Case 18538

Eurorad

Birt–Hogg–Dubé syndrome presenting as recurrent pneumothoraces

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Section: Chest imaging
Area of Interest: Lung Thorax
Imaging Technique: CT
Imaging Technique: CT-High Resolution
Case Type: Clinical Case
Authors: Mandeep Singh Virk, Marc Williams
Patient: 61 years, male

Clinical History:

A 61-year-old gentleman presented to A&E with shortness of breath and cough for 1 month, with no history of chest pain or trauma. CXR done showed left-sided pneumothorax. Past medical history revealed that the patient presented with similar complaints in 2016. Skin examination revealed multiple skin-coloured papules on the face, neck and trunk.

Imaging Findings:

A chest X-ray (CXR) was performed which revealed left-sided moderate pneumothorax. The patient underwent non-contrast CT thorax. CT revealed multiple thin-walled elliptical para-mediastinal air-filled cysts without internal structure in a basilar distribution, with preserved lung volume and no evidence of interstitial lung disease, and a left-sided pneumothorax (Figures 1a, 1b, 1c, 1d, 1e and 1f). Previous records were checked, and the patient had undergone CXR and CT in 2016, which showed similar findings.

Family history revealed a sibling with similar complaints and early onset renal cell carcinoma (RCC). MRI kidney done for this patient was normal, and no evidence of RCC was found. Biopsy from the skin lesions (Figures 2a, 2b and 2c) had been performed in the past and was consistent with fibrofolliculomas.

Discussion:

Background

Birt–Hogg–Dubé syndrome (BHDS) is a rare, inherited syndrome known to involve the skin, lungs and kidneys [1]. It is an autosomal dominant disorder caused by constitutional mutations in the FLCN gene [2–4]. Folliculin (FLCN) gene is currently the only known causative gene for BHDS and has been mapped to chromosome 17p11; over 200 types of mutations have been identified affecting this gene locus in BHDS patients. These mutations are often inherited but can also arise de novo.

Skin-related clinical features in BHDS encompass fibrofolliculomas, trichodiscomas and acrochordons, primarily manifesting on the facial region, neck and upper torso [1,5]. A distinctive hallmark of lung involvement in BHDS is the presence of cysts, which heightens the risk for spontaneous pneumothorax [6,7]. The syndrome's most severe manifestation lies in its association with a predisposition to RCC [8].

Clinical Perspective

BHDS usually manifests in the 3rd–4th decade of life. The phenotype of families affected by BHDS can be quite diverse, and not all patients exhibit the classical triad of lung, skin and renal findings, making the diagnosis of BHDS challenging. All patients suspected of having BHDS should undergo CT chest to look for lung involvement and MR/CT kidneys to look for RCC. Patients complicated by pneumothorax should undergo early pleurodesis to reduce the risk of recurrence. Nephron-sparing surgery is recommended for RCCs bigger than 3cm. Patients without any RCC should undergo routine screening MRI kidneys throughout their lifetime (done every 3–4 years).

Accurate diagnosis not only plays a crucial role in patient management but also helps identify undiagnosed family members. In this case, one family member was diagnosed with unilateral RCC. Due to its rarity, BHDS is unknown to many physicians and is likely to be under-diagnosed.

Imaging Perspective

The diagnostic criteria for Birt–Hogg–Dubé syndrome (BHDS) include:

- One major criterion: (A) Presence of five adult-onset fibrofolliculomas; (B) Proven pathogenic FLCN germline mutation.
- Two minor criteria: (A) Typical lung cysts with no alternative reasonable explanation; (B) Multifocal or bilateral RCC, or early onset (before age 50) RCC, or RCC showing mixed chromophobe-oncocytic histology; (C) A first-degree relative with BHDS.

The lung cysts in BHDS are lower lobe predominant, located in paramediastinal and subpleural locations and usually have oblong shape (floppy cysts) [9]. Lung involvement in BHDS does not lead to respiratory insufficiency, in contrast to other cystic lung diseases (LAM or PLCH).

