Chemodectoma in the region of the aortic arch

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A morphological study of the carotid bodies led de Castro (1926, 1928) to suggest the chemoreceptor function of these structures. His ideas were confirmed by Schmidt (1932) and by Heymans and Bouckaert (1933). Bodies or glomera had been described at several sites long before their function became known. They are aggregates of chemoreceptor cells and are now acknowledged to have a wider distribution than was at first supposed; they have been described in the limbs, in the abdomen, and in the orbit, as well as in the commoner sites shown in Table I. Mulligan suggested in 1950 that a tumour of the chemoreceptors should be called a 'chemodectoma'.

TABLE I
CHEMORECEPTORS AND CHEMODECTOMATA IN MAN

	Body First Described by	Tumour First Reported by	Number of Tumours Reported in British and American Papers
Carotid body	von Haller (1743)	? Morgagni (1761) Marchand (1891)	About 500
Jugular body	Valentin (1840)	Rosenwasser (1945)	About 170
Aortic body	Busacchi (1913)	Lattes (1950) Monro (1950)	28
Vagal body	White (1935)	Stout (1935)	About 15

Von Haller is generally thought to have been the first anatomist to describe the carotid body, which he did in 1743, and Marchand (1891) is usually referred to as the first to report a carotid body tumour; Morgagni, however, had already reported what was probably such a case in 1761 when referring to one of the patients of his teacher Valsalva, a woman aged 50, with 'a hard tumour, in the right part of the neck, being oblong in its figure equal to the size of a turkey's egg, and having its basis in the carotid artery of the same side, from whence going upwards, quite in the division of that artery, it terminated there'.

Reports of tumours arising from chemoreceptor bodies have helped to map the chemoreceptor system. Stout described a vagal body tumour in 1935, Rosenwasser a jugular body tumour in 1945, and the independent reports of aortic body tumours in the mediastinum published by Lattes and by Monro appeared in the same month of 1950. Only recently has the multicentric origin of chemodectoma been appreciated.

The degree of malignancy in the majority of chemodectomata is still uncertain. Harrington, Clagett, and Dockerty (1941) considered half of their 20 cases to be malignant, but this estimate was based on microscopic features (the presence of mitoses, cellular pleomorphism, and capsular invasion) rather than on the behaviour of the neoplasms. Pryse-Davies, Dawson, and Westbury (1964) conclude that 'a satisfactory separation into benign, locally invasive, and malignant metastasising tumor cannot readily be made on histological appearances alone'. Weibull (1961) considers that about 12% of carotid body tumours are malignant. He listed four main behaviour patterns of the malignant tumours: (1) local recurrence; (2) metastases to lymph nodes; (3) metastases to the skeleton, especially the cervical vertebral column, but also to other bones such as the humerus; and (4) metastases to viscera, such as the lungs, brain, and thyroid.

On the other hand, the occurrence of a multicentric chemodectoma is well recognized and documented (Kipkie, 1947; Lattes, 1950; McNeill and Milner, 1955; Marcuse and Chamberlin, 1956; Zacks, 1958; Dibble, 1963). Furthermore it is probable that many small glomera are present in the body, apart from the larger collections which have been found and named by anatomists (Dallachy and Simpson, 1960). The development of tumours from such small and previously unrecognized glomera may make it difficult to distinguish in any particular case between multicentric tumour origin and metastasis.

All the known chemoreceptors are related to large blood vessels; they are themselves highly vascular and have a sensory innervation. They are said to be sensitive to changes in the chemical

composition of the circulating blood, especially to changes in hydrogen-ion, oxygen, and carbon dioxide concentration. 'They appear to act as sensory elements of a reflex arc that aids in the regulation of blood flow and, more especially, respiration' (Mendelow and Slobodkin, 1957).

There is clinical evidence of two types of functional activity of chemodectomata:

(1) The tumours may function as enlarged chemoreceptors, producing an exaggeration of normal physiological responses. The patient may develop dizziness, 'black-outs', hypotension, and nystagmus after slight exertion or even after minimal hyperventilation (Huppler, McBean, and Parkhill, 1955 ; Coldwater and Dirks, 1956).

