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Case report

Crazy paving pattern as a rare radiological manifestation of peripheral T-cell lymphoma (PTCL) with lung involvement: A case report

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ABSTRACT

We report on a 70-year old woman with dyspnea, systemic lymphadenopathy and abnormal chest computed tomography (CT) findings. A complete laboratory testing as well as mediastinal tissue sampling via Endobronchial Ultrasound (EBUS)-guided Transbronchial Needle Biopsy (TBNB) did not reveal a definite diagnosis. After experiencing acute respiratory failure which led to intensive care unit, the patient underwent a cervical lymph node biopsy which revealed peripheral T-cell lymphoma not otherwise specified (PTCL-NOS). A CT-guided *trans*-thoracic lung biopsy was performed that showed involvement of the lung parenchyma in the context of PTCL-NOS. Lung involvement is a rare extra-nodal manifestation of PTCL. The imaging patterns of this lymphoma have not been well described. We conclude that the finding of crazy paving pattern is a rare manifestation of this disease. In patients with pre-existing lymphoma, lung involvement should be included in the differential due to high pre-test probability.

1. Case report

A 70 - year old woman, with a history of hypothyroidism and pemphigus (20 years ago) presented with non-productive cough which progressively worsened for one month. The patient was a smoker (25 pack-years). She was examined by a private practice pulmonologist who reported crackles at auscultation. Complete blood count revealed only mild lymphocytopenia (WBC = 6610 with 1000 lymphocytes, Hct = 47.4 and PLT = 208000) whereas biochemical tests were within normal range. A chest radiograph was made and followed by a chest-CT which demonstrated lymphadenopathy up to 13mm, diffuse ground glass opacities with superimposed interlobular thickening creating a crazy paving pattern (Fig. 1).

A complete lab test examination was performed including the following: erythrocyte sedimentation rate (ESR) = 10mm (normal range 0–20mm), C-reactive protein (CRP) = 0.39mg/dl (0.02–0.80 mg/dl), serum angiotensin-converting enzyme (SACE) = 7 U/L (8–52 U/L) and antinuclear antibodies (ANA) negative. The patient also underwent an EBUS bronchoscopy which demonstrated a high percentage of lymphocytes with no clonality in BAL (M 33%, L 58% PMN 9%, CD4/CD8: 1.91), whereas neither cytologic examination of washing and TBNA nor pathologic examination of the lymph nodes displayed malignancy. Cultures for aerobes and anaerobes were negative and Ziehl-Neelsen stains as well as Lowenstein Jensen culture were negative for *M. Tuberculosis*.

After 15 days the patient suffered of acute dyspnea and was examined in the emergency department of the regional hospital where she lived. In the emergency room she presented with acute respiratory failure with SO2 = 83% (FIO_2 = 21%). Lab tests demonstrated WBC = 13.870 with 90% neutrophils and CRP = 4.40mg/dl. The patient was admitted to the hospital and was treated with broad-spectrum antibiotics as well as oseltamivir. She also presented multiple enlarged lymph nodes in the neck and therefore an ultrasound was made which demonstrated bilateral cervical lymphadenopathy up to 24mm. In addition, a chest CT was performed which showed bilateral infiltrations in lower lobes as well as diffuse ground glass opacities, pleural effusion in the right lung and multiple swollen lymph nodes. The patient was transferred to our hospital, which is a referral center for chest diseases, for further investigation.

At the time of the admission the patient was in respiratory failure (pH = 7.43, PaO_2 = 77.8, $PaCO_2$ = 36.9, HCO_3 = 25.1, Lactate acid = 2.8, Venturi Mask 50%). Despite the step up of antibiotic therapy and the addition of corticosteroids, the patient worsened. After 10 days she was intubated and admitted to intensive care unit (ICU).

