MALIGNANT LYMPHOMAS OF THE NOSE AND THROAT

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Introduction

Sarcomas occur infrequently in the nose and throat so that the number which pass through any individual surgeon's practice tends to be small. As a consequence the description of these tumours in textbooks on diseases of the ear, nose and throat, and malignant lymphomas in particular, has been almost uniformly sketchy, and their pathological features virtually neglected.

Sarcomas are malignant tumours arising from tissues of mesenchymal origin, being considerably rarer than their epithelial counterparts, carcinomas. The commonest are those which arise from bone (osteosarcomas) and from tissues of the reticuloendothelial system (malignant lymphomas). Other less frequent examples are neurofibrosarcoma and leiomyosarcoma, while others such as liposarcoma, rhabdomyosarcoma and angeiosarcoma are very rare.

An analysis has been carried out of sixteen histologically proven cases of malignant lymphoma, presenting in the nose and throat, seen at St. Thomas's Hospital between 1934 and 1954. The natural history of these cases is reviewed, particular attention being paid to the correlation of their pathological and clinical details.

Nomenclature

There has been no little confusion with respect to nomenclature in this group of disorders, so it will not be out of place to define the terms used in this study. The term malignant lymphoma is used to designate a
tumour involving one or more cell types of the reticuloendothelial system which if untreated will lead to the death of the patient (Gall and Mallory, 1942). Synonyms that have been in common use to describe this group are reticulosis (Pullinger, 1932; Ross, 1933) and reticulo-sarcoma (Robb-Smith, 1938). The cells most commonly involved in this disease process are the white blood cells and reticulum cells. If the disease leads to a pathological increase in the number of white cells in the blood stream, with an increased proportion of immature forms, it is usually termed a leukaemia. Of all the theoretically possible cell combinations which could give rise to a non-leukemic malignant lymphoma, there are four more common than the remainder: follicular lymphoma, lymphosarcoma, reticulum cell sarcoma and Hodgkin’s disease (Willis, 1953). The first two arise when there is a proliferation of lymphocytes. Follicular lymphoma is characterized by a numerical and dimensional increase in lymphoid follicles, and lymphosarcoma by a diffusely uniform increase of lymphocytes. The term reticulum cell sarcoma is used when the reticulum cell is the principal cell involved in the lymphoma. A characteristic feature of this tumour is the tendency for the cells to be associated with the production of reticulin fibrils in the stroma, demonstrable by silver impregnation. The fourth common variant is Hodgkin’s disease, and here the characteristic feature is the formation of a pleomorphic tissue, consisting of reticulum cells, lymphocytes and granulocytes, the individual cell types participating to a varying degree from case to case. A proportion of the immature reticulum cells may be multinucleate, the so-called Hodgkin giant cells.

The clinical behaviour of reticulum cell sarcoma, lymphosarcoma and Hodgkin’s disease is frequently similar, though Hodgkin’s disease sometimes has distinguishing features, such as a greater tendency to present with febrile reactions and to produce pruritus. Follicular lymphoma represents a benign form of this disease process, though sooner or later the disease will change over to one of the other three variants. When this takes place, the relatively good health of the patient changes to one of a more obviously malignant progress (Wetherley-Mein et al., 1952).

Multiple myeloma or plasmacytoma is another well known disorder of the reticuloendothelial system which principally affects the bone marrow but which occasionally may form tumours elsewhere, such as the nasal cavity (Carson et al., 1955; Dolin and Dewar, 1956). Because the disease has such constant features and rarely involves lymphoid tissue, it is not commonly classified as a form of malignant lymphoma. As it is a tumour of bone marrow, which occasionally involves other sites implicated in malignant lymphoma, and as it is difficult sometimes to distinguish it histologically from reticulum cell sarcoma, it should clearly also be included under the broad heading and will be discussed in this paper.
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Case Histories

The cases are grouped according to the site of first presentation.

A. The Tonsil: Nine Cases

Case I

A thirty-seven year old woman was admitted to hospital in January, 1952. A month previously she had suffered from a cold and had noticed that the right tonsil was swollen. She had also observed a swelling on the right side of the neck and some difficulty in swallowing. The right tonsil was found to be grossly enlarged, firm, ulcerated anteriorly and surrounded by hyperaemic mucosa. A firm painless swelling the size of a hen's egg was present below the angle of the jaw and attached to deeper structures. No other abnormality was found. Haemoglobin 76 per cent. (Haldane), white cell count 13,400, polymorphs 75 per cent., lymphocytes 22 per cent., monocytes 3 per cent. Tonsillectomy was performed. Histology. The tonsil is partially replaced by malignant lymphoma, which is predominantly reticulum cell sarcoma but in places the picture is that of lymphosarcoma. There is early ulceration of the mucous membrane. Progress. Radiotherapy was given to the area of the tonsillar bed and right side of the neck. The patient's general condition, already good, was improved during treatment in hospital and there was no evidence of recurrence for nine months. In October, 1952, a glandular swelling appeared in the right supraclavicular fossa, there was evidence of an upper abdominal mass and involvement by tumour of the lumbar vertebrae. Radiotherapy was instituted to the affected areas, but a month later a left pleural effusion appeared and the general condition steadily deteriorated. The patient died one year after diagnosis. Post mortem. The body was emaciated. Bilateral pleural effusions were present. There were deposits of reticulum cell sarcoma in both parietal pleurae, mediastinum, pericardium diaphragm, mesenteric lymph nodes, liver, kidneys, left ovary and para-aortic glands.

Summary. A thirty-seven year old woman presented with unilateral tonsillar enlargement and swelling of a regional lymph node, due to reticulum cell sarcoma. She was treated by tonsillectomy and local radiotherapy, remaining in fair health for nine months. Four months later, thirteen months after the onset of symptoms, she died of widely disseminated disease.

Case II

A seventy-five year old man came to hospital in March, 1948, complaining of a lump below the angle of the right jaw and some difficulty in swallowing for a month. A tumour was found affecting the right tonsil and posterior faucial pillars extending down into the vallecula on the right side. There was a mobile lymph node, approximately 4 cm. in diameter, anterior to the sternomastoid muscle on the same side. No blood count was done but a biopsy of the tonsil was performed. Histology. The section consists of fibrous tissue containing clusters of reticulum cells, with a tendency to vacuolation of cytoplasm. There is a moderate deposition of reticulin fibrils between some of the individual cells and the tumour is considered to be a reticulum cell
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sarcoma. Progress. The patient’s condition was good and there was no evidence of lymphomatous change elsewhere. Radiotherapy to the affected region and lymph drainage area was begun a fortnight after the patient was first seen. A year later he was in fair health and there was no recurrence at the primary site, but an ill-defined epigastric mass and enlarged lymph nodes in the right axilla and left groin had appeared. Radiotherapy was given at intervals to these regions with temporary regression of the tumours. Nevertheless by August, 1950, radiotherapy ceased to be effective and a month later the patient died, two and a half years after diagnosis. No post mortem was performed.

Summary. A seventy-five year old man presented with involvement of the right tonsil and adjacent mucous membrane by reticulum cell sarcoma. An enlarged regional lymph node was the only other tissue involved. Complete and permanent local regression was achieved by radiotherapy and the patient remained in fair health for a year. Then there was evidence of widespread involvement of lymph nodes by tumour, and despite radiotherapy the patient died two and a half years after diagnosis.