(2) Recent work on the morphology, histochemistry, and chemistry of chemoreceptor tissue and its tumours indicates that they contain cells capable of producing noradrenaline (Costero and Barroso-Moguel, 1961 ; Barroso-Moguel and Costero, 1962 ; Clay and Adenis, 1963 ; Pryse-Davies *et al.*, 1964). Glenner, Crout, and Roberts (1962) have reported a levarterenol-secreting tumour of the neck in a 12-year-old boy. The neoplasm had the typical microscopic structure of a chemodectoma. The patient suffered from hypertension.

Tumours of the chemoreceptors are comparatively rare, but several hundreds have now been reported (Table I), and their natural history and structure are becoming better known. At the Royal Marsden Hospital, chemodectoma was recognized in 25 patients from January 1945 to June 1963: there were 20 tumours of the jugular body, two of the carotid body, one of the vagal body (Greening and Staunton, 1964), one in the region of the aortic arch (reported here), and one retroperitoneal tumour arising near the aortic bifurcation.

'AORTIC BODY TUMOURS'

The first description of aortic bodies in man has been attributed to Biedl and Wiesel (1902), but their paper dealt with the organs of Zuckerkandl, the paraganglia found in the retroperitoneum of infants near the bifurcation of the aorta. Busacchi (1913) may have been the first to describe the aortic-arch bodies in humans when he drew attention to two 'chromaffin' bodies near the heart of a full-term foetus. Palme (1934) described paragangliomas situated above the heart in man, and Boyd (1937) showed the position of four aortic bodies in the mediastinum of a human embryo ; it is Boyd's diagram of the chemoreceptors near the branchial-arch arteries that has so frequently been reproduced by other authors.

Table II gives a summary of the 28 cases in which, with the exception of those at the periphery of the lungs, primary intrathoracic chemodectoma was thought to be present. These seem sufficiently rare and interesting to merit collection for study.

Our own case report follows.

CASE REPORT

H. F., 029998, a retired postman aged 67 in November 1956, had had an operation for the removal of a tumour of the right side of the mandible at another hospital in 1952 ; the tumour was at that time thought possibly to be of salivary gland origin, but was said to have 'some resemblance to granular-cell "myoblastoma" and to non-chromaffin paraganglioma'. In 1956 when he came to us he had had pain in the back for nearly two years, and radiographs had shown some destruction of the fifth lumbar vertebra and a large mediastinal mass.

On examination he was found to have a tumour some 5 cm. in diameter involving the right mandible and visible in the bucco-alveolar sulcus ; it pulsated, the pulsation being eliminated by carotid artery compression. There was some fullness of the veins of the neck, and a loud tuneful murmur could be heard in the second interspace on both sides of the sternum. The radiological appearances were those of a metastasis in the body of the fifth lumbar vertebra, and there was a large superior mediastinal mass lying anteriorly, displacing the trachea to the right (Figs. 1 a and 1 b). A clinical diagnosis of primary thyroid carcinoma was made, and a radioactive iodine uptake study was done, but no tumour uptake was demonstrated. Sections of the tumour excised in 1952 were then reviewed and the diagnosis of chemodectoma was established.

Radiotherapy was given in November and December 1956 to the lumbar spine, 2,750r in 15 days, and again in March and April 1957 to the jaw (3,250r) (Fig. 2 a), the mediastinum (1,750r), and the lumbar spine (1,900r) in 21 days ; further irradiation was given in September and October 1957 to the mediastinum (2,330r), the lumbar spine (2,750r), and the jaw (2,700r) in 30 days. After treatment he was able to walk without pain for the first time for nearly three years, and he both looked and felt much better, but the tumour masses in the jaw and mediastinum (Fig. 1 c) showed incomplete regression. In August 1958 he developed pain in the left shoulder and was thought to have another metastasis in the greater tuberosity of the left humerus. This was treated (2,550r in 16 days), but relief of pain was slower than before ; he was, however, almost free of discomfort and had full movement of the arm by February 1959. In the course of the ensuing year growth of the tumour of the right jaw recurred (Fig. 2 b), and in June and July 1960 it was again treated, this time with 2 MeV *x* rays to 5,000r in 32 days ; a painful new lesion in the left fibula received 4,200r

