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CASE REPORT

Pulmonary hyalinizing granuloma

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Pulmonary hyalinizing granuloma. S.J.M. Gans, A.M.C. van der Elst, W. Straks.
ABSTRACT: A patient with pulmonary hyalinizing granuloma (PHG) is presented. PHG is a rare disease with very specific histological characteristics. Roentgenograms display multiple bilateral pulmonary nodules which may be cavitated. Evidence exists that the nodules are the result of an exaggerated chronic immune response. The course of the disease is generally favourable. PHG should be considered in patients showing multiple bilateral pulmonary nodules.
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In 1977 ENGLEMAN *et al.* described pulmonary hyalinizing granuloma (PHG) as a separate entity [1]. Predominant features are multiple bilateral pulmonary nodules. The precise aetiology and pathogenesis are unknown. Overall prognosis is favourable.

Case Report

A 57 yr old female was referred to our department because of abnormalities on plain chest roentgenograph. Her medical history was extensive. In 1970 she underwent hemistrumectomy for Riedel's disease. From 1970 until 1974 she was treated with corticosteroids for chronic active hepatitis. Since 1975 she had on a number of occasions experienced swelling of the nasal mucosa, which was diagnosed as a typical Quincke's oedema. C1-esterase inhibitor activity was normal. Allergy for nickel and salicylates was demonstrated. Apart from this she had recurring urticarial lesions on hands and face. In 1981 chest roentgenograms revealed a small opacity in the apical segment of the left lower lobe. A histamine releasing tumour was considered and the patient underwent thoracotomy with resection of the lesion. The tumour measured 1.3 x 1.3 x 0.9 cm and was at this time diagnosed as a sclerosed hamartoma.

The atypical oedema of the nasal mucosa and the sublaryngeal region kept on recurring and eventually resulted in a severe subglottic stenosis, which necessitated a permanent tracheostoma. In 1985 our patient developed a persistant cough with expectoration of tenacious white sputum. She denied anorexia, fever, night sweats or weight loss. She was a nonsmoker and the only medication she occasionally used was codeine. On physical examination, her pulse rate was 76/min and her blood pressure 170/90 mmHg. Surgical procedures had mutilated her nose and a gold plated tracheal cannula was *in situ*. The expirium was slightly prolonged and rhonchi were present. The remainder of the examination was normal.

Laboratory studies disclosed an erythrocyte sedimentat rate (ESR) of 24 mm/h, normal haemoglobin (Hb), white blood corpuscle (WBC) and serum chemistry. Serum protein electrophoresis showed a mild acute phase reaction. Antinuclear antibodies, rheumatoid factor, cryoglobulins and circulating immune complexes were not present. Serum levels of CH50, C3 and C4 were slightly elevated. There were no anti-cytoplasmatic antibodies present (ACPA-test). Microbiological investigations were negative. Chest roentgenograms, tomography and CT-scans revealed a cavitated lesion, measuring 3 cm, with ill-defined margins, in the apical segment of the left lower lobe. The right upper lobe showed a small solid lesion. The mediastinum was normal (fig. 1).

Fibreoptic bronchoscopy revealed no abnormalities apart from some tracheal oedema. Biopsy material was recovered from the left side lesion. Near the margin of this biopsy a field was seen which showed severely sclerosed hyaline fibres with a somewhat concentric course. This finding prompted a recision of the tumour which was surgically removed in 1981 (fig. 2). In this material well-defined areas were found with haphazardly-arranged hyaline fibres. The margin of the lesion showed some infiltration of plasma cells and lymphocytes. Stains for acid-fast bacteria, fungi and amyloid material were negative. Diagnosis was re-evaluated as pulmonary hyalinizing granuloma.

The patient was treated with ipratropium bromide and budesonide by inhalation, in order to alleviate her troublesome cough. This therapy was not successful. The radiological appearance was unchanged six months afterwards.

