases (CM) are neoplastic lesions of the skin originating from a primary tumor elsewhere. CM originating from primary thymic carcinoma is rare, and its incidence remains uncertain. A case of CM from thymic carcinoma in a 57-year-old man was reported. The patient complained about lumps on the skin of the chest, right shoulder and neck that appeared eleven months before the diagnosis of thymic carcinoma was established. Physical examination revealed tumors on the chest, right shoulder and neck. Histopathological examination results were consistent with CM. An immunohistochemical (IHC) examination was performed to determine the primary tumor, with a positive result for CK7. The diagnosis of thymic carcinoma was established based on the results of enhanced chest CT-scan and immunohistochemistry on lymph node biopsies. The patient was treated with a chemotherapy regimen of cyclophosphamide, doxorubicin, and carboplatin scheduled for six cycles. However, the patient did not survive his third cycle of chemotherapy. Establishing the diagnosis and managing CM are challenging for clinicians. This requires careful historical and physical examination, supported by histopathological examination and specific immunohistochemical marker in accordance with the suspected tumor.

Keywords: cutaneous metastases, immunohistochemistry, thymic carcinoma

Introduction

Cutaneous metastases (CM) are defined as the spread of malignant cells from a primary malignancy to the skin. Skin metastases have been reported with an increasing frequency, ranging from 0.7% to 9% in patients with cancer.¹ The most common malignant tumors that metastasize to the skin were lung carcinoma (24%), colorectal carcinoma (19%), and oral squamous cell carcinoma (19%) in men; while in women CM mostly originated from breast cancer (69%), colorectal carcinoma (9%), melanoma (5%), and ovarian carcinoma (4%).² Thymic carcinoma is an aggressive neoplasm arising from the thymus gland, usually with a poor prognosis.³ It is a rare disease, with an incidence of less than one percent of all cancers in adults.⁴ Metastases at presentation are uncommon, with the pleura being the most frequent site. Extrathoracic spread is observed in less than 10% of all cases, mainly to the kidney, lymph node, liver, brain, adrenal, thyroid, and bones.³ Metastasis to the skin is rare, hence its unknown incidence, and the diagnosis is often challenging.⁵ This case report aims to report a rare case of CM originating from thymic carcinoma.

Case

A 57-year-old male was consulted by the internal medicine department with a chief complaint of painful tumors on the chest, right shoulder and neck. Eleven months prior to the consultation, the patient complained of multiple lymphadenopathies on the right side of the neck, covered by multiple marble-sized tumors overlying the lymphadenopathy after one month. The tumors spread to the chest and neck in two months. The patient also complained of coughing and voice hoarseness. Within two months prior to the consult, the skin lesion increased in number and became painful. The complaint was followed by shortness of breath, voice hoarseness, coughing, and weakness; hence, the patient was treated

by a hematology-oncology specialist. The history of malignancy in the family was unknown. The patient admitted to having a history of smoking as a risk factor.

Physical examination revealed rapid breathing, pale conjunctiva, increased jugular venous pressure, asymmetrical chest movement, diminished vesicular breathing sound on the left hemithorax, and multiple immobile and non-tender lymphadenopathies in the anterior and posterior sides of the neck and around the cervical region. Dermatological status revealed multiple tumors on the chest, right shoulder and neck with well-defined border and serous crust found on several tumor surfaces (Figure 1). In the internal medicine department, the patient had undergone several examinations; chest radiography showed right pleural effusion with lymphocytic effusion on cytologic examination, while enhanced chest CT-scan showed a solid mass in the anterior mediastinum, superior vena cava syndrome, and pleural effusion (Figure 2). Histopathological examination of the lymph node revealed metastatic carcinoma in the right supraclavicular region, and immunohistochemistry (IHC) examination of the lymph node was positive for CK7.

The histopathological result from affected skin revealed round, hyperplastic, and hyperchromatic cells in the dermis consistent with metastases to the skin (Figure 3). We continued the immunohistochemical (IHC) staining to find the primary tumor, resulting in positive CK7. Meanwhile, IHC results for CD5, CD117, p63, CK20, P40, and TTF-1 were negative (Figure 4). It was determined that the primary tumor originated from thymic carcinoma because CK7 was positive on IHC examination of the skin tissue and lymph nodes, and enhanced chest CT-scan revealed a mass in the mediastinum that favors thymic carcinoma.

