Tracheobronchopathia osteoplastica

Its relationship to primary tracheobronchial amyloidosis

A. SAKULA

From Redhill General Hospital, Surrey

An uncommon case of tracheobronchopathia osteoplastica in a 52-year-old woman is reported, the fifth example of this condition to be published in the British literature. The bronchoscopic feature of bony hardness of the bronchial wall was initially suggestive of bronchial neoplasm. The histological feature of bony deposits (containing marrow showing active haemopoiesis) in the submucosa of the lower trachea and major bronchi was superimposed on a background of primary localized amyloid infiltration, and yet the bronchoscopic findings and the naked-eye morbid anatomical appearance suggested tracheobronchopathia osteoplastica. A study of the reported cases of tracheobronchopathia osteoplastica on the one hand, and of primary localized tracheobronchial amyloidosis on the other, reveals considerable similarity and overlap between the two conditions. It is postulated that some, if not all, cases of tracheobronchopathia osteoplastica are merely the advanced ossified stage of primary localized amyloidosis of the lower respiratory tract.

Cases of ossification occurring in the wall of the trachea and bronchi have been reported during the past hundred years. Most of these have been examples of so-called tracheopathia (or tracheobronchopathia) osteoplastica, a rare condition of which only 125 cases have been reported throughout the world, four having been described in the British literature. The English physician, Wilks (1857), was the first to give an account of 'ossific deposits in the larynx, trachea and bronchi' in a 38-year-old man who died of pulmonary tuberculosis. Further descriptions of the condition appeared (Muckleston, 1909), and Aschoff (1910) named it tracheopathia osteoplastica. In modern times Dalgaard (1947, 1955) once again drew attention to the condition. The second British case report was by Bowen (1959), and two further cases have since been described, by Salm (1961) and by Baird and Macartney (1966). Secrest, Kendig, and Beland (1964) suggested that it was more accurate to call the condition tracheobronchopathia osteoplastica.

Ossification in the wall of the trachea and bronchi has also been described in primary tracheobronchial localized amyloid infiltrations or 'tumours'. The first case of primary amyloid tracheo- and broncho-stenosis was reported by Balser (1883), and since then further examples of the condition have been published from other

countries (Falconer, 1938; Whitwell, 1953). The most recent comprehensive British papers on the subject have been written by Prowse (1958) and Prowse and Elliott (1963).

There has been considerable speculation as to the nature of tracheobronchopathia osteoplastica, and many theories have been advanced regarding its aetiology. In the reported descriptions of the bronchoscopic and histological appearances of tracheobronchopathia osteoplastica on the one hand, and of primary tracheobronchial amyloidosis with ossification on the other, there has often been a striking similarity and overlap between the two conditions. Thus, in the case of tracheobronchopathia osteoplastica described by Shuttleworth, Self, and Pershing (1960), the bronchoscopic appearances were identical with those described by other authors for primary tracheobronchial amyloidosis, and amyloid was demonstrated histologically in their case.

In the case described here, the fifth example of tracheobronchopathia osteoplastica to be recorded in the British literature, amyloid was demonstrated histologically. The hypothesis is presented that many, if not all, cases of so-called tracheobronchopathia osteoplastica are merely the advanced ossified stage of primary tracheobronchial amyloidosis.

CASE REPORT

A married woman aged 52, with two children, was first seen in February, 1962. She had never smoked or had a job involving dust or other hazards to the respiratory tract. She had always had recurrent episodes of bronchitis, sometimes associated with wheeziness, but there had not been any serious nasal or sinus disorder. During the past 18 months, however, her breathing had become 'noisy', even when she was not troubled by cough or sputum. She had become more easily dyspnoeic on effort, but without any chest pain or haemoptysis. She was obese, and despite dietetic advice she remained overweight. Her other previous illness was an attack of thrombophlebitis of a leg vein seven years previously.

On clinical examination she was overweight at 13 st. 7 lb. (86 kg.). Her 'noisy breathing' was from an inspiratory stridor arising behind the suprasternal notch. The pharynx and thyroid gland seemed normal, there was no finger clubbing, the chest wall moved normally, and the breath sounds were normal. The heart seemed normal (B.P. 160/80 mm. Hg) and the urine was normal. Blood count: Hb 14.7 g./100 ml., W.B.C. 5,800 per 100 ml. (polymorphonuclear leucocytes 60%, lymphocytes 36%, monocytes 4%).

The chest radiograph showed a virtually normal appearance, with no suggestion of undue calcification

or ossification of the trachea or major bronchi in either the postero-anterior or lateral films (Fig. 1).

Indirect laryngoscopy showed a normal larynx, subsequently confirmed at bronchoscopy, where there was a grossly rugose thickening of the mucosa involving the trachea and extending chiefly into the right main bronchus. In the latter the thickening involved the posterior and lateral surfaces, but the anterior portion appeared to be clear. As the bronchoscope was passed, the wall of the lower trachea, the main carina, and the orifices to the main bronchi appeared to be bony hard and rigid, so that the instrument could not be passed into either main bronchus. Biopsies were taken from the main carina and the orifice of the right main bronchus and were reported as showing necrotic material, with no suggestion of neoplasm. Examination of the biopsy by Ziehl-Neelsen staining showed no acid-alcohol-fast bacilli. Despite the negative histological report, a diagnosis of inoperable primary bronchial carcinoma was made, and radiotherapy was not advised.