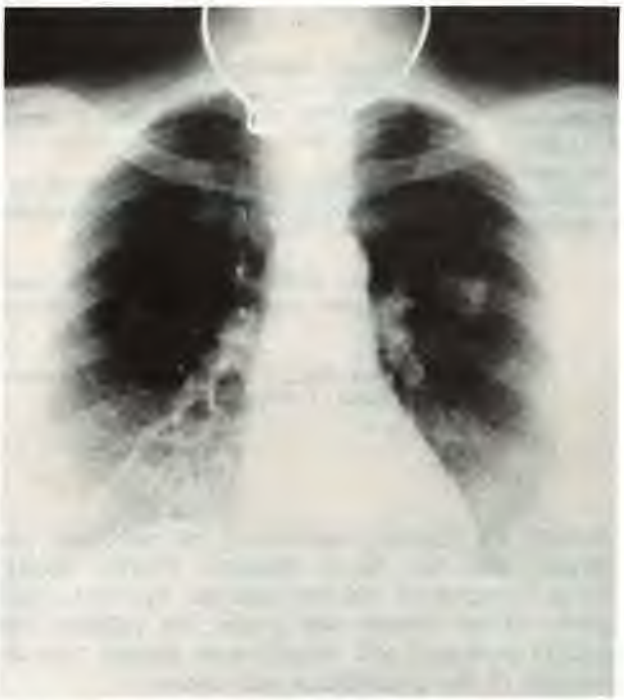

Fig. 1. – Chest roentgenogram revealing bilateral nodular lesions.

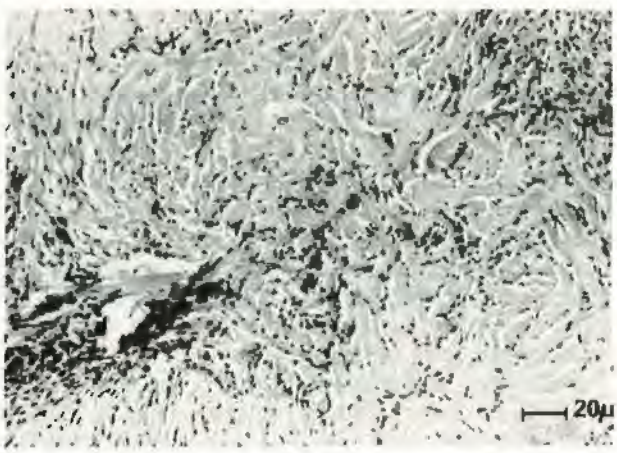

Fig. 2. – Pulmonary hyalinizing granuloma. Haphazardly arranged collagen fibres with a chronic inflammatory cell infiltrate of lymphocytes and plasma cells. H and E stain.

Discussion

Pulmonary hyalinizing granuloma is a rare disease. ULBRIGHT *et al.* found only two cases of PHG in 86 patients with pulmonary granulomas [2]. There is no sex or race predilection. The mean age of presentation is 45 yr. PHG is usually radiologically characterized by multiple and often bilateral nodules without preferential localization. Commonly the lesions are well defined and homogeneous but nodules with blurred margins and cavitation are mentioned. Calcifications are absent. Diameters are variable from a few millimetres to 15 cm [1, 3, 4].

The histological aspect is rather specific [5]. The nodules consist of extracellular, sclerosed, hyaline collagen bundles which are haphazardly arranged. Sometimes there is a more or less concentric pattern, especially around blood vessels. Staining for amyloid material may be slightly positive, although the typical fibrillar structure of amyloid could not be found in electron microscopic studies [6]. A mild infiltration consisting of plasma cells, lymphocytes and sometimes a few giant cells is encountered, especially at the margins of the process. Evidence of vasculitis or active microbiological involvement is never demonstrated.

Patients with PHG are asymptomatic or present with mild symptoms of cough, haemoptysis, fatigue, fever and pleuritic chest pain. Laboratory findings are non-specific. Microbiological tests are negative. No relation to occupational exposure is identified. Several authors suppose PHG to represent an exaggerated chronic immune response to an infectious process, or any process in which antigen-antibody complexes are found [1, 6–8]. The fact that some of the patients described had a history of tuberculosis or histoplasmosis [1] is in agreement with this hypothesis. Furthermore, SCHLOSNAGLE *et al.* demonstrated several auto-antibodies and circulating immune complexes in two patients with PHG [7]. DRASIN *et al.* presented a case of PHG in a patient who developed two different B-cell tumours successively [9]. In our patient, a chronic immunological disorder can also be suspected.