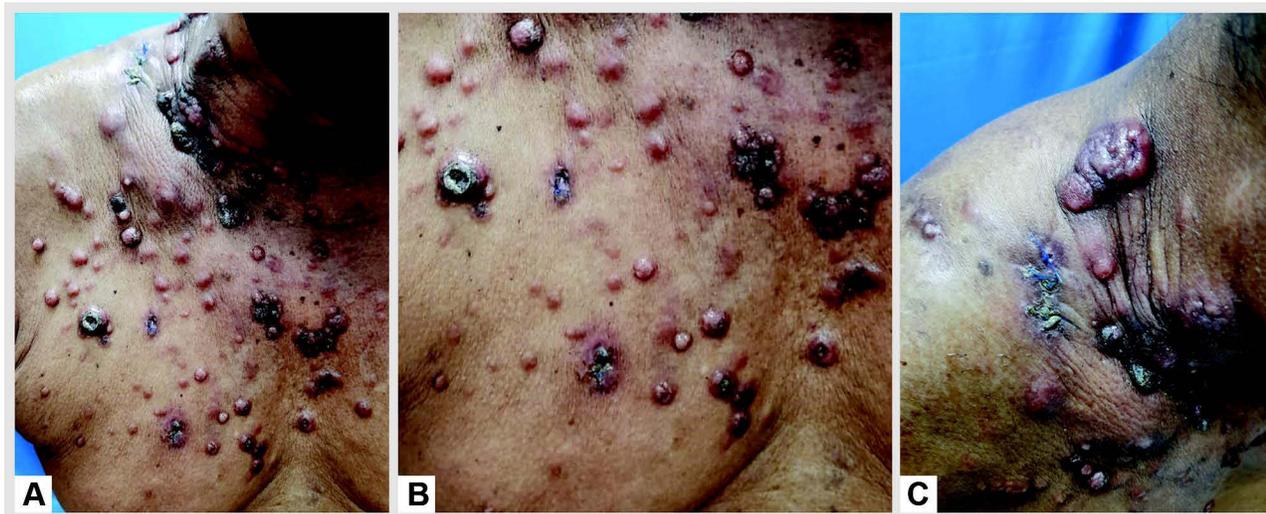


Figure 1 Skin manifestation in form of multiple tumors at right chest (A and B), neck and shoulder (C).



Figure 2 Enhanced chest CT-scan in mediastinal window showed: (A) solid mass in the anterior mediastinum (red arrow) that infiltrate the superior vena cava (blue arrow); (B) right pleural effusion (white arrow); (C) left pleural effusion (yellow arrow).

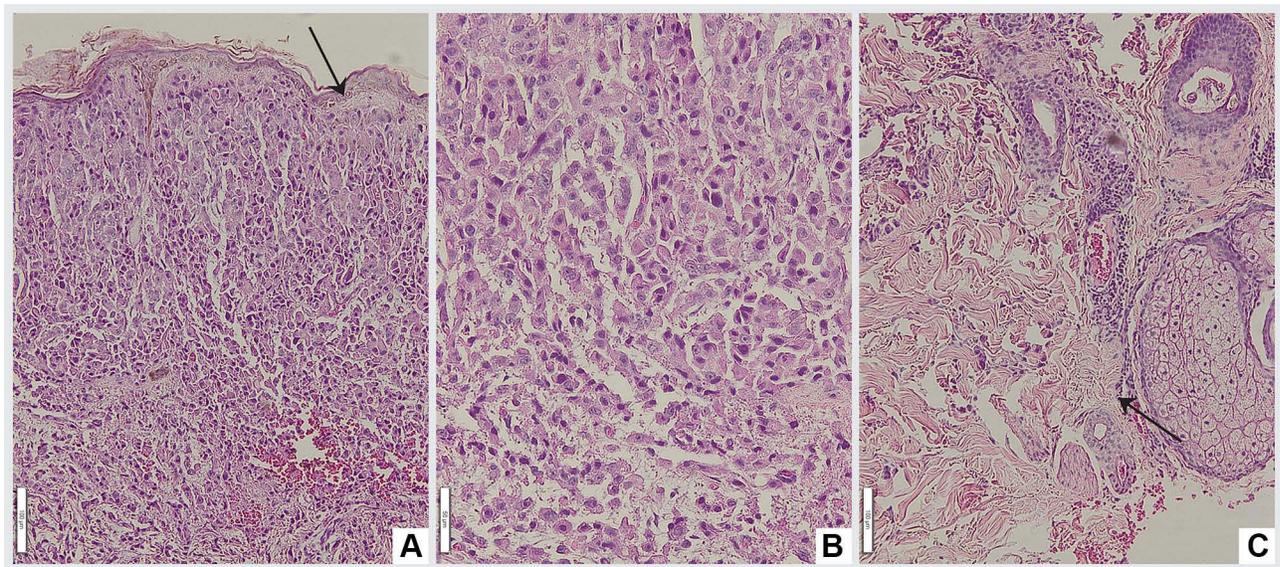


Figure 3 Histopathological result: (A) atrophic stratified squamous cell epithelium (black arrow) in the epidermis; (B) round, hyperplastic and hyperchromatic cells in the dermis; (C) subcutaneous tissue consisting of fibrodysplastic connective tissue (black arrow).