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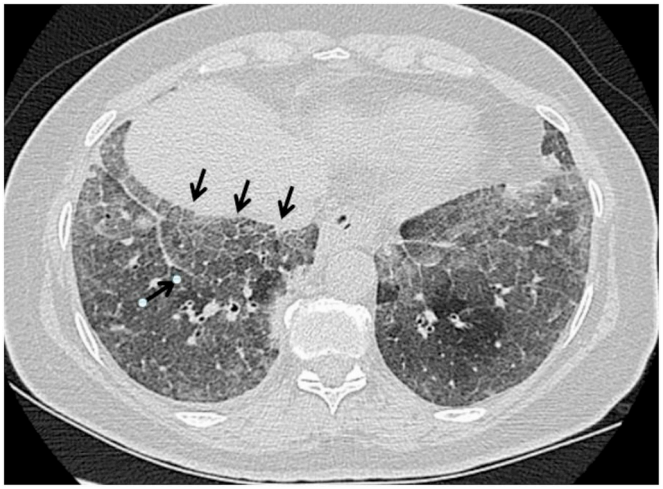

Fig. 1. Diffuse areas of ground glass. Regionally, there is interlobular septal thickening creating a crazy paving pattern (black arrows).

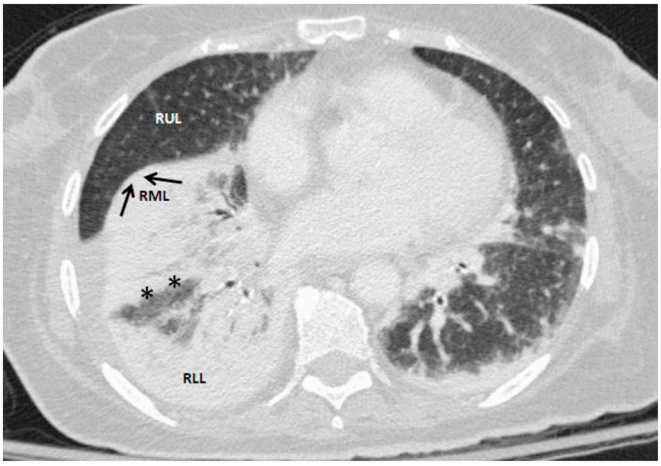

Fig. 3. Mass like consolidations in Right Middle Lobe (RML) and Right Lower Lobe (RLL) with anterior bulky displacement of the right minor fissure (arrows). Loss of volume in RLL (the asterisks indicate the position of the right major fissure).

Cultures of sputum were negative for common pathogens and microscopic examination of sputum was negative for *P. Jirovecii*. The patient underwent a new bronchoscopy and BAL was sent for PCR multiple viruses test which was positive for coronavirus. A chest CT was performed which demonstrated bilateral consolidations in the lower lobes, bilateral pleural effusions and lymphadenopathy. It seemed possible that acute worsening could be caused by a viral respiratory tract infection; however the data so far implied that the patient also suffered from an underlying disease. Therefore, a surgical biopsy of a left supraclavicular lymph node was performed and the tissue examination revealed peripheral T-cell lymphoma not otherwise specified (PTCL -NOS) (Fig. 2). After 3 weeks, the patient was successfully extubated and was transferred to the internal medicine department.

The patient was evaluated by a hematologist and was started on chemotherapy with CHOP. After a few days the swollen cervical lymph nodes reduced in size. However, the patient exhibited progressive respiratory deterioration, even after the 2nd cycle of CHOP. The differential diagnosis included infection, heart failure and lung infiltration of the known lymphoma. Lab testing included complete blood count (WBC = 4100), CRP = 0.69mg/dl (normal range 0.02–0.80mg/dl), Procalcitonin = 0.06 ng/ml (0–0.15ng/ml) and Brain Natriuretic Peptide = 40pg/ml (0–100pg/ml). A new chest CT demonstrated mass-like consolidations in the right middle lobe and right lower lobe (Fig. 3). Although the lung is a rare site of extranodal disease, it was considered a valid possibility due to the high clinical probability and the CT findings. A CT-guided *trans*-thoracic lung biopsy was performed in order to secure final diagnosis and thus firmly guide therapeutic options. Pathologic examination showed diffuse infiltration of lymphocytes in lung parenchyma with the same immunohistochemical markers as those of the lymph node biopsy (Fig. 4). As a result, the diagnosis of PTCL with extranodal involvement of the lung parenchyma was established. Two weeks after the 2nd cycle, the patient improved clinically and was in need of oxygen therapy of 2-3lt/min via nasal cannula. She received the 3rd cycle of CHOP and was in good condition for about 2 weeks. Sadly, before receiving the 4th cycle, the patient worsened and she died of respiratory failure because of disease progression.

