

# 1 **Merkel hücreli karsinomun nadir bir presentasyonu**

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## 3 **Özet**

4 Yetmişbir yaşındaki erkek hastanın sırt ağrısı şikayetiyle hastaneye başvurusu  
5 sonrasında yapılan tetkiklerinde sol paravertebral alan ikinci vertebra düzeyinde kitle tespit  
6 edilmiş ve kitlenin en blok rezeksiyonu sonrasında histopatolojik olarak Merkel hücreli  
7 karsinom tanısı konmuştur. Postoperatif birinci ayında manyetik rezonans incelemede aynı  
8 alanda tespit edilen ve inoperabl olarak değerlendirilen kitle hastalığın hızlı ilerlediğini  
9 düşündürdü. Hasta radyokemoterapinin 6. gününde pnömoni sonucunda ortaya çıkan solunum  
10 yetersizliği nedeniyle hayatını kaybetti. Bu çok nadir görülebilecek bir olgu olmakla birlikte,  
11 intratorasik kitlelerin ayırıcı tanısında Merkel hücreli karsinom da düşünülmelidir.

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13 **Anahtar Sözcükler:** Merkel hücreli karsinom, intratorasik, ekstrakütanöz

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## 15 **An unusual presentation of Merkel cell carcinoma**

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### 17 **Summary**

18 We describe a 71-year-old male patient admitted to the hospital with posterior chest  
19 pain. Following the detection of the paravetebral mass on the level of 2<sup>nd</sup> thoracic vertebra,  
20 the patient underwent a surgical en bloc resection of the mass. The histopathologic  
21 examination revealed a Merkel cell carcinoma. One month after the operation, magnetic  
22 resonance imaging showed an inoperable mass in the same location, which indicated a rapid  
23 progression of the tumor. The patient died of progressive respiratory failure due to pneumonia  
24 on the 6<sup>th</sup> day after the onset of the radiochemotherapy. Although this appears to be an  
25 isolated case, Merkel cell carcinoma must be included in the differential diagnosis of  
26 intrathoracic masses.

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28 **Key words:** Merkel cell carcinoma, intrathoracic, extracutaneous

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33 **Introduction**

34           Merkel cell carcinoma (MCC) is an uncommon primary cutaneous neoplasm of  
35 neuroendocrine cells with a predilection for the head and neck and distal extremities in elderly  
36 patients. It is principally a disease of the Caucasian race with an incidence of 0.44 per 100,000  
37 and is very high (8%) among immunosuppressed patients (1,2). The disease course is difficult  
38 to predict and ranges from relatively indolent to highly aggressive, often spreading to local,  
39 regional, and distant sites (3,4).

40           MCC very rarely arises outside the skin. In the literature, the salivary glands, nasal  
41 cavity, lymph nodes, and subcutaneous fat have been reported as the most common  
42 extracutaneous sites (5-8). We describe a 71-year-old man with Merkel cell carcinoma, which  
43 presented as an intrathoracic mass. To the best of our knowledge, this is the first described  
44 case in the English-language literature of such lesion located intrathoracically with no  
45 detectable primary site.

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47 **Case Report**

48           A 71-year-old male presented to the Thoracic Surgery department with a 11-month  
49 history of a left-sided posterior chest pain. He had smoked one pack of cigarettes daily for 35  
50 years but had given up the habit one year before admission. On physical examination, no rash  
51 or lymphadenopathy were detected. Laboratory results and chest radiography were normal.  
52 Computed tomography of the thorax showed a paravertebral mass (41x21 mm in diameter),  
53 extending the neural foramen of the 2<sup>nd</sup> and 3<sup>th</sup> thoracic vertebrae in the apical-posterior  
54 segment of the left upper lobe. The transthoracic fine-needle aspiration biopsy revealed a  
55 malignant tumor. Positron emission tomography scan showed a hypermetabolic malignant  
56 lesion in the apical-posterior segment of the left upper lobe with no hypermetabolic lesions in  
57 the mediastinum (Figure 1). No other lesions, primary or metastatic, were demonstrated.

58           The patient underwent *en bloc* chest wall resection with parietal pleura, facets and  
59 transvers processes of the thoracic vertebrae (2<sup>nd</sup> and 3<sup>th</sup>), and intercostal muscles. On  
60 exploration, the lesion with a lobulated contour appeared to have an invasion to the thoracic  
61 vertebrae and an intrathoracic but extrapulmonary location.

62           The histopathological examination showed a tumor characterized by small indefinite  
63 nests and solid areas consisted of small and round cells with narrow cytoplasm. Tumor  
64 necrosis and tumor thrombi were also recognised. Macroscopically the tumor did not show  
65 bone invasion. At first glance malignant small round cell tumors namely; metastasis of small

66 cell carcinoma, metastasis of melanoma, PNET/Ewing sarcoma and Merkel cell carcinoma  
67 were thought histologically. By the help of immunohistochemistry some of possibilities were  
68 excluded. Cytokeratin 7 and TTF-1 were negative for metastasis of small cell carcinoma, S-100  
69 and HMB-45 were negative for malignant melanoma and CD-99 was negative for  
70 PNET/Ewing sarcoma. Specific cytokeratin 20 positivity with specific globular pattern did  
71 enable us to label the tumor as Merkel cell carcinoma (Figure 2).