Case III

A sixty-two year old man was admitted to hospital in November, 1952. Three weeks previously he had complained of a sore throat, and a week later had been observed to have enlarged tonsils and a lymph node at the angle of the right jaw. On admission both tonsils were seen to be enlarged, boggy and covered with exudate. The whole buccal mucous membrane was inflamed and covered in places by yellow exudate, yielding no specific organism on culture. Moderately enlarged lymph nodes were palpable in the right posterior triangle and in both jugular chains. The liver was just palpable and the lower limbs oedematous. Haemoglobin 78 per cent., white cell count 17,000, polymorphs 90 per cent., lymphocytes 6 per cent., monocytes 4 per cent. Progress. The patient went downhill rapidly and died in uraemia (blood urea 113 mg. per cent.) five days after admission and almost a month after first seeking advice. Post mortem. The appearances of both tonsils, the right tonsillar and mesenteric lymph nodes were those of malignant lymphoma. The heart was fibrotic and the coronary arteries severely atheromatous. The kidneys were slightly enlarged and paler than normal. The cortico-medullary margin was obliterated in the right kidney. The bladder was hypertrophied. A nodule 1 cm. in diameter and mottled yellow in colour was present in one lateral lobe of the prostate.

Histology. Reticulum cell sarcomatous change is present in both tonsils, lymph nodes of neck and mesentery. There is similar infiltration of the submucosa and mucosa of the stomach. The reticulum cells are small and oat-shaped and associated with a moderate increase of reticulin. The section from the prostate shows a poorly differentiated adenocarcinoma and from the kidneys the picture of nephrocalcinosis. Calcium is also present in the pulmonary alveolar walls and myocardium. The cause for the calcinosis is not determined.

Summary. The presenting symptoms and signs of this sixty-two year old man were those of a throat infection, although the disease was at that time generalized. The patient survived only five days after admission.
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Case IV

A thirty-seven year old man was admitted to hospital in February, 1949, giving a seven-week history of progressive loss of appetite, lassitude and episodes of fainting. The tonsils were moderately enlarged, as also were painless lymph nodes of the right posterior triangle, both anterior triangles, left inguinal region and axilla. The liver and spleen were palpable. The patient was icteric and the blood picture was that of a haemolytic anaemia, the haemoglobin being 38 per cent., reticulocytes 10 per cent., and the direct Race Coombes test positive. White cell count 8,000, polymorphs 83 per cent., lymphocytes 11 per cent., monocytes 6 per cent. Progress. The patient’s general condition deteriorated, an abdominal mass became palpable, signs of cardiac failure appeared and he died in April, 1949, seven weeks after admission and three and a half months after the first symptom. Post mortem. Enlarged lymph nodes were present throughout the body, the enlargement being particularly marked at the root of the mesentery and in the para-aortic region. The tonsils were also increased in size. Peyer’s patches were prominent in the small intestine. The spleen was enlarged to three times its normal size. Histology. The tonsils show malignant lymphomatos change consisting of a lymphocytic and reticulum cell increase, the latter predominating and producing abundant reticulin. A similar change is present in lymph nodes and bowel wall, though the Peyer’s patches in the small intestine are not involved with certainty. The peribronchiolar lymphoid tissue is hyperplastic and foci of lymphomatous tissue are present in the portal tracts of the liver. The spleen is congested and shows no evidence of lymphoma, the Malpighian corpuscles being small.

Summary. A thirty-seven year old man presented with signs of generalized ill health due to widespread reticulum cell sarcoma with an associated haemolytic anaemia. The tonsils were involved in the disease process but did not contribute symptomatically.

Case V

A fifty-seven year old man was admitted to hospital in May, 1951, with the complaint of a painless lump in the throat for a month. His general condition was good but on examination he was found to have a large left tonsillar mass extending across to the uvula and down to the base of the tongue. A firm painless lymph node was palpable at the angle of the jaw on the left side. White cell count 14,000, polymorphs 60 per cent., lymphocytes 35 per cent., monocytes 4 per cent., eosinophils 1 per cent. A biopsy of the tonsillar mass was performed. Histology. The section is of reticulum cell sarcoma, the cells showing a box-like pattern. Progress. A heavy course of irradiation was given to the tonsillar area on the left side and also to the region of the right tonsillar lymph node which was now palpably enlarged. The patient remained well with persistent oedema of the area irradiated until May, 1952, when paraplegia developed, more severe on the right side than the left. This slowly worsened for about six months and then a little later showed some improvement. No evidence of lymphomatos change was found and the lesion was considered to be due to irradiation gliosis of the cervical cord. When last seen in February 1956, four years and nine months after the first symptom, there was no evidence of recurrence and the patient was in excellent health apart from a mild paraplegia.
Summary. A fifty-seven year old man was admitted on account of a symptomless lump in the throat due to a swelling in the left tonsillar region and an enlarged regional lymph node. Biopsy diagnosis was reticulum cell sarcoma. The general condition was good, and after heavy irradiation to the tonsillar area there has been no recurrence four years and nine months later.

Case VI
A man aged thirty-eight was first seen at hospital in April, 1949, complaining of a painless swelling in the throat. A month previously he had suffered from a peritonsillar abscess and the acute symptoms had subsided satisfactorily under penicillin. On examination his left tonsil was considerably enlarged and a soft painless lymph node was palpated at the left angle of the jaw. Total white cells 16,300, polymorphs 61 per cent., lymphocytes 31 per cent., monocytes 5 per cent., eosinophils 3 per cent. Biopsy of the left tonsil was performed. Histology. Somewhat degenerate malignant lymphoma is partially replacing normal tonsillar lymphoid tissue. The cells are pleomorphic, with a tendency to reniform nuclear structure. Reticulin formation is patchy. The tumour, which is considered to be a form of reticulum cell sarcoma, is present in the underlying muscle. Progress. Radiotherapy was given to the tonsillar region and to both sides of the neck, the dosage being spread over one month. The patient remained well but the lymph node at the angle of the jaw still remained enlarged five months after therapy. Block dissection of the lymph nodes on the left side of the neck was therefore undertaken. Microscopic examination showed no evidence of malignant lymphoma and the patient has since remained free from recurrence. He was last seen in December, 1955, six and a half years after diagnosis.

Summary. A thirty-eight year old man had a considerably enlarged left tonsil which was noticed after a peritonsillar abscess had subsided. Biopsy showed this to be a malignant lymphoma. Radiotherapy spread over a month was given to the tonsillar area and six and a half years after diagnosis there has been no extension or recurrence of disease.

Case VII.
A seventy-two year old man came to hospital in November, 1952, complaining of difficulty in swallowing and a lump in the throat which he had had for six weeks. He had lost a considerable amount of weight in recent months but no abnormality was found apart from a very large smooth left tonsil with central ulceration and peripheral hyperaemia, together with a slightly enlarged right tonsil. No blood count was made. Bilateral tonsillectomy was performed. The tonsils were dissected away easily and it was noted that the capsules of both were intact. Histology. Lymphosarcoma is present in both tonsils, the cells being predominantly lymphoblastic (Fig. 1). Replacement of normal lymphoid tissue is only partial on the right side (Fig. 2), but is complete on the left and has led to ulceration of the overlying epithelium. The left tonsil in addition shows a well marked follicular background (Fig. 3), indicating that the tumour probably started as a follicular lymphoma. The tumour forms no
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FIG. 1.
Case VII. Tonsil. H.+E. ×540. Lymphoblastic lymphosarcoma. The tumour consists of a uniform sheet of cells which are predominantly large lymphocytes.

FIG. 2.
Case VII. Tonsil. H.+E. ×42. Lymphoblastic lymphosarcoma. This low power view shows how only part of the lymphoid tissue may be involved.
FIG. 3.
Case VII. Tonsil. H. + E. \( \times 42 \). Lymphoblastic lymphosarcoma. This low power view shows the tendency in this area to a pattern of follicular lymphoma.

FIG. 4.
Case VII. Tonsil. Reticulin stain. \( \times 140 \). Lymphoblastic lymphosarcoma. The scanty reticulin formation is in contrast to the picture in reticulum cell sarcoma.
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increase of reticulin fibrils (Fig. 4). Progress. Radiotherapy was given to the left tonsillar and cervical regions over a period of one month. The patient remained in fair health until three and a half months after diagnosis, when he developed auricular fibrillation. He died two days later in cardiac failure before he could be transferred to hospital. No post mortem was performed.

