CLINICAL REVIEW

Tracheal tumours

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Summary

A brief review of the incidence, clinical features and diagnosis of tracheal tumours is made, and details of ten cases which recently occurred in South East England, are presented and discussed. Theories accounting for the relative rarity of malignant lesions at this site are considered.

Introduction

Tracheal tumours are usually considered to be rare, about 600 cases of primary tumour having been reported in the world literature. However, the impression of extreme rarity of the malignant forms of these growths is exaggerated, as about forty deaths each year are certified as being due to this cause in England and Wales (Table 1).

It seems likely that this figure may represent an underestimate of the true number of cases in a population approaching 50×10^6 , as the diagnosis can rarely be made with certainty on clinical grounds, and is often not even suspected before tracheoscopy. It seems likely that, unless an endoscopic examination is made, a number of malignant tracheal tumours are incorrectly diagnosed and treated, and

that death is finally certified as being due to bronchogenic carcinoma.

In this connection, a new table appearing in the Registrar General's Statistical Review for 1965 reveals that confirmation of the diagnosis of malignant neoplasms of trachea, bronchus and lung at autopsy or operation was only obtained in some 20% of cases certified as dying from these causes (Table 2); this figure is surprisingly low when compared with the 28% confirmation rate of 'all causes' of death.

The recent literature has tended to be concerned with the surgical problems they present. Their apparent rarity has resulted in several publications of one or two cases to add to the older reviews of Culp (1938), Holinger, Novak & Johnston (1950), Gilbert, Mazzarella & Feit (1953) and Moersch, Clagett & Ellis (1954). Salm (1964) has published an excellent survey of pathological aspects of malignant tracheal tumours.

Pathology

Older reviews of the pathology of tracheal tumours are bedevilled by problems of varying nomenclature.

TABLE 1. Yearly numbers of deaths certified as due to primary tumours of the lower respiratory tract in England and Wales

		1958	1959	1960	1961	1962	1963	1964	1965
Larynx	M	662	643	689	652	626	632	571	613
	F	171	180	157	165	153	140	144	163
Trachea	M	27	27	17	33	24	27	33	30
	F	9	11	8	11	11	15	13	14
Bronchus and lung	M	11,397	12,198	12,824	13,323	13,882	14,611	15,027	15,436
	F	1,838	1,866	2,091	2,178	2,321	2,502	2,610	2,816

N.B. Figures for tracheal tumours separately are not available prior to 1958.
Source: Registrar General's Statistical review of England and Wales, 1965.

TABLE 2. Confirmation of diagnosis of malignant tumours of lower respiratory tract in England and Wales for the year 1965, compared with confirmation of cause of death from all causes (modified from the Registrar General's Statistical review of England and Wales, 1965)

	Deaths due to malignant neoplasms of trachea, bronchus and lung			Deaths from all causes
	Males	Females	Totals	Males and females
No. of deaths	22,231	4,167	26,398	549,379
Diagnosis confirmed at autopsy or operation	4,506	944	5,450	154,457
Percentage confirmed	20%	23%	21%	28%

TABLE 3. Primary tumours of the trachea in Southern England during the 5-year period 1960-64 (cases notified to the South Metropolitan Cancer Registry from a population of 8½ million people)

Ten-year age-groups	Histology				No histology	Total
	Carcinoma, not otherwise specified	Squamous cell carcinoma	Anaplastic carcinoma	Adeno-carcinoma		
Males						
40 -	1	3				4
50 -	3	2	3		4	12
60 -	4	12	4		2	22
70 +	1	6	1	1	3	12
Totals	9	23	8	1	9	50
Females						
30 -		1			2	3
50 -		6	2		2	10
60 -	1	4			1	6
70 -	1	5	1	1	1	9
80 +					1	1
Totals	2	16	3	1	7	29
Males and females	11	39	11	2	16	79

It is clear, however, that the majority of definitely attributable malignant tumours in adults are squamous cell epitheliomata, while adenoid and other forms are less common. It will be seen from Table 3, of cases registered from a population of 8½ million people in Southern England over a recent 5-year period, that of seventy-nine cases notified, thirty-nine (49%) were definitely squamous cell carcinomata, and it is likely that a proportion of the twenty-seven (34%) in which the precise pathology was not specified, or not investigated, were also squamous cell in type.