Outcome

Patient was conservatively managed and discharged with an appointment for outpatient follow-up after 6 weeks. The patient will have surveillance renal MRI every 3 years to rule out RCC. Recurrent pneumothorax may need to be treated with pleurodesis.

Take Home Message / Teaching Points

- Patients with lung cysts and recurring pneumothoraces should raise suspicion of BHDS.
- BHDS patients need to be monitored routinely for pneumothorax and RCC development.
- There can be quite diverse clinical presentations, even within a family with BHDS.
- Diagnosing BHDS is of paramount importance not only for patient management but also for identification of previously undiagnosed family members.

Written informed patient consent for publication has been obtained.

Differential Diagnosis List: Lymphangioleiomyomatosis (LAM), Pulmonary Langerhans cell histiocytosis (LCH), Lymphocytic interstitial pneumonia (LIP), Birt–Hogg–Dubé syndrome (BHDS)

Final Diagnosis: Birt–Hogg–Dubé syndrome (BHDS)

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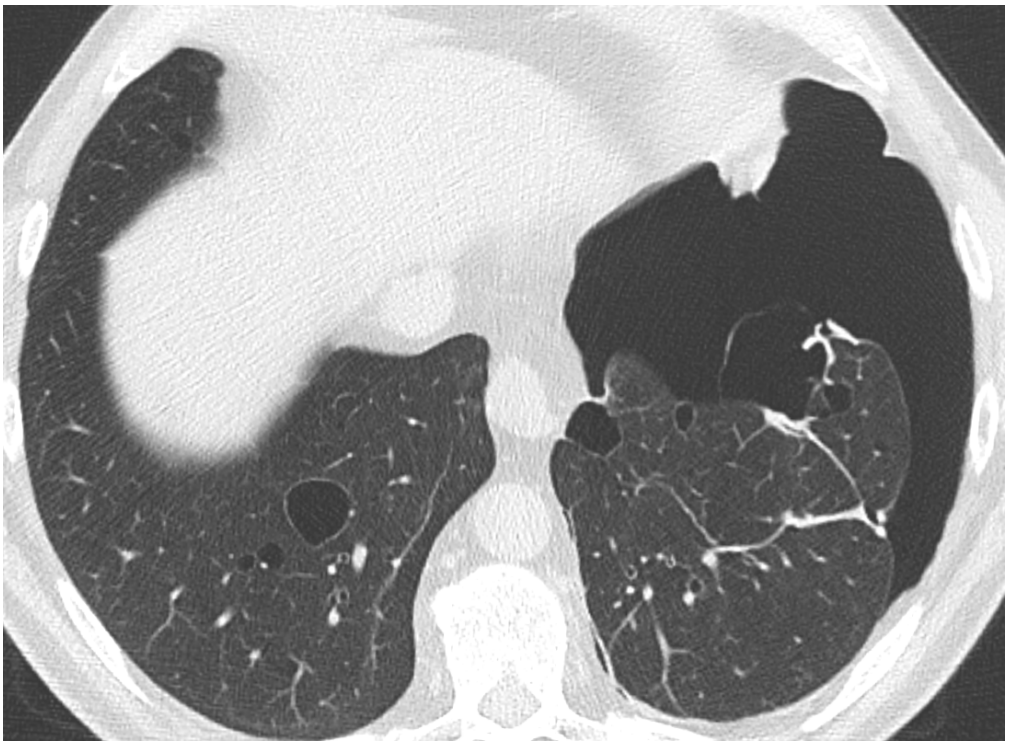
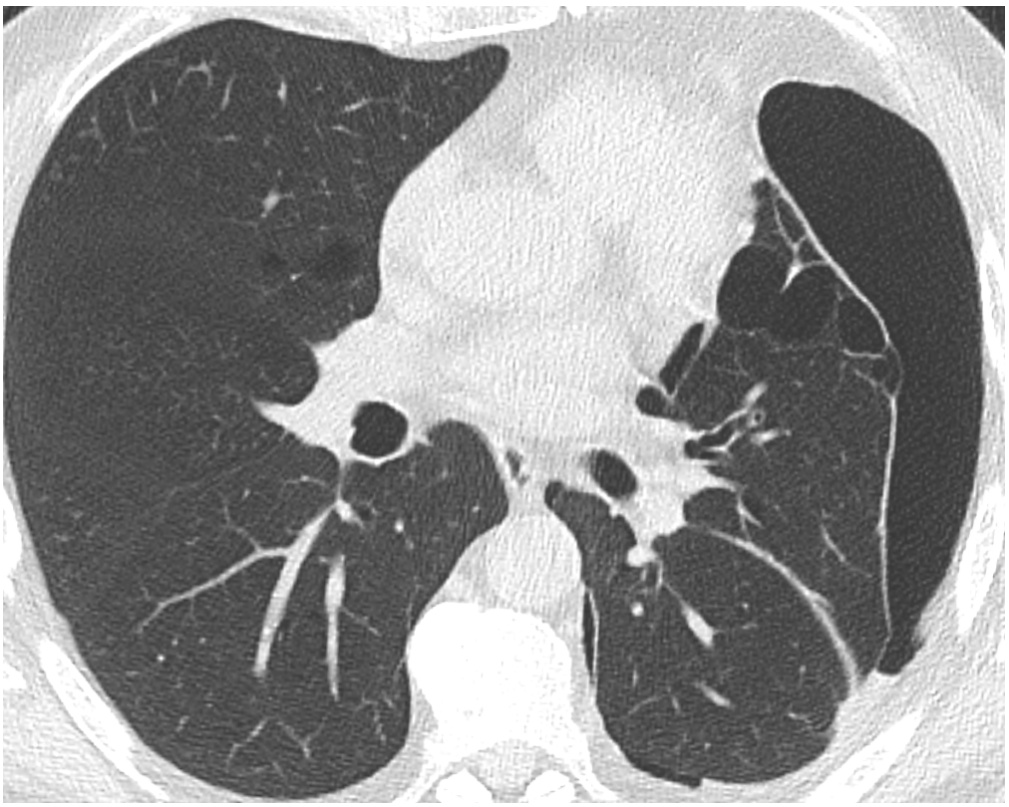
Figure 1