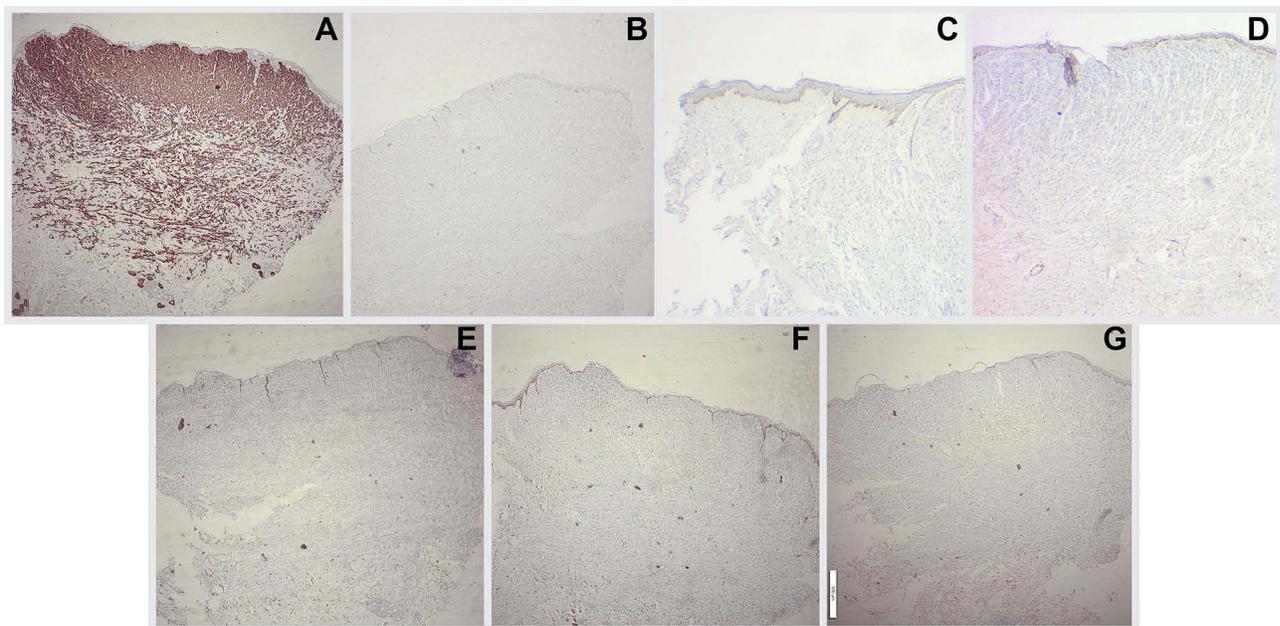


Figure 4 Immunohistochemistry staining result: positive for CK7 (A); negative for CD5 (B), CD117 (C), p63 (D), CK20 (E), P40 (F), and TTF-1 (G).

The patient was treated with a chemotherapy regimen of cyclophosphamide, doxorubicin, and carboplatin planned for six cycles. Unfortunately, the patient passed away after receiving only three cycles of chemotherapy.

Discussion

Cutaneous metastases could be diagnosed prior to the diagnosis of primary malignancy (precocious metastases), simultaneously diagnosed along with the diagnosis of primary malignancy (synchronous metastases), or after the primary malignancy is diagnosed (metachronous metastases). Metastases to the skin are more frequently found in older individuals, with the highest incidence occurring in individuals between the age of 50 and 70 years.^{6,7} The diagnosis

of CM on the patient in this case report is established simultaneously with the diagnosis of the primary malignancy (synchronous metastases).

The mechanism of metastatic spread from a primary tumor to the skin has not been clearly understood. Several proposed theories stated that tumor cells reach the skin through direct invasion of the structures underneath the skin, through lymphogenic spread, hematogenic spread, or direct implantation during a surgical procedure.⁸ Metastasis occurs due to the release of cancer cells from the primary tumor, which spread locally and are eventually implanted on a distant site. Separation of cancer cells might occur due to decreased expression of intracellular adhesion molecules. Implantation at a distant site might occur due to the infiltration of cancer cells into the blood vessels, followed by intravasation and angiogenesis.⁹ CM is usually found in close proximity to the primary tumor.¹⁰ The most frequent location for CM is on the anterior side of the chest and abdomen. Other frequently involved body parts include the scalp area and neck.^{8,10} The location of skin metastases in this case report involved the chest, right shoulder and neck. This finding suited the premise regarding the most frequent CM location and that the location was close to the thymus gland as the primary tumor.