While these squamous carcinomata form about 50% of all malignant tracheal tumours, corresponding with figures for the differing types of bronchial growths (Spencer, 1962), it appears that anaplastic forms occur much less frequently in the trachea than lower in the respiratory tract. The same author, referring to bronchial growths, states that patients

suffering from squamous carcinoma have the longest life expectancy even when untreated. However, in the trachea, these lesions tend to metastasize, and are more resistant to all forms of treatment, so the prognosis is poor. Of the five cases to be described (Table 4), all were dead within 15 months of first attending hospital.

Pathological classification from cellular structure of primary malignant tumours other than squamous cell carcinomata, is less well defined. In recent years, more of these tumours have been ascribed to the category of 'cylindroma' or adenoid cystic carcinoma (Moran *et al.*, 1961), and three of the cases of the present series belong to this category. Although adenoid cystic carcinomata often at first appear to respond well to treatment, extensive local spread and a tendency to persistent recurrence at the original site, or at the edge of an excised area (rather than the formation of metastases), are the rule. These

TABLE 4. Analysis of cases

Case no.	Age at first complaint	Sex	Symptoms	Site	Treatment	Metastases	Survival time	Diagnosis
1	60	M	Cough and haemoptysis	Lower third	Cobalt teletherapy	O	Alive and well 2 years later	Adenoid cystic carcinoma
2	51	M	Cough and dyspnoea	Lower third	Endoscopic resection and radiotherapy	+	4 years	(Probably squamous carcinoma)
3	73	M	Cough, dyspnoea, haemoptysis	Lower third	Cobalt teletherapy	O	9 months	Squamous carcinoma
4	45	M	Cough, haemoptysis	Middle third	Endoscopic resection	++	15 months	Squamous carcinoma
5	46	F	Slight dyspnoea	Upper third	Local excision cobalt teletherapy	O	Alive and well 9 months	Adenoid cystic carcinoma
6	64	M	Dyspnoea, haemoptysis	Lower third	Cobalt teletherapy	+	1 year	Squamous carcinoma
7	52	M	Dyspnoea, cough	Upper third	Cobalt teletherapy	O	8 months	Squamous carcinoma
8	52	M	Cough, haemoptysis difficulty in expiration	Lower third	Radiotherapy	+	3 months	Anaplastic carcinoma
9	68	F	Stridor, discomfort	Upper third	Radiotherapy	O	Alive and well 2 years later	Adenoid cystic carcinoma
10	63	F	Dyspnoea, cough, haemoptysis, stridor	Middle third	Cardiac arrest during endoscopy under G.A.	O		Squamous carcinoma

tumours are relatively radiosensitive, and some years survival may be achieved when the condition is diagnosed at a reasonably early stage. Acquarelli, Ward & Hangos (1967) agree that epidermoid and adenoid cystic carcinoma are the two major types of tracheal malignancy encountered; an exhaustive summary of case reports—particularly of rarer tumours—has been compiled by Huguenin-Dumittan, Kapanai & Rudler (1966), while McCafferty, Parker & Suggit (1964) have presented a survey and detailed reports of eleven malignant cases which occurred in England and Australia.

Benign tumours occur in adults with a frequency similar to that of malignant forms; papilloma, osteochondroma and fibroma are described, and some authors have included the rare disorder—tracheopathia osteoplastica. Excessive calcification of tracheal cartilage, progressing to smooth, hard, nodular indentations into the lumen, simulating true neoplasm, occur in this condition, on which Way (1967) and Gautam (1968) have recently published reports of cases, and reviews of the literature.

Benign lesions occur relatively more frequently in children. As well as reviewing the condition in adults, Gilbert and his colleagues (1953) described

forty-three cases of tracheal tumour in children, of which only three (7%) were malignant; all of these sarcomata.

No case of malignant tumour of the trachea in a child was reported to the South Metropolitan Cancer Registry during the 5-year period under review.

Site

The lower third of the trachea is the most frequent site for tumours of all types, the upper third following; however, it is in the lower third that confusion may most easily arise over the site of origin of the tumour, for primarily bronchial neoplasms often extend to involve this section of the trachea. The lesion originated in the lower third of the trachea in five of the ten cases to be described; several other cases in which there was reasonable doubt over the origin of the tumour were rejected from the study.