a



Description: CT and CXR findings of pulmonary cysts and pneumothorax. Axial and coronal CT images (1a, 1b, 1c, 1d) showing the typical paramediastinal cysts with lower lobe predominance. CXR (1e) with a drainage tube in situ from 2016. Present CXR (1f) showing recurrent pneumothorax.**Origin:**

b



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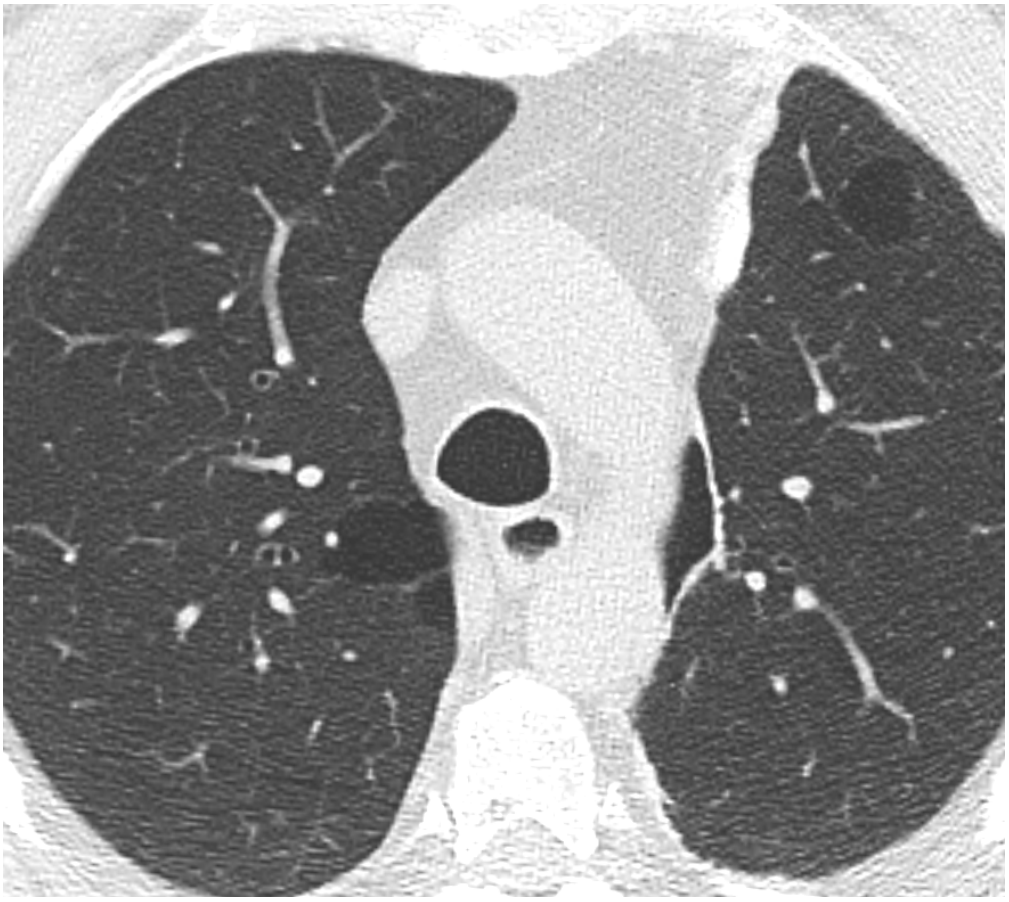
c



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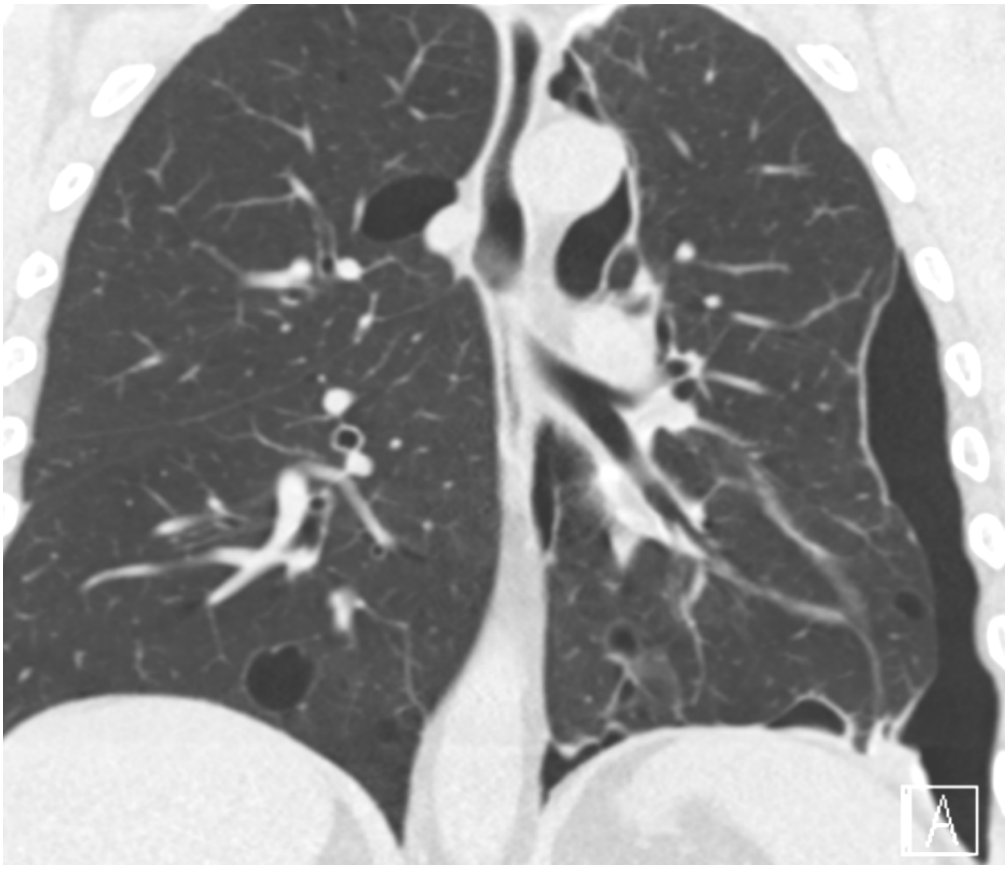
d