TABLE II

CHEMODECTOMATA IN THE REGION OF THE AORTIC ARCH

Author	Sex/Age	Tumour Location, Symptoms, Signs	Treatment	Comment and Follow-up
Lattes (1950)	M 59	Anterior mediastinum, extending upwards behind right clavicle into supraclavicular fossa where a mass was present 14 yrs.	Partial excision of portion of tumour in neck	Alive and well 8 yrs. after surgery
Lattes (1950)	M 35	In adventitia of arch of aorta, near obliterated ductus arteriosus. This tumour and one of the carotid body were incidental findings at necropsy. A third chemodectoma in ganglion nodosum had been detected *ante mortem*	—	Multiple chemodectomata
Monro (1950)	M 22	Anterior mediastinum, extending upwards as a tumour mass at root of neck; biopsy showed metastases in neck lymph nodes; radiological diagnosis of metastases in lungs and liver	Tumour inoperable; irradiation	Proved metastases in cervical lymph nodes; inferred metastases in lung and liver; died 8 yrs. after biopsy; no necropsy
Duncan and McDonald (1951)	M 18	Extrapleural, in right posterior costovertebral sulcus, extending from rib 9–11; tumour asymptomatic, discovered on routine radiography	Excision	Alive and well when last seen 6 yrs. after excision
Duncan and McDonald (1951)	F 33	Extrapleural, in right posterior costovertebral sulcus, at level of Th. 7; tumour asymptomatic, discovered on routine radiography	Excision	Alive and well 14 yrs. after surgery; recurrence suspected at primary site 16 yrs. after treatment
Drews and Groniowski (1953)	F 50	Upper anterior mediastinum, level of second left rib, causing pain in chest; dullness and decreased breath sounds in left chest	Partial excision and irradiation	Died of unknown cause 3 yrs. after treatment
McDonald, Aufderheide, and Fuller (1954)	F 38	Anterior mediastinum, extending upwards behind right clavicle, displacing trachea, oesophagus, thyroid, and common carotid artery; tumour discovered when patient came to hospital for confinement	Excision	Not seen after post-operative discharge
Davies and Randall (1954)	F 67	On anterior aspect of parietal pericardium, overlying right auricle; tumour was an incidental finding at necropsy	—	Death due to suppurative bronchitis and peritonitis
MacDonald (1956)	M 79	Completely encircling, without compressing, left subclavian artery at level just distal to thyrocervical axis; tumour found at necropsy in patient who died of metastasising hepatoma and aneurysm	—	No spread of chemodectoma to lymph nodes or other organs
Gillis, Reynolds, and Merritt (1956)	M 7	Patient admitted to hospital with anorexia, fever, loss of weight, bilateral inguinal lymphadenopathy; radiograph showed circumscribed density right lower lobe of lung; at thoracotomy tumour was found on antero-lateral aspect of right lower lobe	Right lower lobectomy	Post-operatively no symptoms for 2 yrs., then recurrence in scar twice: first excised and proved; second irradiated; patient died; no necropsy
Shaw and Kennedy (1956)	M 30	Behind heart in left paravertebral gutter at ninth intercostal space posteriorly	Excision	Post-operatively alive and well with no sign of recurrence
Mendelow and Slobodkin (1957)	F 31	Anterior superior mediastinum, impinging on azygos vein and superior vena cava, extending posteriorly, fixed to trachea; two pieces taken for biopsy; tumour discovered on routine radiography which led to thoracotomy	Partial excision and irradiation	Alive 3 yrs. after treatment with tumour present
Taylor and Evans (1958)	M 13	At right posterior costovertebral junction, at level of Th. 6, adhering to spine; tumour discovered on routine radiography after trauma; patient died under anaesthetic for thoracotomy	—	Necropsy after operative death; no spread discovered
Madden (1958)	F 28	In mediastinum between trachea and right main stem bronchus; azygos vein overlay tumour which was discovered on routine radiography during sixth month of pregnancy	Excision	Alive and well 19 mths. after surgery
Peräsalo, Dammert, and Sirola (1959)	F 49	First tumour was in anterior mediastinum between and adherent to left lung lobes; excised 1951: second tumour grew on right diaphragm; excised 1956 (thyroid adenoma also removed 1956); metastases suspected at hilum left lung, Th. 7, and in interscapular subskin	Excision of both tumours; radiotherapy after second excision and of unproved metastases spine and shoulder region	Alive and working 21 mths. after excision of second tumour; metastases inferred in lung, spine, and interscapular subskin
LePere and Mani (1961)	F 28	Overlying posterolateral portion of aorta, beginning 1 cm. below origin of left subclavian artery; anorexia, insomnia, and vomiting attacks; tumour discovered on chest radiograph	Excision	Well 6 mths. after operation