Summary. A seventy-two year old man complained of a lump in the throat and difficulty in swallowing for six weeks. There had been recent loss of weight but enlarged tonsils were the only abnormal physical signs. Bilateral tonsillectomy revealed lymphosarcoma. Regional radiotherapy was given for a month. The patient died in cardiac failure three and a half months after diagnosis.

Case VIII

A fifty-four year old man was admitted to hospital in October, 1934, complaining of some difficulty in swallowing with a sensation of "phlegm in the throat" for a year. Tinnitus and a sensation of pressure in the left ear had been present for the same time. On examination an enlarged left tonsil was found and small lymph nodes were palpated in the neck and left supraclavicular fossa. No other abnormality was found and no blood count was made. Bilateral tonsillectomy was performed. Histology. The right tonsil is normal. The left tonsil shows the picture of lymphosarcoma, the normal tonsillar architecture being obliterated by a sheet-like proliferation of small lymphocytes (Fig. 5).
No follicular pattern could be identified. Progress. A course of radiotherapy was given to the left tonsillar fossa and side of neck. Four months later the patient was well but a chest X-ray showed a right basal opacity which was considered to be due to lymphosarcoma. Radiotherapy was applied to this and, although four months later it had increased in size, it had disappeared within a year. The patient remained well apart from developing an X-ray dermatitis over the chest which was successfully grafted in 1948. When last seen at hospital in August, 1949, he was still in good health and remained so until 1953, nineteen years after diagnosis, when he died suddenly from a stroke.

Summary. A fifty-four year old man presented with difficulty in swallowing, tinnitus and a sensation of pressure in the left ear. A large left tonsil and small cervical lymph nodes were the only abnormal physical signs. Bilateral tonsillectomy was performed. The left tonsil showed the histological appearance of lymphosarcoma. Following local radiotherapy, there was no recurrence, except possibly a pulmonary mass, for nineteen years, the patient being in good health until his sudden death from a stroke.

Case IX

A motor mechanic aged 57 was seen in the outpatient department in November, 1947. Two months previously he had had a sore throat which had been treated conservatively as a quinsy. More recently he had noticed a swelling in the throat and left side of the neck with some dysphagia. Examination showed him to be a man of healthy appearance though emphysematous. The right tonsil was small and unhealthy, whilst the left was greatly enlarged, narrowing the pharynx and having the appearance of a peritonsillar abscess, though not tender. There was no glandular enlargement in the neck or elsewhere, and other systems were normal. White cell count 8,800, polymorphs 61 per cent., lymphocytes 33 per cent., monocytes 5 per cent., eosinophils 1 per cent. The left tonsil was removed and was well encapsulated. Histology. Lymphosarcoma of tonsil. The normal architecture of the tonsillar lymphoid tissue is obscured as a result of a widespread proliferation of mature lymphocytes. An ill-defined follicular pattern is present. The overlying squamous epithelium is thin but not ulcerated. Progress. Four days after tonsillectomy radiotherapy to the throat and adjoining neck was begun, the course lasting one month. This resulted in a brisk reaction which did not entirely resolve for three months. Screening of chest showed that there was no mediastinal mass. The patient remained well, though nervous and apprehensive, and was without sign of recurrence at any site when last seen in February, 1950; but he had at this time lost some weight and had had an episode of severe backache for which no neurological or bony abnormality had been found. He died suddenly in May, 1950, two and a half years after first attending hospital. Post mortem. This was performed elsewhere. Death was due to syphilitic coronary arteritis. There were also the appearances of specific aortitis and cardiac dilatation. No sign of lymphosarcoma was found in any system.

Summary. A fifty-seven year old man presented with a month’s history of sore throat and tonsillar swelling in whom a well-encapsulated
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lymphosarcoma was removed at tonsillectomy. Local radiotherapy was followed by a little over two years good health before death two years and six months after first attendance. *Post mortem* showed syphilitic coronary arteritis to be the cause of death. No evidence of lymphosarcoma was found.

B. THE MAXILLA: ONE CASE

*Case X*

A fifty-four year old man was seen at hospital in November, 1953. Six weeks previously a tooth in the left upper jaw had worked loose. The patient now complained of a rapidly increasing swelling in the mouth and left cheek. On examination the left upper alveolus was seen to be largely replaced by a firm ulcerating tumour bulging the cheek forward. No cervical lymph nodes were palpable on the left side, but an enlarged hard node was present in the right submandibular triangle. No other abnormality could be detected. A biopsy was taken of the alveolar swelling. *Histology* (i). The section consists of fragmentary partly ulcerated lymphomatous material which appears to be reticulum cell sarcoma. *Progress*. A week later the mass including the left half of the hard palate and most of the upper jaw on that side was removed. The submandibular lymph node was biopsied. *Histology* (ii). Reticulum cell sarcoma is present in a section from the alveolar mass ulcerating through the squamous mucous membrane (Fig. 6). Abundant reticulin fibrils have been
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laid down (Fig. 7). The lymph node shows partial replacement by similar tumour tissue. **Progress.** Ten days after operation a recurrence had developed in the left cheek and a course of radiotherapy was given for ten days to the left facial and upper cervical regions. The buccal tumour responded to treatment and the patient remained well for nine months, after which he was readmitted with a firm tumour in the right cheek and on the right side of the nose. Blood count at this time showed Hb. 90 per cent., white cells 4,100, polymorphs 69 per cent., lymphocytes 24 per cent., monocytes 7 per cent. No other swellings were observed. Palliative radiotherapy was instituted but the patient’s general condition gradually worsened. He died in February, 1955, thirteen months after diagnosis. **Post mortem** was refused.

**Case X.** Maxilla. Reticulin stain, x 140. Reticulum cell sarcoma. Reticulin fibrils are numerous and closely related to the tumour cells.

**Summary.** A fifty-four year old man complained of a rapidly increasing swelling in mouth and cheek following the loosening of a tooth in the upper jaw. Biopsy of the alveolar swelling showed the presence of reticulum cell sarcoma. The alveolar mass was removed together with the single enlarged lymph node situated in the submandibular region. A local recurrence appeared ten days after operation and responded to radiotherapy. Nine months later the right alveolus became involved by tumour; there was no evidence of extension elsewhere. Despite further radiotherapy, the patient went downhill and died thirteen months after diagnosis. **Post mortem** was refused.

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C. The Nasopharynx: Two Cases

Case XI

A forty-three year old man was admitted to hospital in May, 1945, complaining of numbness and pain in the left side of the face, a lump on the forehead and some weakness of the right leg, all for about three weeks. He was found to have a left palatal palsy together with some loss of function of the Vth nerve on the left side. A small irregular mass was found in the nasopharynx. Lymph nodes were palpable in the left cervical, axillary and supraclavicular regions and also in the right axilla. The lump on the forehead was hard and fixed. There were also signs of a lesion of the thoracic spinal cord in the region of T.5. White cells 9,800, polymorphs 43 per cent., lymphocytes 53 per cent., mono-

FIG. 8.


cytes 4 per cent., eosinophils 1 per cent. A cervical lymph node was removed. Histology. Hodgkin's disease of lymph node. The normal nodal architecture is obliterated by a proliferation of lymphocytes and reticulum cells, with occasional Sternberg cells and eosinophils (Fig. 8). Reticulin fibrin formation is abundant (Fig. 9). Progress. A course of deep X-ray therapy was given with some temporary improvement in the function of the lower limbs. The patient's general condition, however, steadily deteriorated, the liver became readily palpable and a right hilar mass was visible on chest X-ray. He died in January, 1946, eight months after diagnosis. Post mortem. This was performed elsewhere. There was extensive lymphomatous involvement of para-aortic and mediastinal lymph nodes, liver, pancreas and lumbar vertebrae. No record was made of the appearance of the nasopharynx, brain or spinal cord.
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Summary. A forty-three year old man with rapidly advancing Hodgkin's disease presented with signs of cranial nerve and spinal cord involvement. There was also widespread lymph node enlargement. Biopsy of a cervical node showed the picture of Hodgkin's disease. Despite radiotherapy the Hodgkin's tissue extended to other sites and the patient died eight months after diagnosis.