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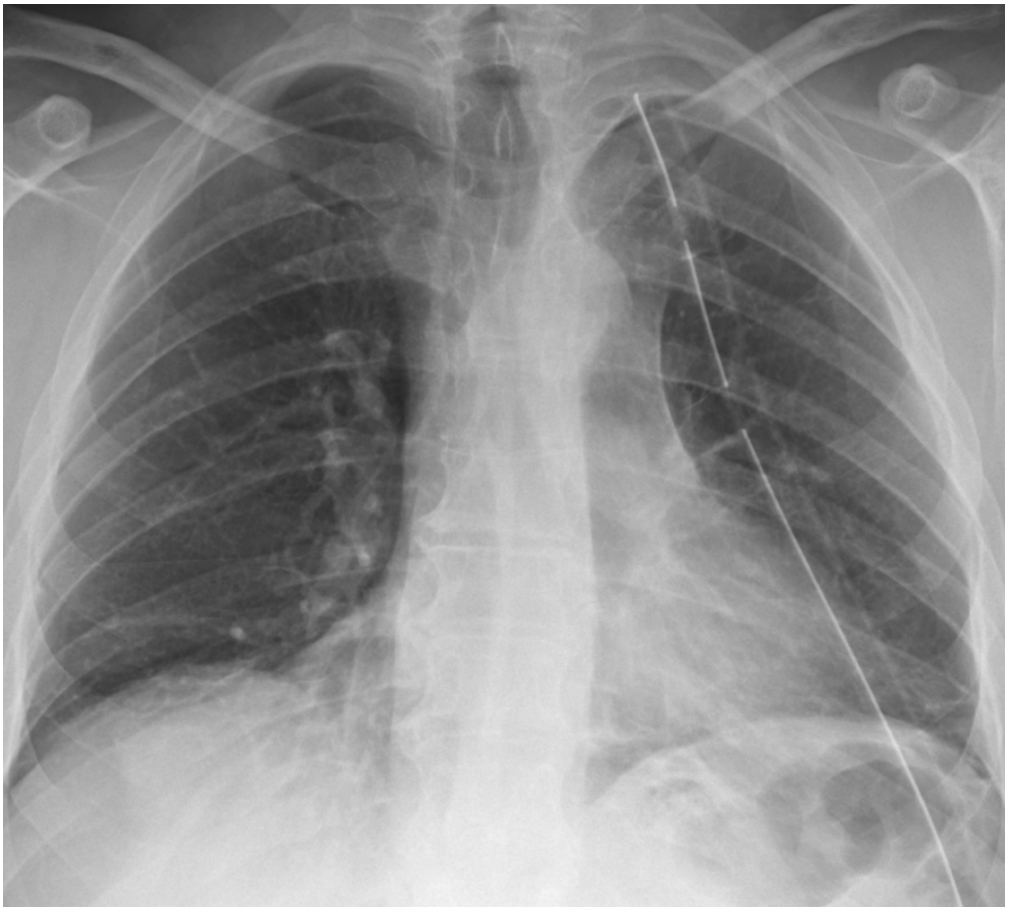
e



