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A Case of Pulmonary Capillary Hemangiomatosis in a Worker with Exposure to Foundry Dust and VOCs

Döküm Dumanına ve Uçucu Organik Bileşiklere Maruz Kalım ile ilişkili Olabilecek Pulmoner Kapiller Hemanjiomatozis Olgusu

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Abstract

Pulmonary capillary hemangiomatosis (PCH) is a rare and progressive vascular disease of the lung that causes pulmonary hypertension, as they frequently overlap. The occupational risk factor associated with PCH is rarely discussed. In the present report, three of the eight patients admitted from the same company had similar radiological findings, and one agreed to undergo a biopsy. A 40-year-old male who was working as a foundry worker with no symptoms underwent CT, which showed moderate peribronchial thickening in both lungs and a mosaic perfusion pattern in the lower zones. There was no evidence of right heart failure. A microscopic examination of the lung by thoracoscopic resection showed capillary-like vascular proliferation in the alveolar septa. As there were workers with similar radiological findings from the same company he was diagnosed with occupational PCH. The etiology of PCH remains unknown. Occupational exposure should be kept in mind if a disease does not meet the classic epidemiological characteristics.

Key words: *Foundry, Occupational disease, foundry dust, VOC.*

Özet

Pulmoner kapiller hemanjiomatozis (PKH) nadir görülen, ilerleyici ve çoğunlukla pulmoner hipertansiyon ile birlikte bulunan akciğerlerin vasküler bir hastalığıdır. Hastalıkla ilişkili mesleksel risk faktörleri ile ilgili araştırma azdır. Aynı işletmeden başvuran 8 olgunun 3 'ünde benzer radyolojik bulgulara rastlandı, olguların yalnızca bir tanesi akciğer biopsisini kabul etti. Kırk yaşında erkek olgunun herhangi bir yakınması yoktu. Bilgisayarlı tomografide her iki akciğerde orta derecede peribronşiyal kalınlaşma ve alt bölgelerde mozaik perfüzyon paterni izlendi. Kardiyak değerlendirmede sağ kalp yetmezliği saptanmadı. Akciğer biopsisinde alveolar septada kapiller benzeri vasküler proliferasyon görünümü izlendi. Aynı işletmeden benzer 3 radyolojik bulgu olması ve literatür bulguları eşliğinde mesleksel maruz kalım ile ilişkili PKH olgusu olabileceği düşünüldü. PKH etiyolojisi halen bilinmeyen bir hastalıktır. Mesleki maruziyetler PKH için potansiyel bir risk faktörü olarak bildirilmektedir. Herhangi bir hastalık için bilinen klasik epidemiyolojik özelliklerin karşılanmadığı durumlarda mesleki etiyolojinin değerlendirilmesi unutulmamalıdır.

Anahtar Sözcükler: *Döküm, meslek hastalığı, döküm dumanı, uçucu organik bileşikler.*

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Pulmonary capillary hemangiomatosis (PCH) is a rare disease with unknown etiologies. It mostly manifests progressive dyspnea, hypoxemia and pulmonary hypertension due to refractory capillary proliferation within the alveolar septae. PCH has been identified in patients aged from newborn to 71 years in literature (1,2).

In radiological assessments, basilar reticulonodular opacities and large-sized ground-grass opacities are common, while air-trapping, cystic lesions and focal bronchiectasis may also be observed in the whole lung fields, mimicking an airway-disease pattern. PCH remains challenging to treat. New agents are currently under examination with positive results (3).

Only around 100 cases of PCH have been reported to date. The cause or risk factors of PCH are yet to be clearly identified, although some cases have suggested an association with connective tissue diseases or hereditary origins (4,5). There have been two different hypotheses put forward with regard to the etiology of PCH. The first suggests a neoplastic process, while the other, a secondary change due to other diseases. Occupational risk factors have rarely been discussed (6,7).