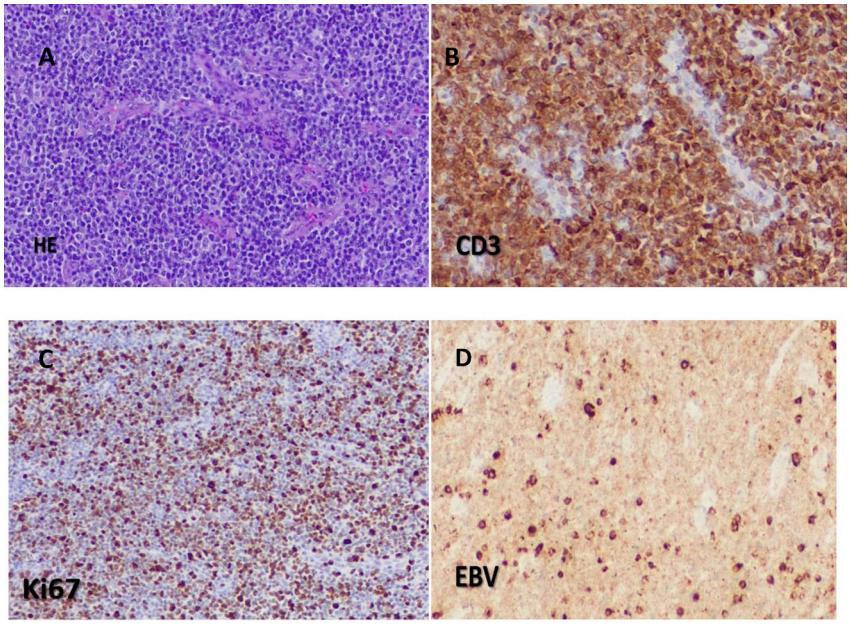

Fig. 2. Specimen detail of supraclavicular lymph node biopsy. **A.** Hematoxylin-Eosin, lymph node is filled with middle to large size cells with perinuclear halo. **B.** Immunohistochemical stain for CD3 highlights neoplastic cells. **C.** Immunohistochemical stain shows high proliferative index Ki67. **D.** In situ hybridization stain for EBV-encoded RNAs was positive.

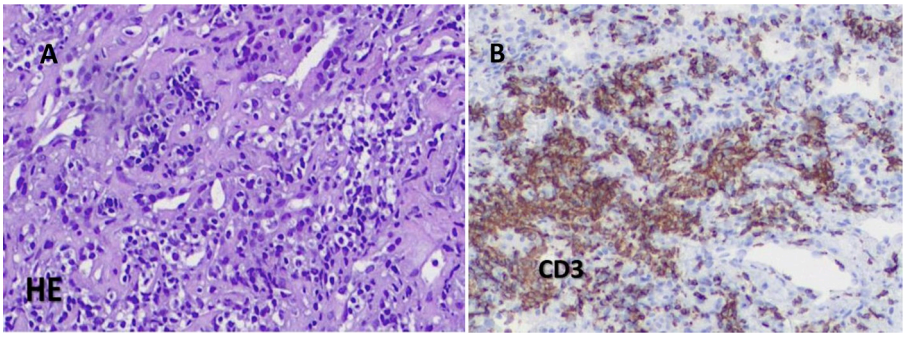

Fig. 4. Specimen detail from *trans*-thoracic lung biopsy. **A.** Hematoxylin-Eosin, infiltration of middle-size cells most of which contain perinuclear halo. **B.** Immunostain demonstrating neoplastic aggregates of CD3 (+) cells.