72 No suspected skin lesion or lymph nodes were detected after careful physical  
73 examination of the patient. The patient had no history to suggest an immuno-compromised  
74 status and human immunodeficiency virus infection was excluded by the appropriate  
75 laboratory tests.

76 The patient was referred to the Oncology department for adjuvant treatment one month  
77 after the operation. Magnetic resonance imaging of the thorax showed a mass with  
78 dimensions of 28x15 mm in the same location, which was apicomediaally adjacent to the  
79 corpus of the 2<sup>nd</sup> thoracic vertebra, and the mass was also expanding to the neural foramen. It  
80 was thought to be a rapid progression of the tumor. The tumor was inoperable and  
81 concomitant radiochemotherapy was planned. He developed a severe pneumonia six days  
82 after the onset of the radiochemotherapy and died despite the rapid onset of broad spectrum  
83 antibiotherapy two days after the diagnosis of pneumonia.

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## 85 **Discussion**

86 MCC is rare, with estimated annual incidence of 0,2 and 0,45 cases per 100,000 (9).  
87 MCC is extremely rare before age 50 years, after which the incidence increases steeply with  
88 age. The incidence is increased approximately 11-fold for people with AIDS and five-fold for  
89 people who have undergone an organ transplantation (9,10). The risk of MCC may be  
90 particularly high with prior psoralen and UV-A treatment, which reinforces the likely  
91 etiologic role of UV radiation (11). In the current case, there was no such history.

92 Fredrick Merkel described first Merkel cells in 1875 as mechanoreceptors in the basal  
93 layer of the epidermis. An epithelial origin is possible, but some data suggest that Merkel cells  
94 may have a neural-crest origin (12). Cyril Toker has first published a series of skin neoplasms  
95 of elderly with special histologic characteristics between 1966-1970 (13).

96 Microscopically, the tumor nodule of MCC is comprised of small cells with scant  
97 neoplasm, large nuclei, finely granular chromatin. Accurate diagnoses of neuroendocrine  
98 carcinoma is difficult due to its similarity to other poorly differentiated “small blue cell  
99 tumors”, like small cell carcinoma of the lung. Immunohistochemistry is an essential tool in  
100 routine diagnosis of MCC. MCC cells stain negatively for S-100 protein which is positive in  
101 melanoma, for TTF-1 and CK-7 which is positive in small-cell lung carcinoma, and for LCA  
102 which is positive in lymphoma. Combined immunostaining for TTF-1 and CK20 can be used  
103 for differentiating MCC from small cell lung carcinoma (14). A CK20 positive and TTF-1  
104 negative result in a tumor morphologically consistent with MCC establishes the diagnosis  
105 (15). In the present case, diffuse globular CK20 positivity and TTF-1 negativity were  
106 detected. Additionally, MCC cells stain positively for neuroendocrine markers chromogranin  
107 and synaptophysin.

108 MCC almost always arises from the dermis. It occurs extremely rare outside the skin.  
109 In the literature, the salivary glands, lymph nodes, subcutaneous fat and nasal cavity, are the  
110 the reported extracutaneous sites with no detectable skin primary (6-8,16). However, no case  
111 of MCC located intrathoracically with no detectable skin primary have been reported.  
112 Actually, it is very difficult to decide that the intrathoracic mass is primary or metastatic in the  
113 current case. The hypothesis that MCC may originate from a pluripotent cell has gained recent  
114 support. This hypothesis could help to explain the origins of both skin and non-skin tumors  
115 (17).

116 Currently, there is no a standart therapy protocol for MCC. The treatment of choice  
117 depends on the extension of disease. Local excision is prefered in localized disease. Whereas  
118 a wide excision with 2 to 3 cm of tumor free surgical margin is prefered for primary lesions  
119 smaller than 2 cm, adjuvant radiotherapy is suggested for tumors greater than 2cm after  
120 surgical excision. The mortality rate could be decreased in cases with lymphatic metastasis  
121 through irradiation of primary tumor bed and lymph node site after wide local excision and  
122 complete lymphatic node dissection. Chemotherapy is the most common preferred modality  
123 for the treatment of metastatic disease. In stage IV MCC, cisplatin, doxorubicin, and  
124 vincristine or the combination of etoposide and platinum are the most common agents used  
125 for chemotherapy (18-20).

126 MCC is a rare, neuroendocrine cancer of the skin. Primaries in other sites may also be  
127 seen. MCC from unknown primary site is an extremely rare entity. Although the presented  
128 patient appears to be an isolated case, MCC should be thought in the differential diagnosis of  
129 intrathoracic extrapulmonary malignant masses even without an identifiable primary site.

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190 Figure 1: A: Computed tomography scan shows the left intrathoracic mass B: Positron  
191 emission tomography and superimposed computed tomography scan shows the left  
192 intrathoracic hypermetabolic malignant mass.

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199 Figure 2: A: Solid tumor areas composed of atypical small round cells (HEx200). B: Globular  
200 cytokeratin 20 positivity in cytoplasm of tumor cells (Immunoperoxidase  
201 cytokeratin 20 x 400).

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