TABLE II—*continued.*

Author	Sex/Age	Tumour Location, Symptoms, Signs	Treatment	Comment and Follow-up
Barrie (1961)	M 63	Attached to pericardium over right auricle; incidental necropsy finding	—	—
Barrie (1961)	F 51	Anterior to aorta and common carotid vessels; discomfort behind sternum; tumour discovered on chest radiograph	Excision	Well 12 mths. after operation
Tama, Ellis, Hodgson, and Dockerty (1962)	M 66	Anterior superior mediastinum, almost completely encircling superior vena cava near azygos vein, causing superior vena caval obstruction and usual symptoms	Tumour inoperable; superior vena caval obstruction treated by shunt and radiotherapy	Septicaemia post-operatively for 5 mths., gastrointestinal bleeding for 1 yr. with radiation fibrosis
Pachter (1963)	F 27	Anterior superior mediastinum; no symptoms	Excision	Alive 6 yrs. after surgery
Pachter (1963)	F 61	Anterior inferior mediastinum; no symptoms	Excision	Alive 4 yrs. after surgery
Pachter (1963)	F 63	Anterior superior mediastinum; dyspnoea	Excision	Alive 6 yrs. after surgery
Pachter (1963)	F 30	Anterior superior mediastinum; no symptoms	Excision	Alive 6 yrs. after surgery
Pachter (1963)	F 68	Anterior inferior mediastinum; no symptoms	Excision	Alive 7 yrs. after surgery
Pachter (1963)	F 29	Anterior superior mediastinum; no symptoms	Incomplete excision	Alive 9 yrs. after surgery
Phillips (1963)	F 58	Anterior superior mediastinum (aortography diagnosis *ante mortem*); thoracotomy biopsy; necropsy showed mass above and external to pericardial sac, thought to have arisen in an aortic body near left subclavian artery	Tumour inoperable	Died after attempted excision; necropsy
Spector, Roper, and Spratt (1963)	F 67	In mid-mediastinum, adherent to inferior aspect of aortic arch, causing deviation of trachea, oesophagus; vague upper abdominal pain for one year before treatment, with one episode of syncope	Excision	Well 5 mths. after operation
Smithers and Gowing (present report)	M 62	Tumour partially removed from right lower jaw in 1952; backache 1956; radiography showed large mediastinal mass and destruction of Lumbar 5; pain left shoulder 1958,? metastasis head of humerus; right jaw tumour recurred 1960 and ? metastasis left fibula. At necropsy mediastinal tumour was seen to lie above arch of aorta, partly surrounding left subclavian artery	Incomplete excision of jaw tumour 1952 and later irradiation of mediastinum, right jaw, Lumbar 5, left shoulder and left leg	Survived 10½ yrs. after surgery in 1952; in this period four other tumours were discovered; died of bronchopneumonia August 1962; necropsy

in the same period. There was further and better regression of the mass in the mouth on this occasion, but it never completely disappeared. In June 1962 he developed tightness in the chest, dyspnoea, rising blood urea, nausea, and vomiting; he was admitted to nospital and died of bronchopneumonia on 4 August 1962.

There can be little doubt that the mediastinal tumour in this patient was a large primary chemodectoma arising from an aortic body. Retroperitoneal chemodectoma has been reported by others (Zacks, 1958), so that the tumour invading the fifth lumbar vertebra of our patient may also have been primary. To our knowledge, a primary chemodectoma has not been reported within the body of the mandible, although the possibility of the growth having arisen from small glomera associated with nutrient arteries of the bone cannot be excluded. The lesions in the left humerus and left fibula may well have been metastases, but, if so, radiotherapy caused their complete destruction, since no histological evidence of neoplasia in these sites could be found *post mortem*. Although the appearances suggest metastases from a primary aortic body tumour, multicentric chemodectoma formation cannot be excluded in this case.