2. Discussion

We report a rare case of PTCL presenting with an unusual radiologic manifestation of that of crazy paving pattern. The term crazy-paving pattern refers to an image of ground glass opacities with superimposed thickening of interlobular septal lines. Although it is considered typical of alveolar proteinosis the actual differential is wide including infections (pneumocystis jirovecii, viral), sanguineous causes (pulmonary edema, diffuse alveolar hemorrhage), interstitial lung diseases (organizing pneumonia, exogenous lipoid pneumonia), malignancy (adenocarcinoma with lepidic growth, lymphatic spread of the tumor) [1]. Although the causes of this pattern are frequently indistinguishable at radiologic evaluation, incorporating data from history and clinical examination (e.g. immune status, acute vs chronic symptoms, history of cancer etc) as well as differences in the location of the characteristic attenuation in the lungs is crucial for suggesting the appropriate diagnosis [2].

PTCL, a subgroup of Non-Hodgkin Lymphoma, is a malignant lymphoproliferative disorder from post-thymic (peripheral T-cells) or mature NK cells [3]. PTCL accounts for less than 15% of all NHLs in the United States and Europe but they are more frequent in the Far East [4,5]. PTCL not otherwise specified (NOS) is the most common group of PTCL and it includes cases that do not correspond to any specific subtype [5,6].Despite aggressive chemotherapy, the majority of patients with most subtypes of PTCL have unfavorable prognosis [7]. The IPI score, including age greater than 60 years, stage III or IV disease according to Ann Arbor staging system, elevated serum LDH, ECOG/Zubrod performance status of 2, 3, or 4 and more than one extranodal site, is the most established prognostic factor, but newer prognostic models have also been proposed [8,9].

Patients with PTCL present predominantly with nodal disease, but extranodal disease is often present, with skin being the most common extranodal site [10].Pulmonary involvement is relatively rare; its frequency has been assessed from 2% to 8% of the cases, while extrapulmonary manifestations in the form of pleural effusions are present in 3%–12% of the individuals with this disorder [6,10]. The chest imaging findings of PTCL have not been well characterized [11]. It should be noted that imaging findings are frequently non-specific and require correlation with clinical findings. However, the radiologist is often the first one to suggest the diagnosis. Common CT findings include nodules or consolidation, cavitation (in aggressive forms) as well as hilar/mediastinal lymphadenopathy [12]. Lewis et al. evaluated CT findings of 31 patients with lung lymphoma and reported that the most frequent finding was a mass/masslike consolidation larger than 1 cm, while the second most common was nodules less than 1cm.The authors did not report any patient with crazy paving pattern in the chest CT [13]. Fu et al. (2016) reported a rare case of pneumothorax as first manifestation of PTCL [14]. Three case reports exist concerning crazy paving pattern of PTCL with lung involvement [15–17]. Recently, Aqeel et al. reported a rare case of acute respiratory failure in the setting of antisynthetase syndrome (ASS) in a patient with PTCL where the chest CT revealed extensive bilateral ground glass opacities [18].

3. Conclusion

In conclusion, this case report represents a rare radiologic presentation of a rare disease. Reviewing the course of the patient, we presume that the crazy paving depicted in the initial chest CT, actually represented early lung infiltration by PTCL. Due to disease progression, the radiological pattern changed from crazy paving pattern to solid consolidations after a few months. We conclude that PTCL of the lungs should be included in the differential of crazy paving pattern and a histological confirmation should be pursued in patients with a high pretest probability for the sake of accurate diagnosis, valid prognostication and proper management.

Learning points

1. EBUS has a low sensitivity in the diagnosis of lymphoma
2. Embedding pre-test clinical probability in clinical practice is of utmost importance
3. PTCL has grave prognosis and therefore clinical trials should evaluate newer regimens

Conflict of interest

We wish to confirm that there are no known conflicts of interest associated with this publication and there has been no significant financial support for this work that could have influenced its outcome.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.rmcr.2018.09.015.

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