Clinical manifestations

It is clear from the literature, that in the past, many of these tumours were not diagnosed until almost total respiratory obstruction had occurred, and this was evident in Case 2 of this series; on the other hand in Case 5 symptoms of respiratory dis-

FIG. 1. Conventional lateral X-ray of neck and thoracic inlet (Case 2).

tress were minimal, yet radiography revealed a large tracheal mass, confirmed on direct inspection.

Usually, however, patients first complain of hacking, irritating cough, wheezing and haemoptysis—particularly in malignant lesions. Stridor and dyspnoea occur later, and hoarseness may develop due to involvement of the recurrent laryngeal nerve by extratracheal spread. Expiratory, and sometimes inspiratory wheeze may vary with posture, but as it is heard over both lung fields, patients are often extensively investigated and treated for 'asthma'. Further developments may cause recognition of the true nature of the disorder. Respiratory obstruction and hypoxia may exacerbate underlying cardiac disease, and alter the approach to diagnosis and treatment.

Osteoarthropathy does not occur, and local pain and swelling in the neck from secondary involvement of lymphatic glands are uncommon, as metastases from malignant tumours are usually relatively late in appearing. In Case 4 of this series on the contrary, multiple pulmonary secondary deposits were a presenting radiological sign. Although local spread is often extensive, it may be difficult to recognize clinically.

FIG. 2. Tomogram of neck and thoracic inlet (Case 2). Tomography confirms the site of the lesion, relating it to the trachea and clarifies details of the tumour.

Increasing weakness, loss of weight, involvement of other vital mediastinal structures, or suffocation, appear terminally in the course of the disease.

Investigations

Radiological investigation, including tomography, may indicate the presence of a tumour, once the site is suspected (Figs. 1–8). Occasionally tracheal irregularities may be apparent on a routine chest X-ray, as in Case 9. Confirmation, perhaps accompanied by excision during tracheoscopy, is invariably necessary. There are frequent reports in the literature of last-minute diagnosis with piece-meal excision of the tumour during emergency bronchoscopy, where near-total respiratory obstruction has supervened. Emergency bronchoscopy was needed for treatment in Case 2 of this series.

Treatment

Three methods of treatment are available, surgical excision—either local or radical—and radiotherapy.

Endoscopic excision of both benign and malignant lesions has been attempted in many cases, with, predictably, better results where the lesion has been benign. In view of the characteristic extensive local spread of malignant tumours, surgical resection of the trachea and either direct anastomosis, replacement by graft, or permanent tracheostomy have been more recently attempted with varying success. Grillo, who has contributed extensively to the literature on the subject, has achieved a 17% 'long-term' success rate in a series of thirty-two cases (Grillo, 1966).

It is perhaps too soon to compare recent surgical results with the radiotherapeutic procedures; Cobalt-60 therapy has been relatively helpful in these lesions, often producing months or even years of regression, and the prognosis in cases of adenoid cystic carcinoma in particular (compared with that for squamous forms) is comparatively good, if adequate treatment, either surgical or radiotherapeutic, is carried out. Local excision and radiotherapy were the only methods of treatment used in this series.

Case reports

Details of ten cases which have occurred during recent years in South-East England, are outlined in Table 4. The following two representative case histories seem fairly typical of the course taken by the more common forms of these tumours.

Case 7

A 52-year-old man, who had previously suffered from chronic bronchitis, attended hospital complaining of increasing cough and sputum, dyspnoea and 'feverishness'. X-rays of the chest showed partial collapse of the left lung, while a lateral film of the neck demonstrated narrowing of the lumen of the trachea by a mass apparently originating from the posterior wall (Fig. 5). Tomography of the region revealed downward extension of the growth, and lateral deviation of the trachea.

At tracheoscopy the trachea was found to be partly blocked by growth from 2 cm below the cords. Histological report of biopsy of the growth was squamous cell carcinoma. Shortly after tracheoscopy, inspiratory stridor developed, and a course of Cobalt teletherapy was started. Considerable temporary improvement took place, and the left lung re-expanded, but he later deteriorated and died 8 months after the first hospital attendance.