Nine months later, in December 1962, she collapsed after a severe bout of coughing and was brought to hospital as an emergency, comatose, dyspnoeic, and cyanosed. The heart was rapid at 140 per minute and regular; B.P. 120/90 mm. Hg. The breath sounds were weak, but crepitations and a loud wheeze were audible over both lungs. The electrocardiogram

FIG. 1. Radiograph of chest on 14.3.62.

showed no evidence of myocardial infarction. Her condition rapidly deteriorated, and 20 minutes after arrival at hospital cardiac arrest occurred. Despite all attempts at resuscitation, including the aspiration of a considerable quantity of blood-stained mucus from the right lung, she died.

NECROPSY FINDINGS The heart showed dilatation of the right ventricle with moderate atheroma of the coronary arteries. The liver, kidneys, and brain were congested, and there were gallstones in the gall-bladder. There was no evidence of amyloidosis affecting any organ. The lungs were oedematous. There was a stenosis of the lower trachea and major bronchi, resulting from gross thickening of their walls. This process extended as far as the main subdivisions of the main bronchi. On attempting to slit open the lower trachea and bronchi, the scissors cut through the bony hard walls with difficulty.

Radiographs of the necropsy specimen of the trachea and bronchi showed clearly the abnormal submucosal calcification and ossification (Fig. 2).

FIG. 2. Radiograph of necropsy specimen of lower trachea and bronchi, showing submucosal thickening, calcification, and ossification.

Histological examination of sections of the trachea and bronchus (Fig. 3) showed the lining columnar epithelium, where present, to be thrown into irregular folds, there being but little lining epithelium remaining in the trachea. Beneath this epithelium, especially in the section of the bronchus, there was an inflammatory infiltrate consisting of plasma cells and a few lymphocytes. The submucosa of both the trachea and bronchus was markedly thickened and was, for the most part, replaced by masses of hyaline material giving the staining reactions for amyloid. Scattered irregularly throughout this material were

islands of atypical cartilage and bone, in a few of which there were areas of haemopoietic tissue (Fig. 4). Some of these areas of atypical cartilage appeared to be intimately associated with the normal cartilaginous rings. There was no evidence of amyloid in the walls of the small vessels.

DISCUSSION

The essential features of tracheobronchopathia osteoplastica are the deposits of calcification and ossification, often with foci of bone marrow and active haemopoiesis, demonstrable in the submucosa of the trachea and bronchi. This must, of course, be distinguished from the changes in cartilage seen in the tracheobronchial tree with age or with conditions such as Paget's disease of bone (Shanks and Kerley, 1962), as well as from other causes of foci of ossification seen in the lung parenchyma, as in mitral stenosis.

Although the case described here was in a woman, tracheobronchopathia osteoplastica usually occurs in men, in the fifth or sixth decades. Occasionally, no definite symptoms are recognized during life, and the condition is discovered incidentally at necropsy. Usually, however, a 'noisy' chest with an inspiratory as well as expiratory element (due more to stridor than to bronchospasm) is a feature for a number of years. There may be haemoptysis or a pulmonary segmental infection. In some cases rhinitis atrophica (ozaena) has been associated (Larsen, 1937). Plain chest radiographs will not show any evidence of the tracheobronchial condition, but tomographs may reveal the lesions narrowing the lumen of the trachea and bronchi (Howland and Good, 1958).

Naturally, bronchial neoplasm is often suspected in these circumstances (Flick, 1950), and bronchoscopy will be performed. The hardness of the tracheal wall, and the almost gritty bony feel as the bronchoscope passes, may confirm the clinical suspicion of bronchial neoplasm, but the bony spicules projecting under the apparently intact normal mucosa are characteristic (Huzly, 1960), and the bronchial biopsy, which is often technically difficult as the forceps tend to slip on the bony tissue (Carr and Olsen, 1954), does not show evidence of neoplasm.

However, primary amyloidosis of the lower respiratory tract needs also to be differentiated. The symptoms in this condition resemble closely those found in tracheobronchopathia osteoplastica, and the bronchoscopic findings may be similar, too. The essential feature of these amyloid infiltra-

FIG. 3. *Histology of portion of trachea ($\times 7.5$). Marked thickening of submucosa, replaced by hyaline material giving amyloid stain. Islands of atypical cartilage and bone seen to be intimately associated in places with the normal cartilaginous rings.*

tions and 'tumours' is that they are confined to the larynx, trachea, or bronchi, occasionally in the lung parenchyma, but there is no evidence of a generalized systemic amyloidosis, either primary or secondary. As already indicated above, and as will be discussed further below, the differentiation of the two conditions may be academic, since the ossification in primary amyloidosis may be responsible for so-called tracheobronchopathia osteoplastica.