Case XII
A forty-seven year old man presented himself in June, 1953, with a six months' history of increasing nasal discharge. This followed three attacks of "influenza" in rapid succession. He had also noticed a swelling on the left side of the neck for three months and during the last month his vision had deteriorated in the left eye, which had also become immobile. Fifteen years previously the patient had suffered from a left-sided proptosis and facial pain which had been cured following a left Caldwell-Luc operation. Examination showed involvement of III, IV, VI, VII and VIII cranial nerves on the left side. A hard mobile lymph node was palpable in the right posterior triangle of the neck, and there was another one beneath the left sternomastoid muscle. An X-ray of the base of the skull showed bone destruction of the tip of the petrous portion of the left temporal bone, extending laterally as far as the internal auditory meatus, and also a large soft tissue mass lying posteriorly in the nasopharynx. Total white cell count was 12,600, polymorphs 71 per cent., lymphocytes 4 per cent., monocytes 5 per cent., eosinophils 3 per cent.

Fig. 9.
Case XI. Lymph node. Reticulin stain. ×140. Hodgkin's disease. The stain confirms the presence of an increased amount of reticulin fibre.
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Examination under anaesthesia disclosed a deeply fixed firm swelling of the nasopharynx covered by normal mucosa and lying behind and above the Eustachian orifice. The lymph node in the region of the sternomastoid muscle was removed for diagnosis. Histology. Reticulum cell sarcoma. The normal lymphoid tissue of the lymph node is replaced to a varying degree by box-like, rather immature, reticulum cells (Fig. 10). Abundant reticulin formation can be demonstrated (Fig. 11). Progress. A course of radiotherapy spread over a fortnight was given to the primary nasopharyngeal tumour and the lymphatic drainage area in the neck. A month later all cranial nerve palsies had recovered except for total deafness and absent vestibular reactions on the left side. The nasopharyngeal tumour and lymph nodes were no longer palpable. The patient remained well until December, 1955, when he complained of upper abdominal pain and was found to have an enlarged spleen to which radiotherapy was given. Splenic size decreased and he was well and at work when last seen in April, 1956, over three years since the first symptoms.

Summary. A forty-seven year old man presented with nasal discharge, cranial nerve palsies and cervical lymph node enlargement. Examination revealed a nasopharyngeal tumour and X-ray showed extensive involvement of the petrous part of the temporal bone. Biopsy showed the tumour to be a reticulum cell sarcoma. Radiotherapy caused regression of all tumours and recovery from all palsies except for residual deafness. The
patient is well, though there is splenic enlargement, two years and ten months after diagnosis.

D. THE ETHMOID REGION AND NASAL CAVITY: FOUR CASES

Case XIII

A housewife aged fifty-seven attended the outpatient department in March, 1954, complaining of left-sided nasal obstruction which had been present since a cold two months previously. On examination a fleshly polyp was observed arising in the middle meatus of the left nasal cavity which filled the latter and which was seen to be extending into the left posterior choana. A similar but much smaller polypoid mass was found to be arising from the lateral nasal wall in front of the right inferior turbinate. The remainder of the upper respiratory tract and the ears showed no abnormality on clinical examination. There were no palpable lymph nodes in the neck. X-ray of the sinuses showed the left antrum to be opaque. A clinical diagnosis was made of a neoplasm arising from the left antrum. Under general anaesthesia the polyp in the left middle meatus was found to be very vascular and friable. Many pieces were removed for histological examination. The polyp on the floor of the right nasal cavity was also removed for section. Histology. The sections from both sides of the nose consist of fragments of nasal mucous membrane showing a heavy infiltration with plasma cells and their precursors. The tumour, a plasmacytoma, is associated with the deposition of abundant reticulin fibrils (Figs. 12 and 13). Progress. Further investigations showed a normal blood count and an E.S.R.
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Fig. 12.
Case XIII. Nasal tumour. H. + E. ×540. Plasmacytoma. The presence of plasma cells with small eccentrically placed nucleus in abundant cytoplasm is well shown.

Fig. 13.
Case XIII. Nasal tumour. Reticulin stain. ×540. Plasmacytoma. The stain shows how this tumour may be associated with an excess of reticulin fibre formation.
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(Westergren) of 9 mm. in 1 hour. The serum proteins were normal, in correct ratio and showed a normal electrophoretic pattern. No Bence Jones proteose or protein was present in the urine. X-rays of chest, ribs, spine, pelvis, upper ends of both femora and humeri were all normal. A course of high voltage radiotherapy (250 KV.) was instituted and the nasal airway rapidly improved. A month later there was no evidence of polypi on either side of the nose. The patient was last examined two years after the onset of symptoms and was still free from symptoms and signs.

Summary. A fifty-seven year old woman presented with a two-month history of left-sided nasal obstruction. Examination revealed polypi on both sides of the nose. X-ray showed the left antrum to be opaque. The polypi were removed and shown to consist of plasmacytoma. All laboratory tests and bone X-rays were normal. The tumour resolved with radiotherapy and the patient is well two years after the onset of symptoms.

Case XIV

A fifty-eight year old male pensioner first attended the outpatient department in March, 1954, complaining of left-sided nasal obstruction, which he had noticed for a week. There was some clear discharge from the nose. On examination the nasal septum was deviated to the left and the left nasal cavity filled with a large fleshy polyp. The right nasal cavity was healthy. The remainder of the upper respiratory tract was normal. There were no palpable lymph nodes in the neck. X-rays of the paranasal sinuses were clear. Clinically the polyp appeared neoplastic. Hb. 108 per cent., white count 11,300, polymorphs 67 per cent., lymphocytes 22 per cent., monocytes 7 per cent., eosinophils 4 per cent. Under general anaesthesia it was seen to be a large sessile friable polyp arising from an area the size of a penny on the left side of the nasal septum. There was no attachment to the lateral wall of the nose. The polyp was removed. Histology. The sections consist of fragments of nasal mucous membrane showing a heavy infiltration with plasma cells and their precursors. The tumour, a plasmacytoma, was associated with the production of abundant reticulin. Progress. As this polyp appeared to be a single lesion, it was decided to excise the septal area of origin with the underlying cartilage (left lateral rhinotomy with Moure-type incision). No further plasmacytoma could be seen histologically in this tissue. The wound healed by first intention and the patient was discharged with no abnormal physical signs in April. Three months later an adhesion was present on the left side of the septum high up but otherwise there was nothing to suggest recurrence. X-ray examination, however, showed the skull to contain deposits characteristic of multiple myeloma. In May, 1955, deposits had appeared in the IVth, Vth and VIth cervical vertebrae. The urine has been consistently negative for Bence Jones proteose, and the plasma proteins have been within normal limits. When last seen in February, 1956, the patient was very well and the clinical picture unchanged.

Summary. A fifty-eight year old male complained of left-sided nasal obstruction of a week's duration, associated with a little clear discharge.
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A large fleshy polyp obstructed the left nasal cavity. On removal this was seen to be a plasmacytoma. The patient was discharged free of symptoms but four months after the onset there was radiological evidence of myeloma in the skull and when last seen two years from the first symptom, deposits were also observed in the cervical vertebrae. All laboratory tests have so far been normal.