NECROPSY   Only positive findings are given.

*Cardiovascular system*   There was moderate hypertrophic thickening of the right ventricular wall.

A lobulated tumour mass, 8 × 7 × 6 cm., was present above the aortic arch. It partly surrounded the left subclavian artery; the left common carotid was stretched over its anterior surface, and the innominate artery was displaced downwards and to the right. The tumour was generally reddish in colour but displayed greyish areas of fibrosis on the cut surface (Fig. 3).

Respiratory system   The trachea was compressed and displaced to the right by the mediastinal tumour. The bronchi contained mucopus, and there were multiple patches of bronchopneumonic consolidation in both lower lobes. The right pleural cavity contained 320 ml. of pale yellow fluid.

*Urinary system*   Both kidneys showed coarse pyelonephritic scarring.

*Skeletal system*   The body of the fifth lumbar vertebra was invaded and surrounded by a dark
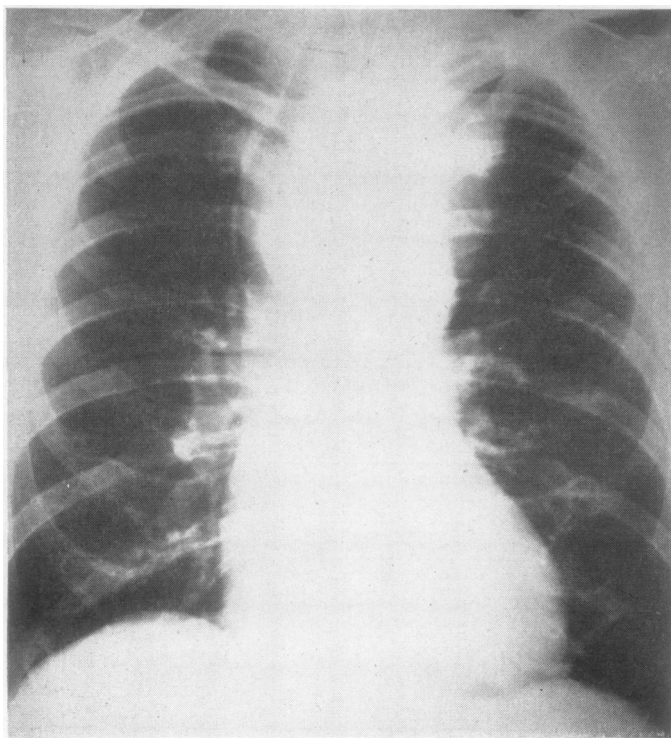