Clinical and radiographic differential diagnosis of the lung lesions includes primary and secondary neoplasmata, rheumatoid nodules, Wegener's granulomatosis, lymphomatoid granulomatosis, the macronodular variant of sarcoidosis, nodular amyloidosis and plasma cell granuloma. For a certain diagnosis histological examination of a representative tissue specimen is required. The ACPA-test which is thought to be specific for Wegener's granulomatosis is negative in PHG.

The prognosis of PHG is generally favourable. Usually the nodules tend to grow slowly, but spontaneous regression and a *status quo* are also described [1]. Prognosis is significantly worse when sclerosing mediastinitis develops in the course of PHG. This dangerous complication occurs in 20% of the patients and patients with a positive histochemical staining for amyloid material in their lesions are especially at risk. Perihilar situated nodules are able to progress to sclerosing mediastinitis by direct extension. Apart from this, compression of hilar structures is possible. DENT *et al.* described PHG in association with retroperitoneal fibrosis [10]. Because of the simultaneous occurrence of the above mentioned diseases and their similar histopathological features, some authors suspect them to be different expressions of the same immunological disorder [1, 6, 7].

In view of the usually benign nature of PHG, the

therapeutic regimen should be expectative. In patients who show a rapid progression, immunosuppressive drugs can be considered. Considering their earlier mentioned risks, perihilar situated nodules may be resected preventively.

References

1. Engleman Ph, Liebow AA, Gmelich J, Friedman PJ. – Pulmonary hyalinizing granuloma. *Am Rev Respir Dis*, 1977, 115, 997–1008.
2. Ulbright ThM, Katzenstein A-LA. – Solitary necrotizing granulomas of the lung. *Am J Surg Pathol*, 1980, 4, 13–28.
3. Macedo EV, Adolph J. – Pulmonary hyalinizing granulomas. *J Can Assoc Radiol*, 1985, 36, 66–67.
4. Chalaoui J, Grégoire P, Sylvestre J, Lefebvre R, Amyot R. – Pulmonary hyalinizing granulomas: A cause of pulmonary nodules. *Radiology*, 1984, 152, 23–26.
5. Katzenstein A-LA, Askin FB. – *In*: Major problems in Pathology, vol. 13: Surgical pathology of non neoplastic lung disease. Saunders, Philadelphia, 1982, 373–379.
6. Guccion JG, Rohatgi PK, Saini N. – Pulmonary hyalinizing granuloma, electron microscopic and immunologic studies. *Chest*, 1984, 85, 571–573.
7. Schlosnagle DC, Check IJ, Sewell CW, Plummer A, York RM, Hunter RL. – Immunologic abnormalities in two patients with pulmonary hyalinizing granuloma. *Am J Clin Pathol*, 1982, 78, 231–235.
8. Maijub AG, Giltman LI, Verner JL, Peace RJ. – Pulmonary hyalinizing granuloma. *Ann Allergy*, 1985, 54, 227—229.
9. Drasin H, Blume MR, Rosenbaum EH, Klein HZ. – Pulmonary hyalinizing granulomas in a patients with malignant lymphoma, with development nine years later of multiple myeloma and systemic amyloidosis. *Cancer*, 1979, 44, 215–220.
10. Dent RG, Godden DJ, Stovin PGI, Stark JE. – Pulmonary hyalinizing granuloma in association with retroperitoneal fibrosis. *Thorax*, 1983, 38, 955–956.

RÉSUMÉ: Présentation d'un cas de granulome hyalinisant du poumon, affection rare à caractéristiques histo-pathologiques très spécifiques. Les clichés thoraciques montrent des nodules pulmonaires bilatéraux multiples, parfois excavés. La preuve existe que ces nodules résultent d'une résponse immunitaire chronique excessive. Le décours de la maladie est généralement favorable. Il faut prendre en considération le granulome pulmonaire hyalinisant chez les patients présentant des nodules pulmonaires bilatéraux multiples.