In 2018, eight workers from the same factory were referred to the outpatient clinic with suspicion of pneumoconiosis. A work history and job analysis, a qualitative exposure assessment (QEA), PPE use, and any specific self-reported exposure to high-risk substances were obtained by occupational medicine specialists (Table 1). Of the eight workers, three had similar radiological findings, although only one patient agreed to a lung biopsy. In this case report we present a case of PCH diagnosed by biopsy to draw attention to the occupational risk factors in the etiology of PCH.

CASE

A 40-year-old married male, living in Manisa and with four healthy children, had been working at a foundry factory since 2016. A normal physical examination revealed no symptoms. He reported a 15 pack years smoking history, and but had quit 2 years ago. PA Chest X-ray: digital graphy, quality 1, p/s 1/0 (Figure 1c). Thorax HRCT: Moderate peribronchial thickening in both lungs and a mosaic perfusion pattern in the lower zones (Figure 1a and b).

Respiratory functional test (RFT) (% predicted): FEV1: 3.39 L (97%), FVC: 4.17 L (99%), FEV1/FVC: 85%, PEF: 6.17 L (101%), DLCO test normal

The patient's work history and job analysis is presented in Table 1. He had been working as a foundry operator since 2016, before which, he was employed in the leather sector. He was exposed to high risk of VOC in both work histories. No health records were available from the leatherworking period. Health records were obtained from the last workplace. According to the documents submitted by the occupational physician (initial and periodical examination forms): normal, RFT, and blood tests were normal, ILO assessment quality 2, p / p 1/1 (January 2019).

A biopsy was planned due to the patient's work history and atypical radiological findings.

A video thoracoscopic wedge resection of the right bottom lobe was performed for histopathologic diagnosis. A microscopic examination of the lung wedge resection showed patchy involvement of pulmonary capillary hemangiomatosis (H&E, X1.25) (Figure 2a); a capillary-like vascular proliferation in the alveolar septa with hematoxylin & eosin sections and CD34 in pulmonary capillary hemangiomatosis (Figure 2b and c); and a thickening of vessel walls in pulmonary capillary hemangiomatosis (H&E, X10) (Figure 2d). The findings were consistent with PCH.

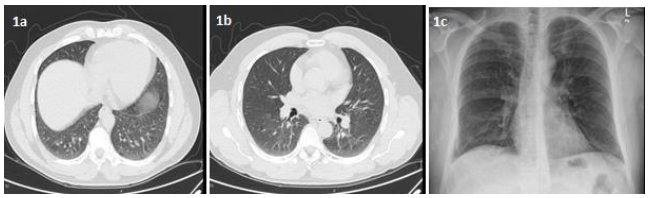

Figure 1a, b and c: *Radiological imaging of the case; Thorax HRCT images show that moderate peribronchial thickening in both lungs and mosaic perfusion pattern in the lower zones (a and b), PA chest X-ray, ILO classification: p/p 1/1*

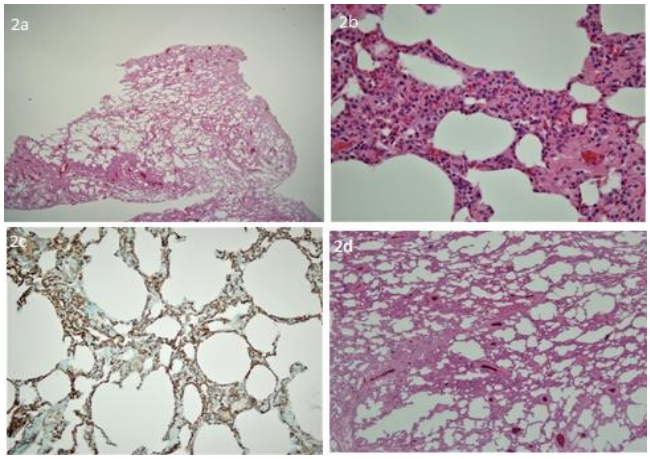

Figure 2a, b, c and d: *Histologic findings of the case; patchy involvement of pulmonary capillary hemangiomatosis (H&E, X1.25) (a), capillary-like vascular proliferation in alveolar septa with hematoxylin & eosin sections and CD34 in pulmonary capillary hemangimatosis (b and c), thickening of vessel walls in pulmonary capillary hemangiomatosis (H&E, X10) (d)*