A histopathological examination must be conducted to establish the definitive diagnosis after finding skin lesions with a suspicion of CM.^{8,11} The histopathological features of CM include the appearance of malignant cells around the blood vessels, dermis, hypodermis, and along the collagen bundles. Signs of cell malignancy in the histopathological examination include atypical cells marked by increased relative nucleus size compared to the cytoplasm, darker nucleus due to increased DNA content (hyperchromatic), and pleomorphic nucleus with various shapes and sizes. Furthermore, increased mitotic activity was also found.¹² The histopathological examination of the patient in this case report revealed dense hyperplastic cells with partial coarse chromatin, which supported the diagnosis of CM.

IHC examination of CM is required to identify the primary tumor, especially in cases with a non-specific histopathological appearance.^{8,13} Some standard IHC examinations to be tested if the primary tumor is unknown include CD45 for lymphoid tumors, pan-cytokeratin AE1/AE3 for carcinoma, S100 for melanoma, and CD34 for blood vessels malignancy and leukemia.⁸ In our case, the IHC result from the skin biopsy sample was positive for CK7 and negative for CK20, which included the differential diagnoses of primary tumor from the lung, breast, thyroid, mesothelioma, endocrine, thymus, and germ cell origin. IHC examination for TTF-1 was negative, excluding the diagnosis of primary thyroid tumor.⁸ IHC for P40 was also negative, excluding the diagnosis of squamous cell carcinoma of the lung.¹³ In thymic carcinoma, IHC result may be positive for pan-cytokeratin, CK5, CK7, CD5, CD117, and p63.^{4,5} Examination for CD5 IHC was initially presumed to be specific to thymic carcinoma and may distinguish thymic carcinoma from other malignancies. However, in serial studies on thymic carcinoma, positive CD5 results were only found in less than 40% of cases.⁴ Previous studies reported positive immunoreactivity for CD117 in 65–91% of thymic carcinomas, as opposed to 0–5% of thymoma. Kojika et al showed that the positivity of CD117 was 8 out of 11 of thymic carcinoma cases.¹⁴ However, CD117 can be found to be negative in enteric-type adenocarcinoma of the thymus. In this type, tumor cells are negative for TTF-1 and CD117.¹⁵ In our patient, the diagnosis of primary tumor of thymic carcinoma was established based on positive CK7 result from IHC examination of samples taken from the skin and lymph node and enhanced CT-scan finding of mediastinum mass, which supported the diagnosis of thymic carcinoma.

Thymic carcinoma may spread through hematogenous and lymphogenous metastases. In a study involving 72 patients with thymic carcinoma, it was reported that 31% of patients experienced metastases, with the most frequent locations being the pleura (71%), lungs (38%), and lymph nodes (38%). In this published study, no evidence of skin metastasis was reported.¹⁶ Vladislav et al¹⁷ reported that among 35 cases of thymic carcinoma, extrathoracic metastases were found in the lymph nodes, liver, spleen, pancreas, bones, gastrointestinal tract, kidneys, ovarium, breast, central nervous system, and the skin. Choi et al⁵ reported a case of CM from primary thymic carcinoma in a female aged 44 years. The patient had previously undergone thymectomy and radiotherapy. A histopathological examination revealed infiltration of malignant cells, and an IHC examination showed a negative CD5 result.⁵

The management of CM was solely based on the management of the primary tumor.¹¹ In cases of thymic carcinoma metastasizing through the lymphogenous or hematogenous route, the disease should be treated with chemotherapy.³ Combined chemotherapy showed complete and partial resolution. The regularly used combined chemotherapy regimen included cyclophosphamide, doxorubicin, and carboplatin (PAC). This regimen provided a 50% response rate and a complete response rate with a median of 12 months and a 5-year survival rate of 50%.¹⁸ The patient in this case report had received three out of six planned chemotherapy regimen sessions. The patient opted out of continuing chemotherapy sessions due to the worsening condition.

Conclusion

Cutaneous metastasis of thymic carcinoma primary tumor is rare, and establishing the diagnosis and managing such conditions are challenging. Thorough history taking and physical examination are keys to a successful diagnosis. Histopathological examination and specific immunohistochemical marker based on suspected primary tumor should be conducted to diagnose the primary tumor.

Consent for Publication

The patient's family has signed the consent forms for the use of case details, images for publication, and for scientific purposes. The case report has been approved by the institutional ethics committee of Dr. Hasan Sadikin General Hospital, Bandung, Indonesia (Ethical Clearance Number: LB.02.01/X.6.5/120/2022).

Acknowledgments

The authors would like to thank the staff of the Dermatology and Venereology Department, Faculty of Medicine, Universitas Padjadjaran, Bandung, West Java, Indonesia.

Funding

The authors declare that this study has received no financial support.

Disclosure

The authors report no conflicts of interest in relation to this work.

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