Case XV

A forty-five year old woman was admitted to hospital in August, 1951, complaining of blocking of the left nostril with a blood-stained nasal discharge, together with some deafness and tinnitus, worse in the left ear, which had been present for three months. Examination showed the left nostril to be obstructed by a closely packed mass of polypi. Both tympanic membranes were indrawn and there was a bilateral conductive deafness, worse on the left, due to Eustachian obstruction. X-ray showed a completely opaque left antrum. No blood count was made. A left Caldwell-Luc operation was performed and a mass of polypi was found in the anterior ethmoidal region. These were removed, including the left middle turbinate. Histology. The nasal polypi showed involvement by reticulum cell sarcoma producing a moderate amount of reticulin fibrils. Following the histological report a left external ethmoidectomy was performed, but no further lymphoma could be identified either macroscopically or histologically. Progress. At the beginning of October, 1951, lymph nodes had become palpable in both anterior triangles of the neck, and radiotherapy was instituted to this region with recession of the lymphoid swellings. The patient remained well for a further three months, when multiple small purplish nodules appeared in the skin of the trunk. One was biopsied and showed the presence of reticulum cell sarcoma in the region of the sweat glands and small vessels. Palliative radiotherapy was given to these nodules without effect. The patient’s general condition grew steadily worse, tenderness of the lumbar regions and bones of lower limbs suggested further deposits of neoplastic tissue, and she died in April, 1952, eight months after diagnosis. Post mortem was refused.

Summary. A forty-five year old woman presented with left nasal obstruction and blood-stained discharge. Polypi were removed from the left ethmoid region and the left middle turbinate was excised as it appeared abnormal. Both showed the presence of reticulum cell sarcoma. Two months later enlarged lymph nodes appeared in the neck, which disappeared after radiotherapy. Three months after this a crop of skin deposits of reticulum cell sarcoma developed which proved resistant to radiotherapy. The patient’s condition steadily deteriorated and she died eight months after diagnosis.

Case XVI

A fifty-two year old man who had suffered from bronchitis and emphysema for many years was admitted to hospital in July, 1952. He complained of a foul purulent discharge from the left nostril for six weeks. On examination his general condition was poor and he had lost a considerable amount of weight.
The mucous membrane of the nasopharynx was swollen, roughened and ulcerated, and a hard lymph node was palpable at the angle of the right jaw. Under anaesthesia a friable mass was identified in the ethmoid and sphenoid regions. A left Caldwell-Luc operation was performed and the mass was biopsied. No blood count was made. Histology. Fragments of nasal mucous membrane and underlying tissue contain partly necrotic malignant lymphoma. The tumour shows considerable pleomorphism, particularly marked in the more cellular, pseudo-follicular areas. The pleomorphic tissue includes multinucleate giant cells and many cells in mitosis. The tumour is associated with well-marked reticulin fibril formation and therefore is considered to be a reticulum cell sarcoma with a high proportion of immature cells. Progress. Shortly after the operation the patient bled profusely from the nasopharynx and became acutely obstructed. He failed to regain consciousness and died six hours after induction. Post-mortem examination showed the growth to be filling the left nasal fossa, maxillary antrum and invading the ethmoid on that side. Other organs of the body were normal and there was no sign of malignant lymphoma elsewhere.

Summary. A fifty-two year old man was admitted with a six week history of purulent nasal discharge. His general condition was poor. A friable mass was detected in the ethmoid and sphenoid regions and a hard lymph node at the angle of the right jaw. Biopsy of tissue obtained at Caldwell-Luc operation showed the tumour to be an immature form of reticulum cell sarcoma. The patient bled severely from the operation site and died with respiratory obstruction without regaining consciousness.

Discussion

Frequency

There were seventeen cases of histologically proven malignant lymphoma of the nose and throat at St. Thomas's Hospital, London, between 1934 and 1954. No clinical details are available of one case presenting in the tonsil: the remaining sixteen have been described above.

A total of 955 cases of sarcoma of all forms and in all situations were admitted to hospital during the same period and 578 (60.5 per cent.) of these were examples of malignant lymphoma, not including leukemia. The true incidence is probably higher as many of the earlier examples of the tumour called round cell sarcoma would now be classified as malignant lymphoma. Hodgkin's disease accounted for half of the total of malignant lymphoma, the remainder consisting chiefly of lymphosarcoma and reticulum cell sarcoma. The seventeen examples of lymphoma affecting the nose and throat form 2.9 per cent. of all lymphomas.

Table I shows the relative incidence in the different situations in the nose and throat and also gives the comparative frequency of carcinomas in each area. Figures are also included of similar cases seen at the Royal Marsden Hospital, London, for the nine years since 1945. It will be seen
## Malignant Lymphomas of the Nose and Throat

TABLE I.

<table>
<thead>
<tr>
<th>Location</th>
<th>Carcinoma</th>
<th>Malignant Lymphoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oro-pharynx</td>
<td>T 149</td>
<td>Nil</td>
</tr>
<tr>
<td>Maxillary antrum</td>
<td>M 20</td>
<td>11</td>
</tr>
<tr>
<td>Nasal cavities</td>
<td>T 6</td>
<td>M 1</td>
</tr>
<tr>
<td>Tonsil</td>
<td>T 41</td>
<td>M 54</td>
</tr>
<tr>
<td>Tongue</td>
<td>T 170</td>
<td>M 43</td>
</tr>
<tr>
<td>Tongue</td>
<td>M 11</td>
<td>10</td>
</tr>
<tr>
<td>Tongue</td>
<td>M 22</td>
<td>8</td>
</tr>
<tr>
<td>Tongue</td>
<td>M 93</td>
<td>8</td>
</tr>
<tr>
<td>Total</td>
<td>T 446</td>
<td>M 603</td>
</tr>
<tr>
<td>Malignant Lymphoma</td>
<td>Nil</td>
<td>17</td>
</tr>
</tbody>
</table>

(3-7\%)

(4-7\%)
that there were 17 cases of malignant lymphoma among 466 patients
with malignant disease of the nose and throat at St. Thomas’s Hospital
(3.7 per cent.) and 30 among 603 patients at the Royal Marsden Hospital
(4.7 per cent.). The tonsil was the site most frequently involved in the
nose and throat accounting for 59 per cent. and 63 per cent. of all
lymphomas at St. Thomas’s Hospital and the Royal Marsden Hospital
respectively. There was a higher incidence in the nasopharynx at the
Royal Marsden Hospital, compared with that found at St. Thomas’s
Hospital.

Clinical Features

The clinical features of the cases under review are summarized in
Table II.

The disease is one of the middle and old age groups, the ages of our
cases ranging from 37 to 75 years with an average of 55 years. The cases
at the Royal Marsden Hospital showed a similar incidence, the average
age there being 59 years. The disease has been reported in children in
whom, as might be expected, the course is altogether more acute (Hirst
and Charland, 1951; Metson, 1954).

All but three of the sixteen St. Thomas’s Hospital cases were male,
in contrast to the eighteen males among the thirty Royal Marsden
Hospital cases. The combined series shows a 2:1 ratio in favour of males
which is similar to that for malignant lymphomas as a whole (Lumb,
1954).

Malignant lymphoma may present in the nose and throat either as an
isolated primary tumour or as part of a generalized lymphoma. The
generalized case is usually seen by a physician on account of systemic
symptoms, such as lassitude, loss of weight and anaemia. Symptoms may
however be particularly prominent in the nose and throat in the first
place, so that the patient may be referred to a Nose and Throat Clinic
as a case of tonsillitis or suspected tumour in the throat. Two examples
of this group are included in the present series (Cases III and IV). One
presented with asthenia and sore throat, the latter being due to a stomatitis
resembling Vincent’s angina and similar to that seen in many acute
leukæmias. The other presented with systemic symptoms largely attribut-
able to a severe anaemia but which were complicated by a clinical picture
of acute follicular tonsillitis. It is of some interest that the anaemia was
found to be an acquired haemolytic anaemia, a type now recognized as an
occasional but severe complication of malignant lymphomas (Dacie,
1954).