Tablo 1: Work history and job analysis

Job	Task	Time	Suspected Risks	Occupational Hygiene Measurements	QEA*
2016-ongoing Foundry operator	Cleaning	1 h/per shift	Dust (silica, mix metal dust, graffits)	Poor	Medium
	Melting and pouring metal into molds	4 h/per shift	Heavy metal dust (aluminum, iron, lead)	Poor	High
	Removing castings from molds and dressing castings (para-occupational exposure)	8h/per shift	Silica and organic solvents	Poor	Low
Between times (1995-2016) Leather sector	Leather Tanning and Processing	8h/per shift	Chemical risks (Chromium, sulfuric acid, leather dust, H2S, DDT, formaldehyde, phenols)	Very poor	High

**: Qualitative Exposure Assessment by occupational medicine specialist*

Cardiology assessment: Normal cardiac function, EF%60; right and left ventricles normal; and normal pulmonary wedge pressure. The patient had no symptoms or laboratory findings associated with connective tissue disorder.

He was diagnosed with occupational PCH due to the fact that the initial and periodic examinations were normal (based on the principle of temporal relationship in the diagnosis of OD), and workers with similar radiological findings were employed in the same enterprise (based on the principle of having cluster case groups in the diagnosis of OD). The case was reported to the Social Security Institution.

DISCUSSION

PCH is a rare disease that is classified as a subgroup of pulmonary arterial hypertension. We identified pathologically diagnosed PCH in a young male who was exposed to occupational risk factors (mixed foundry dust and volatile organic solvents) without elevated right ventricular systolic pressure.

The etiology of PCH remains unknown, and the occupational risk factors associated with PCH are rarely discussed. Montani et al. (6) conducted a case-control study using the job-exposure matrix (JEM), and stated that occupational exposure to organic solvents (trichloroethylene) may be a risk factor for PCH. Yeo et al. (7) reported the case of a female worker who had worked in a bathtub factory without proper respiratory protection. The authors stated that based on her occupational history, the worker could have been exposed to silica or organic solvents. A lung biopsy and revealed a microscopic atypical proliferation of capillary channels within the alveolar walls.

Bone morphogenetic protein receptor type 2 (BMPR2) gene and bi-allelic EIF2AK4 mutations have been identified as the main predisposing factor behind heritable PCH (8). We did not perform this test; however there was no family history of any suspected respiratory or cardiac diseases.

Most cases of PCH present with pulmonary hypertension and progressive clinical symptoms, aside from in a few reports (1,9). The typical clinical course of PCH includes rapid deterioration due to the progressive increase in pulmonary artery pressure, which leads to right ventricular failure and death. The uncontrolled proliferation of pulmonary capillaries infiltrating the vascular, bronchial and interstitial pulmonary structures could be a reason for this (10). Our case has no PHT findings, even on echocardiography. In the present case, the histology revealed capillaries infiltrating the alveolar and bronchial walls and a moderate thickening of the vessel wall, which may have contributed to the maintenance of pulmonary blood flow in the early stage of the natural disease course.

Radiographic findings are typically nonspecific and include changes consistent with pulmonary hypertension. Chest HRCT scans usually show lobular ground-glass opacification in the area of increased pulmonary perfusion, a mosaic pattern of attenuation of pulmonary parenchyma and a thickening of the interlobular septa (11). In our cases, a mosaic perfusion pattern was dominant, but the other suspected cases also had centrilobular

ground-glass opacities. The definitive diagnosis of PCH is based on histopathological findings (12).

Finally, it is necessary to state how OD is diagnosed. We evaluate according to causality criteria in occupational disease evaluation. The various definitions, however, have two main mandatory elements in common: the fact that the disease occurs in groups of exposed workers with a higher frequency rate than in the rest of the population; and the temporality criteria that define the exposure of interest preceded the disease by a period of time (13). Our case met these two main criteria, being diagnosed with occupational PCH based on clinical and radiological findings, besides his occupational history.