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f

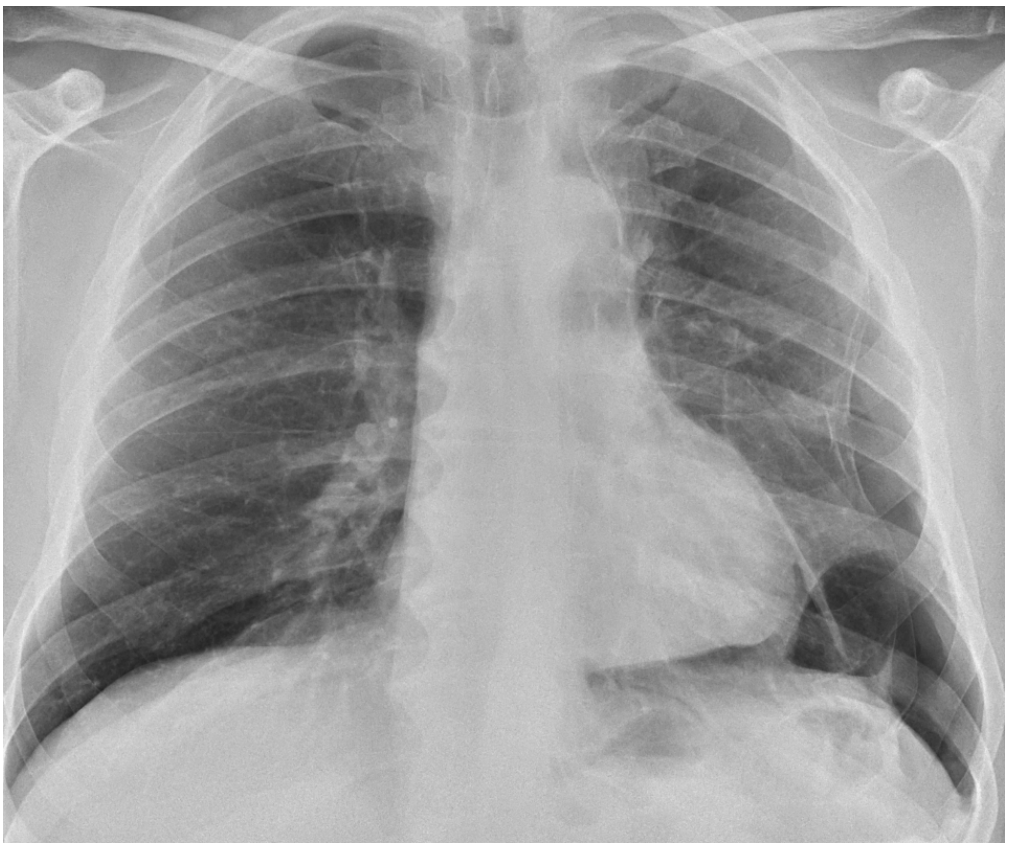