AETIOLOGY OF TRACHEOBRONCHOPATHIA OSTEOPLASTICA Many theories have been advanced to explain the histogenesis of tracheobronchopathia osteoplastica (see Clerf, 1944).

Congenital deformity This explanation was originally advanced by Ribbert (1895). The youngest reported case was in a girl aged 12 years.

After careful consideration of the evidence this theory was rejected by Dalgaard (1947) and by Hempel and Gläser (1958).

Chronic infection Often there is evidence of associated chronic infection and inflammation, resulting from chronic bronchitis. In the first description by Wilks (1857) there was an association with phthisis. Syphilis has also been suggested as a cause. However, histological examination usually reveals a normal tracheobronchial mucosa, overlying the abnormal calcification and ossification in the submucosa. It is therefore unlikely that chronic infection is the cause of the condition.

Chemical or mechanical irritations In the case described by Jackson and Jackson (1932) chemical fumes were incriminated, and Jepsen and Sørensen (1960) ascribed the cause of their case of tracheo-

FIG. 4. Same section as in Fig. 3 ($\times 28$). Area of submucosal cartilage and bone formation containing haemopoietic tissue.

bronchopathia osteoplastica associated with ozaena to certain oil vapours. However, in the majority of cases described no such an association has been demonstrated.

Metabolic disturbance Hempel and Gläser (1958) postulated that the bony islet development was due to metabolic and local inflammatory disturbances, leading to acidosis, hyaline swelling, transformation to cartilage, and then bone formation. This armchair speculation has been rejected by Spencer (1962), who emphasizes that there is no alteration in calcium or phosphorus metabolism and no connexion with pulmonary calcinosis.

Degenerative process Hiebaum (1934) and, more recently, Delord (1954) ascribed the change essentially to a metaplasia of the tracheobronchial wall, but due to functional changes associated with ageing.

Ecchondrosis and exostosis The earlier writers (Virchow, 1863) considered the condition to be due to a cartilaginous outgrowth from the normal tracheal rings, these outgrowths becoming ossified and forming 'ostomata'. The fact that the bony spicules tend to be absent from the membranous portion of the trachea and bronchi tended to support this explanation. Liebow (1952) described multiple ecchondrosis in the trachea with or without secondary ossification. Recently, Baird and Macartney (1966) have supported the original Virchow theory. However, the fact that the submucosal bony islets appear to be predominantly bony and do not represent merely secondary ossification makes it unlikely that the condition develops from ecchondrosis. Moreover, the bony spicules may overlies the interspaces between the tracheal rings and appear not to be connected with them.

Metaplasia of elastic tissue Aschoff (1910) maintained that the condition was a systemic disease

of the tissues in the region of the internal elastic membrane in the submucosa of the trachea and major bronchi, and he named it tracheopathia osteoplastica. The fusion of the bony islets and the tracheal rings, which is sometimes seen, he explained as a coincidental or secondary phenomenon. Dalgaard (1947) attempted to expand the Aschoff hypothesis further, and described how the elastic fibre cells were transformed to elastic cartilage by metaplasia. These cartilage cells then grew into islets of cartilage, which became calcified, and were then invaded by connective tissue including blood vessels, with the production of bone marrow cavities lined by osteoblasts, resulting in bone formation. Dalgaard (1955) demonstrated in one patient that even further metaplasia might occur, leading to bronchial carcinoma as a complication. This theory does not explain the absence of bony spicules over the membranous portions of the trachea or bronchi, where elastic fibres predominate, and the presence of active bone marrow cells in the bony islets means that the metaplasia must have arisen from undifferentiated uncommitted mesenchymal cells (Freund, 1914).

RELATIONSHIP TO PRIMARY TRACHEOBRONCHIAL AMYLOIDOSIS From the above consideration of the various theories attempting to explain the nature of tracheobronchopathia osteoplastica it is evident that no completely satisfactory cause has been demonstrated. As already suggested, several of the cases described in the literature as tracheobronchopathia osteoplastica must, in fact, have been examples of primary amyloidosis localized to the lower respiratory tract (Shuttleworth *et al.*, 1960). Similarly, in a case described by Prowse (1958), the bronchoscopic appearance of primary amyloidosis appeared to be identical with that seen in tracheobronchopathia osteoplastica. Prowse and Elliott (1963) also demonstrated the submucosal bony islets enclosing bone marrow spaces and foci of active haemopoiesis in their cases of primary tracheobronchial amyloidosis. In the reports of cases of tracheobronchopathia osteoplastica, no specific mention has usually been made of an attempt to demonstrate amyloid. I think that the apparent overlap between these two conditions may well indicate a common aetiology and suggest that the condition of tracheobronchopathia osteoplastica is intimately connected with primary localized amyloidosis of the lower respiratory tract and probably represents a late stage of that condition.

I should like to thank Mr. R. Rowlandson for the bronchoscopy report, and Dr. T. N. Gledhill for the histological report.

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