Case 9

A 68-year-old woman had suffered from stridor for about 2 months following an attack of 'bronchitis'. In retrospect, it is of interest to note that a routine chest radiograph taken during this period shows

FIG. 3. AP tomogram of Case 4. An irregular mass is shown in the trachea.

FIG. 4. Lateral X-ray of the neck (Case 5). A rounded opacity overlies the trachea just above the thoracic inlet.

FIG. 5. A large irregular mass invades the upper trachea (Case 7).

FIG. 7. Routine PA film of neck (Case 9), showing stenosis of upper third of trachea.

FIG. 6. AP tomogram of Case 8. This shows narrowing of the lower third of the trachea.

FIG. 8. Tomogram of neck (Case 9), showing stenosis of upper third of trachea.

considerable tracheal narrowing (Fig. 7), but this was unremarked at the time. Following admission to hospital, tracheoscopy was performed with difficulty under local analgesia, and a biopsy taken of an intratracheal mass which was causing marked stenosis. Tomography had demonstrated the extent of the lesion (Fig. 8). Histology of the biopsy specimen was later reported as adenoid cystic carcinoma.

A course of radiotherapy consisting of 6874 rad over 43 days was carried out, and the patient rapidly became symptom-free. She remains well 2 years later; there is no sign of recurrence.

Discussion

This group of cases, all of which have occurred during recent years in East Kent, illustrate variations in the clinical course of malignant lesions of the trachea. Corresponding with the statistical analysis from the South Metropolitan Cancer Registry (Table 3) there was a preponderance of males, but the figures for the histological nature of the tumours from any source must be interpreted with caution, for although it is clear that squamous cell carcinomata predominate in the adult, it seems likely that difficulties of histological interpretation and pathological nomenclature have unduly diminished the numbers of adenoid forms of these growths.

Accurate diagnosis from histology is, as always, of considerable importance in planning treatment and considering prognosis. Because of the rarity of adenoid cystic carcinoma of the trachea, and the recent evolution of improved methods of radical surgical treatment, it will be some time before an assessment of the relative merits of radiotherapy as opposed to surgery, can be made in this condition.

Enterline & Schoenberg (1954) considered that cylindromatous carcinoma was a relatively fatal form of tracheal tumour, while Moran *et al.* (1961) felt that radiotherapy was only of palliative value in this condition, and it will be of interest to continue observation of the three surviving cases described here, who were treated by radiotherapy.

Each of the five cases in which the definite histological diagnosis of squamous cell carcinoma was made, conform with the usual gloomy outlook accorded by previous writers to patients suffering from this type of tracheal growth. All were dead within 15 months of the diagnosis being made. A very few cases, detailed by Engler (1948), have been described in which some years' survival after radiotherapy has been achieved.

Two of the five squamous cell carcinomata developed metastases, suggesting a closer relationship with bronchogenic neoplasms, rather than with squamous forms of laryngeal cancer, which are usually slow in forming secondary tumours. Unfortunately, full details of the smoking habits of the

reported cases are not available, and, while it would be attractive to incriminate the same aetiological factors for tracheal lesions as are generally thought to be important in the causation of bronchial growths, two considerations from the statistical surveys and our knowledge of the lesions merit attention.

Firstly, the obvious great rarity of tracheal tumours compared with bronchial growths, when the cellular structure of the lining of the two adjacent parts of the respiratory tract is very similar, if not identical, and where exposure to inhaled carcinogens would, at first sight, appear to be equal.

Secondly, the interesting position which tracheal tumours adopt statistically, when considering the mortality from tumours of the lower respiratory tract (Table 1). While deaths from bronchial carcinoma steadily increase, there is a small but steady fall in mortality from laryngeal malignancy. Can this latter fall be related purely to improvements in treatment, or is there a fall in the incidence of these lesions?

The mortality rate for tracheal tumours is perhaps comparable to their anatomical position. While there seems to be no diminution in the number of deaths from this cause, the rate of increase is not so consistent as that for bronchial tumours, and, were the figures large enough to adjust sensibly as Standardized Mortality Ratios (i.e. to compensate for absolute increases in the number of the population at risk), they would probably show that there has been little change year by year in the mortality—and, therefore, presumably the incidence—of tracheal tumours in England and Wales.