CONCLUSION

We explain here the pathological diagnosis of PCH. The worker had been exposed to occupational chemical risks. We were unable to assess other workers from the same company, although this group may lead to the identification of a new disease associated with occupational exposure. The occupational etiology should be kept in mind if a disease occurs at the same time in a group of workers that does meet the classic epidemiological characteristics.

CONFLICTS OF INTEREST

None declared.

AUTHOR CONTRIBUTIONS

Concept - A.C.B., A.C., D.G.; Planning and Design - A.C.B., A.C., D.G.; Supervision - A.C.B., A.C., D.G.; Funding -; Materials -; Data Collection and/or Processing - A.C.B.; Analysis and/or Interpretation - A.C.B., A.C., D.G. A.C.B., A.C., D.G.; Literature Review - A.C.B., A.C., D.G.; Writing - A.C.B., A.C., D.G.; Critical Review - A.C., D.G.

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REFERENCES

1. Ito K, Ichiki T, Ohi K, Egashira K, Ohta M, Taguchi K, et al. Pulmonary capillary hemangiomatosis with severe pulmonary hypertension. Circ J 2003; 67:793–5. [CrossRef]
2. Cavallo SLS, Sobrino LAM, Altamar LJM, Alquichire AFM. Congenital pulmonary capillary hemangiomatosis in a newborn. Arch Argent Pediatr 2017; 115:e17–20. [CrossRef]
3. O'Keefe MC, Post MD. Pulmonary capillary hemangiomatosis a rare cause of pulmonary hypertension. Arch Pathol Lab Med 2015; 139:274–7. [CrossRef]
4. Odronic SI, Narula T, Budev M, Farver C. Pulmonary capillary hemangiomatosis associated with connective tissue disease: a report of 4 cases and review of the literature. Ann Diagn Pathol 2015; 19:149–53. [CrossRef]
5. Ogawa A, Takahashi Y, Matsubara H. Clinical prediction score for identifying patients with pulmonary veno-occlusive disease/pulmonary capillary hemangiomatosis. J Cardiol 2018; 72:255–60. [CrossRef]
6. Montani D, Lau EM, Descatha A, Jaïs X, Savale L, Andujar P, et al. Occupational exposure to organic solvents: a risk factor for pulmonary veno-occlusive disease. Eur Respir J 2015; 46:1721–31. [CrossRef]
7. Yeo CD, Han D, Lee J, Chung WB, Jung JI, Lee KY, et al. A case of early diagnosis of pulmonary capillary hemangiomatosis in a worker with exposure to silica. BMC Pulm Med 2019;19:133. [CrossRef]
8. Best DH, Sumner KL, Austin ED, Chung WK, Brown LM, Borczuk AC, et al. EIF2AK4 Mutations in pulmonary capillary hemangiomatosis. Chest 2014; 145:231–6. [CrossRef]
9. Umezu H, Naito M, Yagisawa K, Hattori A, Aizawa Y. An autopsy case of pulmonary capillary hemangiomatosis without evidence of pulmonary hypertension. Virchows Arch 2001; 439:586–92. [CrossRef]
10. Frazier AA, Franks TJ, Mohammed TLH, Ozbudak IH, Galvin JR. From the archives of the AFIP: Pulmonary veno-occlusive disease and pulmonary capillary hemangiomatosis. Radiographics 2007; 27:867–82. [CrossRef]
11. Miura A, Akagi S, Nakamura K, Ohta-Ogo K, Hashimoto K, Nagase S, et al. Different sizes of centrilobular ground-glass opacities in chest high-resolution computed tomography of patients with pulmonary veno-occlusive disease and patients with pulmonary capillary hemangiomatosis. Cardiovasc Pathol 2013; 22:287–93. [CrossRef]
12. Bal SK, Thangakunam B, Irodi A, Gupta M, Christopher DJ. Small sample lung biopsy findings in patients with clinicoradiologic suspicion of pulmonary venoocclusive disease-pulmonary capillary hemangiomatosis. J Bronchol Interv Pulmonol 2016; 23:308–15. [CrossRef]
13. Verbeek J. When work is related to disease, what establishes evidence for a causal relation? Saf Health Work. 2012; 3:110–6. [CrossRef]