Those lymphomas occurring primarily in the nose and throat usually
presented as bulky tumours with a short history. The great majority were
treated within three months of the onset of symptoms. The rate of
# TABLE II.


<table>
<thead>
<tr>
<th>No.</th>
<th>Sex</th>
<th>Age</th>
<th>Site</th>
<th>First Symptom</th>
<th>Delay Before Admission</th>
<th>Ulceration</th>
<th>Regional Glands</th>
<th>Histology</th>
<th>Treatment</th>
<th>Survival after Admission</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>F</td>
<td>37</td>
<td>R Tonsil</td>
<td>Cold and mass in throat</td>
<td>1 month</td>
<td>+</td>
<td>+</td>
<td>Mixed reticulum cell S. + lymphosarcoma</td>
<td>R tonsillectomy + radiotherapy</td>
<td>13 mths.</td>
<td>Died of generalized disease</td>
</tr>
<tr>
<td>2</td>
<td>M</td>
<td>75</td>
<td>R Tonsil</td>
<td>Mass in neck, Dysphagia</td>
<td>1 month</td>
<td>+</td>
<td>+</td>
<td>Reticulum cell S.</td>
<td>Radiotherapy</td>
<td>1 month</td>
<td>Died of generalized disease</td>
</tr>
<tr>
<td>3</td>
<td>M</td>
<td>62</td>
<td>R+L Tonsils</td>
<td>Sore throat and asthenia</td>
<td>2 months</td>
<td>+</td>
<td>+</td>
<td>Reticulum cell S.</td>
<td>Radiotherapy</td>
<td>5 days</td>
<td>Died of generalized disease</td>
</tr>
<tr>
<td>4</td>
<td>M</td>
<td>37</td>
<td>R+L Tonsils</td>
<td>Anorexia, lassitude</td>
<td>3 weeks</td>
<td>+</td>
<td>+</td>
<td>Reticulum cell S.</td>
<td>Radiotherapy</td>
<td>4 weeks</td>
<td>Died of generalized disease</td>
</tr>
<tr>
<td>5</td>
<td>M</td>
<td>57</td>
<td>L Tonsil</td>
<td>Painless mass in throat</td>
<td>1 month</td>
<td>-</td>
<td>+</td>
<td>Lymphosarcoma</td>
<td>Radiotherapy</td>
<td>2 months</td>
<td>Alive, no sign of disease</td>
</tr>
<tr>
<td>6</td>
<td>M</td>
<td>38</td>
<td>L Tonsil</td>
<td>&quot;Peritonsillar abscess&quot;</td>
<td>1 month</td>
<td>+</td>
<td>-</td>
<td>Reticulum cell S.</td>
<td>Radiotherapy</td>
<td>2 months</td>
<td>Alive, no sign of disease</td>
</tr>
<tr>
<td>7</td>
<td>M</td>
<td>72</td>
<td>L+R Tonsil</td>
<td>Dysphagia + lump in throat</td>
<td>1 month</td>
<td>+</td>
<td>-</td>
<td>Reticulum cell S.</td>
<td>Radiotherapy + block dissection of neck</td>
<td>1 month</td>
<td>Died of heart failure</td>
</tr>
<tr>
<td>8</td>
<td>M</td>
<td>54</td>
<td>L Tonsil</td>
<td>Dysphagia, Pressure and noises in left ear</td>
<td>2 months</td>
<td>+</td>
<td>-</td>
<td>Lymphoma</td>
<td>Tonsillectomy + radiotherapy</td>
<td>1 year</td>
<td>Died of stroke aged 74. No clinical evidence of disease</td>
</tr>
<tr>
<td>9</td>
<td>M</td>
<td>57</td>
<td>L Tonsil</td>
<td>Sore throat and quinsy</td>
<td>2 months</td>
<td>+</td>
<td>-</td>
<td>Lymphoma</td>
<td>Excision</td>
<td>3 mths</td>
<td>Died of syphilitic coronary arteritis, No sign of disease</td>
</tr>
<tr>
<td>10</td>
<td>F</td>
<td>43</td>
<td>Maxilla</td>
<td>Loose tooth, Swelling of cheek</td>
<td>1 month</td>
<td>+</td>
<td>-</td>
<td>Reticulum cell S.</td>
<td>Excision</td>
<td>8 months</td>
<td>Died of generalized disease</td>
</tr>
<tr>
<td>11</td>
<td>M</td>
<td>47</td>
<td>Nasopharynx</td>
<td>Nasal obstruction and discharge</td>
<td>6 months</td>
<td>+</td>
<td>-</td>
<td>Reticulum cell S.</td>
<td>Excision</td>
<td>2 years</td>
<td>Alive, No sign of disease</td>
</tr>
<tr>
<td>12</td>
<td>M</td>
<td>47</td>
<td>Nasopharynx</td>
<td>Nasal obstruction and discharge</td>
<td>6 months</td>
<td>+</td>
<td>-</td>
<td>Reticulum cell S.</td>
<td>Excision</td>
<td>2 years</td>
<td>Alive, No sign of disease</td>
</tr>
<tr>
<td>13</td>
<td>F</td>
<td>57</td>
<td>Ethmoid</td>
<td>Nasal obstruction and discharge</td>
<td>6 months</td>
<td>+</td>
<td>-</td>
<td>Reticulum cell S.</td>
<td>Radiotherapy</td>
<td>2 years</td>
<td>Alive, No sign of disease</td>
</tr>
<tr>
<td>14</td>
<td>M</td>
<td>54</td>
<td>Ethmoid</td>
<td>Nasal obstruction and discharge</td>
<td>6 months</td>
<td>+</td>
<td>-</td>
<td>Reticulum cell S.</td>
<td>Radiotherapy</td>
<td>8 months</td>
<td>Alive, No sign of disease</td>
</tr>
<tr>
<td>15</td>
<td>F</td>
<td>47</td>
<td>Ethmoid</td>
<td>Nasal obstruction and discharge</td>
<td>6 months</td>
<td>+</td>
<td>-</td>
<td>Reticulum cell S.</td>
<td>Excision</td>
<td>3 months</td>
<td>Died of generalized disease</td>
</tr>
<tr>
<td>16</td>
<td>M</td>
<td>54</td>
<td>Ethmoid</td>
<td>Nasal obstruction and discharge</td>
<td>6 months</td>
<td>+</td>
<td>-</td>
<td>Reticulum cell S.</td>
<td>Excision</td>
<td>1 year</td>
<td>Died of generalized disease</td>
</tr>
</tbody>
</table>

### Malignant Lymphomas of the Nose and Throat

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*https://doi.org/10.1017/S0022215100053093*
growth of the tumours appeared to be more rapid than that of carcinomas in this region.

The tonsillar cases most frequently complained of a sensation or the actual presence of a lump in the throat. Dysphagia was commonly present but was not usually severe. A lump in the neck was noted only by one patient.

The two nasopharyngeal cases both had symptoms due to cranial nerve paralysis, whereas those with nasal and ethmoid lymphomas complained of nasal obstruction combined with serous, purulent or blood-stained discharge. Pain was conspicuous by its infrequency in this series. Even rapidly growing lymphomas invading bone did not seem to cause more than occasional discomfort.