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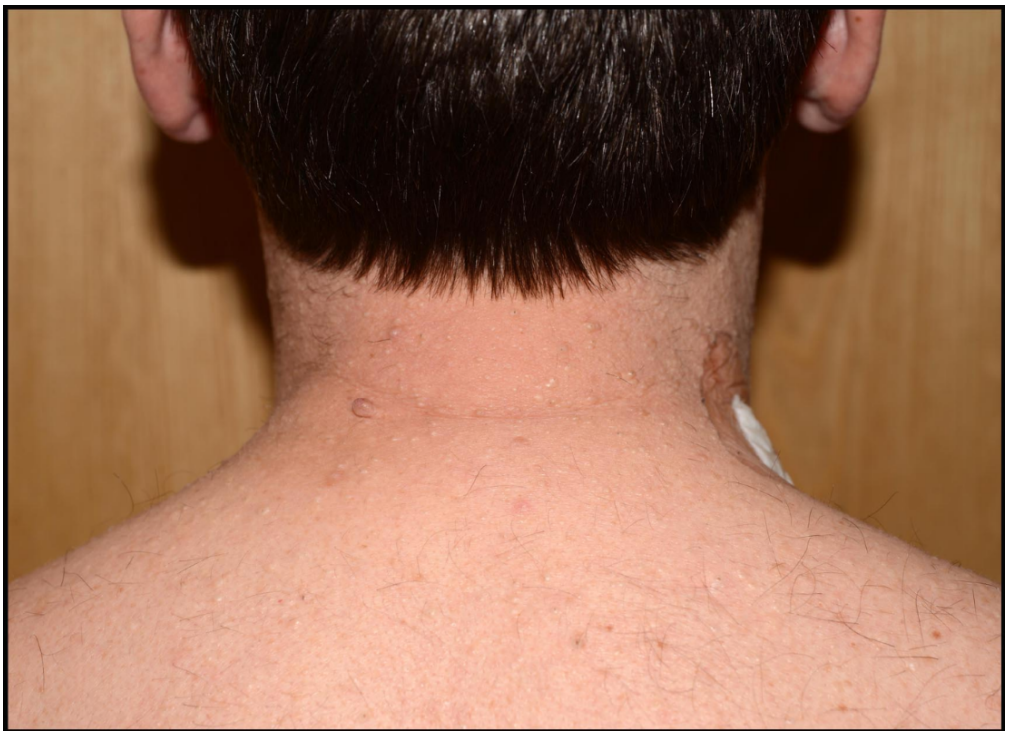
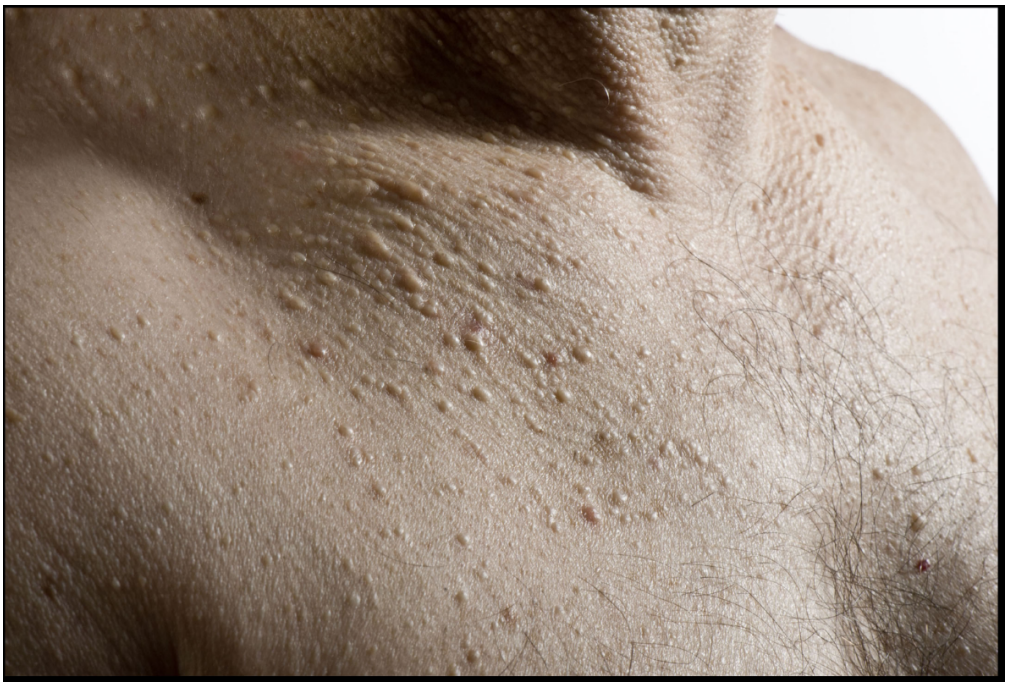
Figure 2