FIG. 1.   a, *Chest radiograph taken in November 1956 shows an anterior mediastinal mass with the appearances of a retrosternal thyroid.* b, *A more penetrating radiograph taken in March 1957 before irradiation of the mediastinum shows that the mass has increased in size and that the trachea is displaced further to the right.* c, *Little change is seen in the appearances of the mediastinal mass after the second course of irradiation in November 1957.*
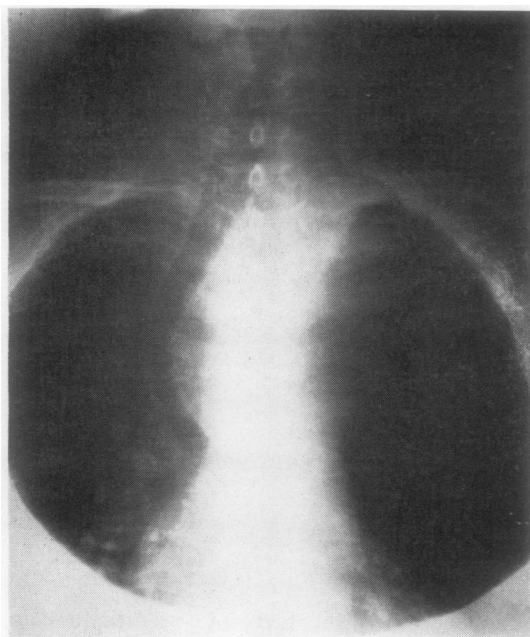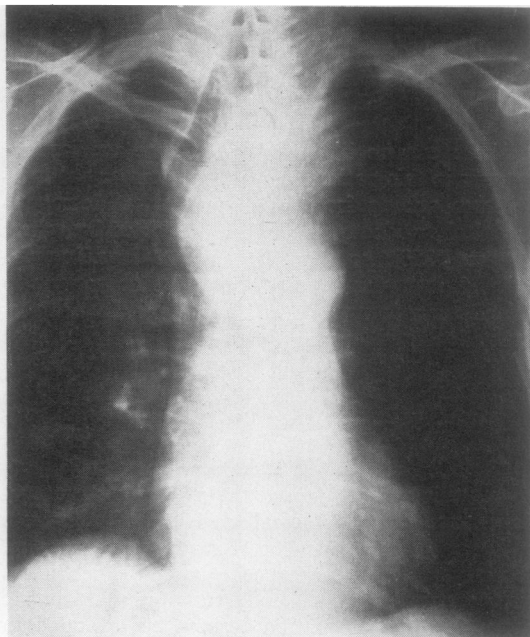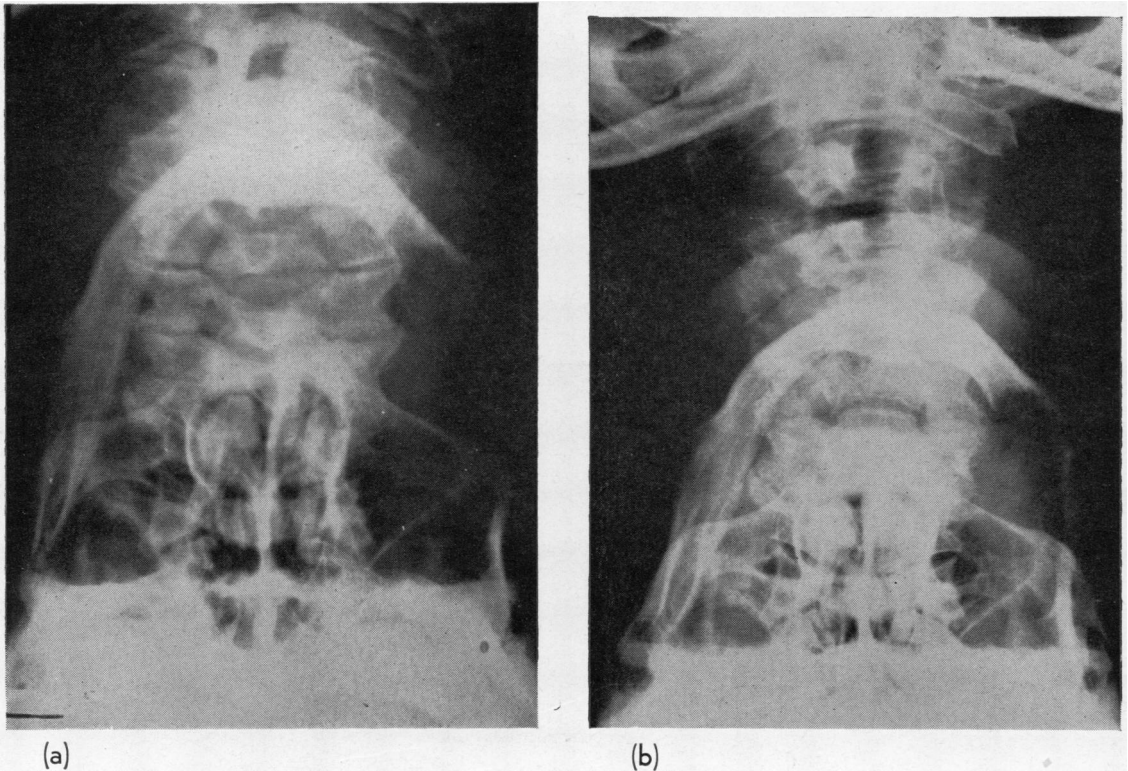
FIG. 2. a, *March* 1957. *An extensive area of destruction is seen in the right mandible. The tumour had been partially excised in* 1952. b, *Although radiotherapy had led to some tumour regression and new bone formation in the right mandible, by June* 1959 *the tumour was enlarging again.*

red, lobulated tumour. This tumour mass was firmly adherent to the anterior aspect of the vertebral body; it curved round the lateral surfaces, passed into both foramina, and infiltrated beneath the dura on the dorsal aspect.