The consistency of the tumours varied from firm or rubbery to a jelly-like and rather amorphous mass. The latter were especially seen in the nose, where soft friable very vascular polypi formed. The appearance in the throat of a firm vascular tumour involving the tonsil and bulging into the soft palate presented a picture very like a peritonsillar abscess. Three of our cases were of this type and more recently two further cases have been seen by one of us (J.K.) in whom the "quinsy" had been lanced. Ulceration was noted in a third of our cases. This tends to be a late sign and may be entirely absent even with large tumours. The ulcer may resemble that of an epithelioma or gumma or may be nothing more than a superficial loss of epithelium. The tonsillar lymphomas appeared frequently to be circumscribed, the tonsillar capsule being apparently intact in most of the operated cases. Elsewhere the lymphomas were often extensive and in the nasopharynx showed a disposition to involve the underlying bone.

Enlarged cervical lymph nodes were present in both nasopharyngeal cases, all but one of the tonsillar tumours and in two of the ethmoid lymphomas. The enlargement was almost certainly due to secondary infection in some instances. The presence of enlarged nodes in other superficial situations indicated that the disease was already widely disseminated and correspondingly that the outlook was more grave.

White cell counts were usually normal in those cases presenting primarily in the nose and throat. There was a slight relative lymphocytosis in Case XI but this cannot be regarded as significant.

Pathology

The reticuloendothelial system is widespread throughout the body. Its component cells lie chiefly in the bone marrow, spleen, lymph nodes, liver (the Kupffer cells) and in perivascular connective tissue. The types of cell that exist in the different situations are constant under normal conditions. For example, the bone marrow consists largely of haemopoietic cells, the lymph nodes of lymphocytes and the Kupffer cells are
Malignant Lymphomas of the Nose and Throat

histiocytes, whereas the cells in the region of the blood vessels are dormant. All these cells have a common ancestor, the multipotential primitive mesenchymal cell described by Maximow (Maximow and Bloom, 1948). Many pathological states call for an increased physiological activity of one or more of the component cells. This leads to an increased number of these cells, which are usually supplied by the relevant tissues. For example, an acute infection calls for an increased production of neutrophil polymorphs, which are readily supplied by the bone marrow, and conditions calling for extensive tissue repair will lead to the mobilization of histiocytes derived in large measure from the local perivascular connective tissue. Occasionally, however, the stimulus is so great that cells are produced in situations within the reticuloendothelial system which in the adult are not normally concerned in their formation. For example, in diffuse carcinomatous infiltration of the bone marrow, extramedullary erythropoiesis may take place in lymph nodes and spleen.

It is a matter of no great surprise, therefore, that when malignant disease arises affecting the reticuloendothelial system, cell proliferation occurs in situations which are not commonly associated with the formation of the component cells. Myeloid leukaemia affects predominantly the bone marrow, but the spleen and liver commonly take part in the proliferative process; lymphosarcoma affects chiefly the lymph nodes but organs like the stomach and intestines may on occasion become involved in the hyperplasia. It is a feature of malignant lymphomas as a group that not all the sites containing reticuloendothelial cells will undergo proliferation at the same time. The diseases usually appear first where they might be expected, for example myeloid leukaemia in bone marrow, or lymphosarcoma in lymph nodes, and then affect other situations later, if at all; but it is not infrequent for them to reveal themselves as proliferations at unusual sites, only later showing evidence of involvement of the expected sites. Leukaemia can present by way of skin nodules (Wintrobe and Mitchell, 1940) and reticulum cell sarcoma by way of intestinal perforation (Skrimshire, 1955). When the diseases arise in more than one situation, it is clear that they always do so through primary proliferation at the various sites. Theoretically it is possible that some of the tumour masses could arise as a result of metastasis from elsewhere with secondary proliferation. This may well be the reason for some tumours but evidence is strong that primary proliferation is the more important feature.

With these theoretical considerations in mind, it would be expected that the nose and throat would at times participate in malignant lymphoma, either as a part of a proliferation already widespread, or sometimes as the first indication that the disease exists. We have been able to confirm this behaviour in our study of sixteen cases. These all presented with symptoms referable to the nose and throat. Most showed evidence of tumour either only within this cavity or in association with
R. R. M. Harman, J. Kodicek and J. L. Pinniger

regional lymph node enlargement, though Cases III, IV and XI are examples where local enlargement formed but one aspect of a disease already widespread. It is not surprising that this region should participate in malignant lymphoma, as it is so rich in tissue of the reticuloendothelial system, and it is to be expected that the tonsil should show a particular liability to be involved, as occurred in over half our cases.

There are only five survivors in our series; among these one has radiological evidence of foci of plasmacytoma in the skull and spine (Case XIV) and another has recently had further radiotherapy to a splenic tumour (Case XII). Seven of our patients who have died showed evidence of widespread involvement by the disease process (Cases I, II, III, IV, X, XI, XV) and this was proved by post-mortem examination in four. Of the remaining four cases, one died of a stroke 19 years after treatment (Case VIII), one of cardiac failure (Case VII), another of post-operative haemorrhage (Case XVI) and one of syphilitic coronary artery disease (Case IX).

The evidence from this group of cases, therefore, indicates that lymphoma starting in the nose and throat will sooner or later extend to other situations in the body, confirming the conclusions of Jackson, Parker and Brues (1936) in the case of the tonsil alone.

**Histological Features**

The nomenclature outlined in the opening section has been followed in the study of these cases. Nine have been considered to be examples of reticulum cell sarcoma, three of lymphosarcoma, two of plasmacytoma, one of Hodgkin's disease and one of a mixed lymphosarcoma and reticulum cell sarcoma. Reticulum cell sarcoma is by far the commonest variant. The cell picture varies quite appreciably. The individual cells can appear predominantly mature taking oval or polygonal forms, lying on or attached to threads in haematoxylin and eosin preparations as in Fig. 6. Occasionally they are surrounded in a box fashion by the fibrils, there being clear zones between the nucleus and fibrils. In other cases maturation of the cells is less well marked, the nucleus shows a more open network and often the cell has more abundant cytoplasm as in Fig. 10. Deposition of reticulin fibrils as judged by silver impregnation is a very common feature as seen in Figs. 7 and 11, this being in contrast to the scarcity of such fibrils seen in lymphosarcoma (Fig. 4). The absence of these fibrils, however, does not necessarily invalidate the diagnosis because tumour cells do not always reproduce the activity of their normal counterparts. Lymphosarcoma occurred in three instances, all being tonsillar tumours. In Case VII the cells were predominantly immature (Fig. 1), consisting of large round cells with open nucleus and little cytoplasm, and showing no fibrillar support. In Case VIII the cells were typical small lymphocytes (Fig. 5). This is the one case who survived for nineteen years, which is
Malignant Lymphomas of the Nose and Throat
to be correlated with the fact that chronic lymphatic leukaemia will at
times run a very benign course (Tivey, 1954).

Case XI has been termed one of Hodgkin’s disease, as the proliferation
is distinctly pleomorphic, including reticulum cells, lymphocytes, and
giant cells (Figs. 8 and 9). Eosinophils were rare, but their presence in
these cases is far from being invariable. The rarity of Hodgkin’s disease
presenting with symptoms in the nose and throat region has been observed
by Jackson, Parker and Brues (1936).

Study of our series of malignant lymphoma serves to emphasize that
while it is helpful in the interests of simplicity to designate a tumour as
being one of the three subtypes, such a designation is only based on the
majority of cells forming the tumour. It is not infrequent to see a few
lymphocytes in a reticulum cell sarcoma and a few reticulum cells in
lymphosarcoma. Occasionally the proportion of each becomes nearly
equal, when one can only term the tumour a malignant lymphoma as in
Case IV. Such a case might well be termed Hodgkin’s disease but its histo-
logical picture is rather remote from the classical features of that disease.

Two other histological findings are worthy of note. One tonsil in
Case VII showed an indistinct follicular pattern (Fig. 3) indicating that
the lymphosarcoma here had been through a stage of follicular lymphoma.
There is no indication how long a benign clinical phase had been present,
if at all. The symptoms were of short duration but the swelling was large
and could well have only slowly increased in size. As a result of the
histological picture, one would have expected a transition clinically to a
more malignant phase at about the time of operation, as lymphosarcoma
was already present, but the patient’s sudden death from cardiac failure
and lack of an autopsy invalidated any conclusions that might have been
drawn from a study of the post-operative phase.