a



Description: Skin changes, with fibrofolliculomas on chest and back. **Origin:** © Department of Radiology, Royal Albert Edward Infirmary, WWL NHS Trust, Wigan, United Kingdom, 2023

b



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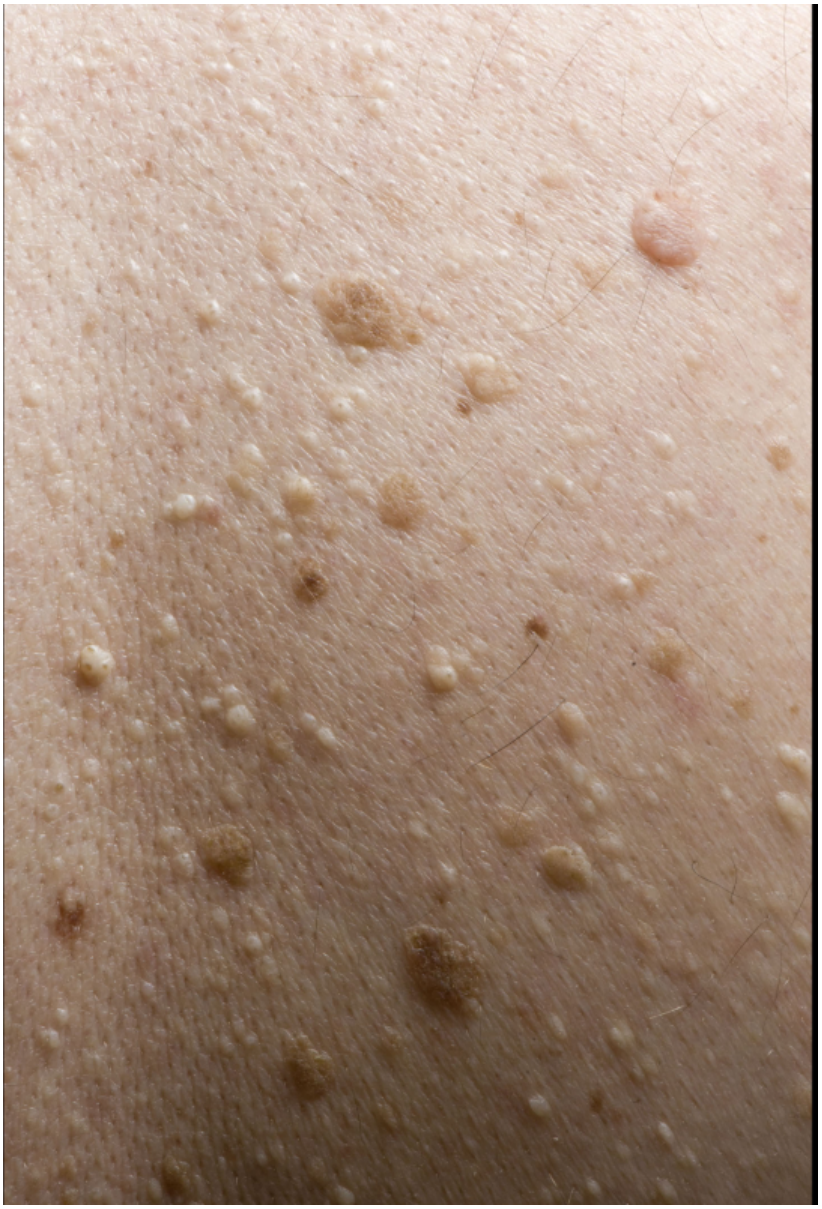

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