Residual tumour was present in the right ramus of the mandible. The bone was expanded and the cortex thinned. No residual tumour tissue could be identified in either the left humerus or the left fibula.

Histology Similar microscopic features are seen in the tumour removed from the jaw in 1952 and in the mandibular, mediastinal, and retroperitoneal tumours examined *post mortem*. The neoplasms consist of polyhedral cells which have fairly regular nuclei and finely granular, palely eosinophilic cytoplasm. The cells are disposed as clusters in a highly vascular stroma. Most of the blood vessels have thin walls comprising little more than a single layer of endothelial cells supported by a delicate basement membrane. The

tumour cells at the periphery of the clusters lie in intimate relation to these vascular channels (Figs. 4 a and b).

The histological appearances are considered to be those of the chemodectoma. Attempts to demonstrate argentaffin, argyrophile, and chromaffin reactions in the cells produced negative results. However, the 1952 material was received in formalin, and post-mortem tissues often give weak or negative reactions.

SUMMARY

The twenty-eighth case of tumour of an aortic-arch body is reported. The relevant literature on chemoreceptors and their tumours is reviewed with special reference to intrathoracic chemodectoma in the region of the aortic arch.
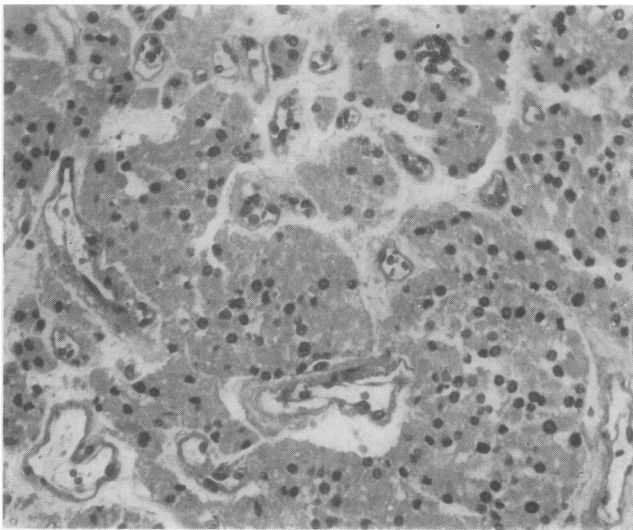
FIG. 3. *Necropsy specimen showing the large tumour mass above the aortic arch, displacing and distorting the blood vessels and trachea.*
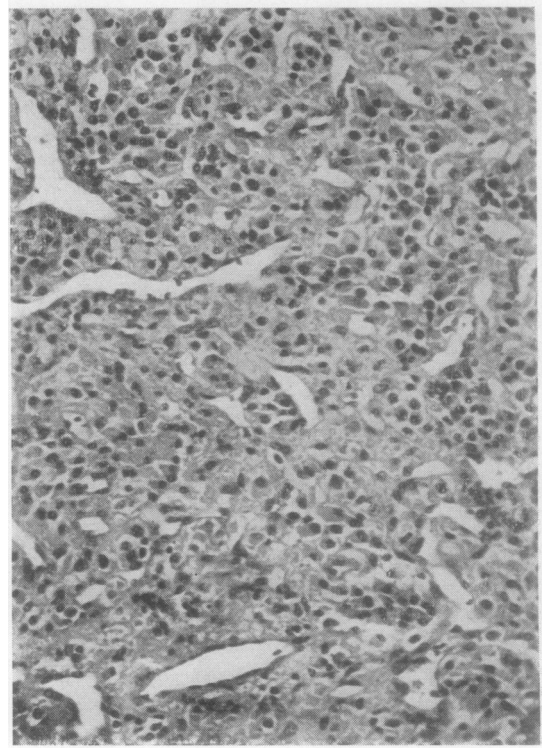
(a)

(b)

FIG. 4. a, *Section of the jaw tumour excised in 1952. Note the polyhedral cells and the abundant thin-walled vascular channels. H. and E., × 205.* b, *Section of the aortic body tumour found* post mortem. *The cells have abundant granular cytoplasm, and there are numerous thin-walled capillary blood vessels. H. and E., × 205.*

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