The second feature of interest is that in two cases (Nos. VI and VII)
the lymphoid tissue of the tonsil was only partially replaced by tumour
(Fig. 2). This serves to emphasize a common finding in this group of
diseases that the reticuloendothelial tissues are only patchily involved by
tumour. If normal lymphoid tissue can be seen in a diseased tonsil, then
it would not be unexpected that lymphoid tissue elsewhere would also
be normal at that time.

The two cases of plasmacytoma show histologically the features
characteristic of this disease, consisting of sheets of myeloma cells, often
resembling plasma cells, having abundant cytoplasm and eccentric nucleus
(Fig. 12). In some areas the cells become a little less differentiated and
are here difficult to distinguish from immature reticulum cells. That there
is in fact a real relationship between these two types of cell is supported
by the finding in these cases of a dense reticulin fibril network (Fig. 13),
a feature which has also been observed by us in the marrow of orthodox
multiple myeloma.
The only two histological pictures likely to cause problems in differential diagnosis are those of severe chronic inflammation on the one hand and anaplastic carcinoma on the other. On occasions it may be quite impossible to decide on scrutiny of a single section, in which case a decision will be influenced by the consequent natural history of the disease. However, chronic inflammation rarely produces the intense and uniform proliferation of most of the lymphomas and the pleomorphism of most cases of Hodgkin’s disease is sufficiently characteristic for this to be identified. That a tumour is an anaplastic carcinoma can usually be determined by the following features. In places it will form solid alveolar or trabecular masses, clumps of tumour cells will be seen to lie in lymphatics and reticulin fibrils will not be seen to run between the individual cells.

**Prognosis**

A follow-up of those cases in which the disease has been localized to the nose and throat in the first instance shows that five are still alive (Cases V, VI, XII, XIII and XIV) from two years to six and a half years after diagnosis, one died immediately after operation (Case XVI), another after the onset of auricular fibrillation (Case VII), one from a stroke (Case VIII) and the remaining five following extension of the disease to other situations, death taking place from eight to thirty months after diagnosis (Cases I, II, IX, X and XV). A consideration of the cases still alive has to take into account three reasons for the survival. One is that the follow-up time is short, a second is that the diagnosis, usually histological, is incorrect, and the third that a cure has been effected by adequate local treatment. The first possibility can well be the explanation for all the cases, for it is well known that occasional cases of lymphoma survive for longer than ten years (Jackson, Parker and Brues, 1936; Wintrobe, 1951). However, as most sufferers from this disease die within three years of the onset of symptoms, the adequacy of diagnosis in those surviving a longer time must be critically examined before acceptance. As has already been stated, the histological picture of chronic inflammation shows considerable variations and at times can be so proliferative as to make differentiation from lymphoma a matter of real difficulty. Bearing this in mind, the histological pictures in those of our cases which survived beyond three years without recurrence (Case V, 4 years; Case VI, 6 years; and Case VIII, 19 years) have been re-examined and submitted to another individual for second opinion, with the result that the original diagnoses have been upheld. Further, a large number of routine tonsillectomy slides have been studied to ensure that a knowledge exists of the range of chronic inflammatory changes in this situation. It is still possible that Cases V, VI and VIII represent clinical cure. The likelihood is, of course, greatest in the last case but cannot be regarded as definite. Nevertheless, so long a
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survival as this is clearly a testimony to the adequacy of therapy and an encouragement to its application in similar cases.

We have not sufficient material to give an opinion as to the prognostic significance of the histological features. One case of lymphocytic lymphosarcoma which involved the tonsil survived nineteen years after treatment but the other died two and a half years after the first attendance. The one case of Hodgkin's disease survived only eight months. Those cases with reticulum cell sarcoma have shown a wide range of survival up to five years but there has been no correlation between the times and type or maturity of reticulum cell seen histologically. Plasmacytoma occurring primarily in extramedullary situations is uncommon but is a recognized entity. It is most frequent in the upper respiratory tract and particularly so in the nasal fossa (Carson et al., 1955; Dolin and Dewar, 1956). These authors have shown that the tumours are quite unpredictable in their course and may remain stationary for many years before they develop into diffuse myeloma or expand rapidly as an invading tumour, destroying bone. One of our cases (No. XV) has developed evidence of skeletal involvement a year after the onset of the nasal symptoms. Both cases have so far shown normal chemical findings, which is in accordance with other reported cases of extramedullary tumour (Carson et al., 1955; Dolin and Dewar, 1956).

Treatment

This consisted of high voltage radiotherapy with or without surgical removal of affected tissues in most cases of lymphomas confined to the nose and throat.

It has been shown that if malignant lymphoma is confined to soft tissues in the nose and throat, it is almost invariably highly sensitive to radiation (Hilton, 1948). We confirm that radiotherapy is the treatment of choice for this group of cases and that surgery plays no useful role except for the purpose of establishing the diagnosis by biopsy. Local recurrence after treatment is exceptional and the locally enlarged lymph nodes commonly also revert to normal. Lymphomatous tissue appearing in other sites subsequently usually proves increasingly less sensitive to radiotherapy.

The involvement of neighbouring bony structures carries a more serious prognosis. In the nasopharynx involvement of the base of the skull is often more extensive than clinical and radiological examinations indicate and tumour tissue is liable to remain in this inaccessible territory after an apparently adequate course of radiotherapy (Snelling, 1954).

The nose and sinuses are rather more accessible than the nasopharynx and local excision of the ethmoid region is usually performed in order to establish the exact extent of the involved area prior to radiotherapy.
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If the maxillary antrum is affected there is a case for resecting the involved antrum and hard palate after a course of radiotherapy. This provides an opportunity for direct examination of any doubtful areas and for further treatment if necessary. The palato-antrostomy also makes follow up examination more effective while the dental prosthesis which is fitted allows the patient to lead a very nearly normal life both from the functional and cosmetic points of view.

If the disease is already generalized when the patient is first seen, then the lines of treatment available are those which are directed at reducing the lymphomatous masses on the one hand, and supportive measures, such as transfusions for anaemia on the other. The specific treatment to be adopted has to be assessed for each individual patient. If localized masses are present, then radiotherapy is the treatment of choice. If, however, the disease is widespread, without any particular localization, then the newer chemotherapeutic lines should be considered (Wilkinson, 1955). These have their greatest success in the control of leukaemias. Results are moderate and inconstant for Hodgkin’s disease, reticulum cell sarcoma and lymphosarcoma and are uniformly bad in multiple myeloma.

Summary

(1) Sixteen cases of malignant lymphoma of the nose and throat have been studied. The patients were predominantly male and of middle or old age. The tonsils were involved in nine cases, the maxilla in one, the nasopharynx in two and the ethmoid in four.

(2) Clinically the tumours were bulky and appeared to grow rapidly. They behaved in the nose and throat in a similar way to lymphomas presenting in other situations and they showed the same tendency to become generalized.

(3) Reticulum cell sarcoma was the commonest in the series but the histological picture varied both in maturity and uniformity of cell types. The difficulty of sharp differentiation between the various manifestations of malignant lymphoma and the frequent finding of mixed types served further to emphasize the unity of this group of tumours.

(4) Radiotherapy was the treatment of choice and proved consistently effective in causing regression of the primary tumours, although its subsequent application to further foci of disease was progressively less useful.

(5) In the majority of cases prognosis was poor; occasionally individuals survived many years. As expected the outlook was worst where the local swellings formed part of an already widespread disease. Those who died with evidence of generalized disease survived on average only fourteen months. No clear relation could be established between the histological picture and the clinical course.
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