Theories which endeavour to account for the apparently anomalous position of tumours of the trachea, when compared with those of adjacent structures of the lower respiratory tract, may be grouped according to their concern with: (a) the tissues at risk, (b) the mucous blanket covering the epithelial surfaces, and (c) the presumed inhaled carcinogens and their deposition.

There is little evidence to differentiate, on a structural basis, tracheal from bronchial mucosa; and lesions suspected of being pre-cancerous may be found both above and below the carina. Exemplifying this, Ide, Suntzeff & Cowdry (1959) in a comparison of the histopathology of tracheal and bronchial epithelium of smokers and non-smokers, found that although the percentage of individuals exhibiting basal cell hyperplasia and squamous metaplasia (which were also found to exist in non-smokers), was increased in smokers, these epithelial lesions developed to the same degree in both tracheas and bronchi of their subjects.

Differences in the chemical composition of the mucous blanket covering various parts of the lower

respiratory tract have been postulated, but not demonstrated. On the other hand it has been suggested, notably by Hilding (1959), that characteristics of the movement and conformation of the mucous blanket, particularly in the root of the lung, where there are large bronchial openings impeding flow, might result in certain defined areas being more exposed to inhaled carcinogens. This theory nearly accords with the known high incidence of bronchial tumours originating near the orifices of the major and minor bronchi.

As a corollary, this author points out that carcinoma rarely occurs in the trachea, where ciliary streaming is free and uninterrupted, and where the postulated protective mucous blanket is, therefore, unbroken.

The common sites of malignant neoplasms of the respiratory tract are said to reflect the main points of deposition of inhaled potential carcinogens. Ermala & Holsti (1955), found that only very small amounts of tobacco tar were deposited on the simulated tracheal wall in their experiments, compared with the deposition on those parts of the respiratory tract where narrowing or deviation of the air flow occur. They concluded that there was a striking correlation between the clinical incidence of cancer and the localization of deposition of tobacco tars (although heavy deposition of tars predictably occurred on the simulated vocal cords during these experiments, it is presumed that one reason for the relative infrequency, compared to the bronchi, of tumour formation at this site, is the different epithelial covering).

Blocks form in mucus-streaming at the anastomoses if normal tracheal ciliary activity is interrupted, as in experiments on dogs described by Beattie *et al.* (1961), where autogenous grafts were inserted in the reverse direction in their original sites. When the carcinogen, benzantracene, was introduced, carcinomata developed at the distal anastomoses, where there was pooling of mucus, and interruption of its free flow, due to the paradoxical ciliary activity at this area. Squamous metaplasia and incipient carcinoma were seen to develop at those places where drying of mucosa was produced at the proximal anastomoses.

These pieces of evidence reinforce the view that inhaled carcinogens are responsible for neoplasia in the tracheo-bronchial tree. What factors may be responsible for the points of deposition of inhaled substances in the lower respiratory tract in man?

Gas flow through tubes may be laminar, i.e. smoothly parallel to the walls of the tube; or turbulent. Turbulence occurs where sudden alterations in the bore of tubes, or changes in the direction of gas flows take place, and also when a 'critical flow rate' is exceeded.

The term 'critical flow rate' indicates the rate of flow of a gas (or a liquid) in a smooth walled tube, at which the type of flow changes from laminar to wholly turbulent flow, and is dependent upon the diameter of the tube for any particular gas.

For a tube of 2 cm diameter (say, the trachea), critical flow rate for air is approximately 28 l/min. In an adult, breathing quietly, with a minute volume of 8 l/min, maximum flow rate will not usually exceed 25 l/min (though this rate may be greatly exceeded when breathing deeply) (Macintosh, Mushin & Epstein, 1958). Laminar flow of air, therefore, may be expected in the trachea under ordinary conditions of breathing, but turbulence will normally occur at the main and subsidiary carinae, where sudden changes of direction of air flow take place (West & Hugh-Jones, 1959).

It seems reasonable to assume that particulate matter, perhaps inhaled carcinogens, will be deposited from the air-stream at these points of turbulence, rather than where the flow is smooth and laminar, in the trachea. Can this then, explain the distribution of growths of the lower respiratory tract, in which the great majority originate in the region of the carinae and bronchial orifices—points of air turbulence where the mucus blanket is weak—while neoplasms of the trachea are of great rarity?

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