by way of the lymphatics was rather small. The theoretical background for transposition of the greater omentum in cases of lymphoedema was questioned. The course and ramifications of the drainage channels from the omentum to the large praevertebral lymph trunks are not yet completely known.

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Primary Plasmacytoma of Lymph Nodes

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Solitary plasmacytomas may occur in a variety of organs and tissues, including the conjunctivae, paranasal sinuses and upper respiratory tract, tonsils, stomach, small bowel, kidney, ovaries, lung, and elsewhere. More commonly, however, solitary plasmacytomas have been described as originating in bone, although multiple myeloma subsequently appears in most of these patients. Four cases of plasmacytoma arising in lymph nodes have been reported (1–4), in which there was no abnormality of the bone marrow or of the serum proteins, or other evidence of systemic dissemination. Especially interesting is the relationship of so-called „solitary" plasmacytomas to multiple myeloma, since some solitary plasmacytomas progress, after months or years, to a clinical picture indistinguishable from multiple myeloma (5).

We report two patients who presented with solitary plasmacytomas arising in cervical lymph nodes. After no other foci of disease could be found, the local lesion was widely resected. Results of treatment of solitary plasmacytomas of lymph nodes and the relationship of this lesion to multiple myeloma are discussed.

Case reports

Case 1: (G. V., M. H. # 141949): A seventy-two year old white male was first seen at Memorial Hospital in April 1954, with a seven-month history of a painless mass in the upper left side of his neck. There were no local or systemic symptoms. Physical

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examination revealed a 6 × 4 cm, non-tender, firm, smooth, mobile mass in the left mid-cervical area. Thorough examination of the oral cavity, nasopharynx, and larynx showed no abnormality. There was no peripheral lymphadenopathy and the remainder of the physical examination was unremarkable.

Routine laboratory studies were within normal limits except for a blood urea nitrogen level of 26 mg/100 ml. The urine showed a 2+ test for albumin, but did not have Bence Jones protein. Roentgenograms of the chest and skeleton did not demonstrate bony lesions. Needle aspiration biopsy of the cervical mass yielded tissue diagnostic of plasmacytoma. The patient underwent left radical neck dissection. Pathologic examination of the specimen demonstrated involvement with plasma cells of lymph nodes at all levels. The postoperative course was uneventful.

He was readmitted in December 1955 with a cerebrovascular accident. No clinical evidence of recurrent or disseminated plasmacytoma was found, but the patient left the hospital against medical advice before other studies could be done. He remained well for the next twenty months, after which he returned to his native Italy and was lost to follow-up. He is known to have died in 1960 at the age of seventy-eight, but the state of his disease and the circumstances of death are unknown.

Case 2: (R. J., M. H. # 270364): A sixty-seven year old white male noted a painless lump in the left side of his neck in December 1966. This slowly enlarged during the next several months but was otherwise asymptomatic. Incisional biopsy was done elsewhere in July 1967 and pathologic examination of the specimen showed a histologic picture characteristic of plasmacytoma. The patient denied any systemic complaints.

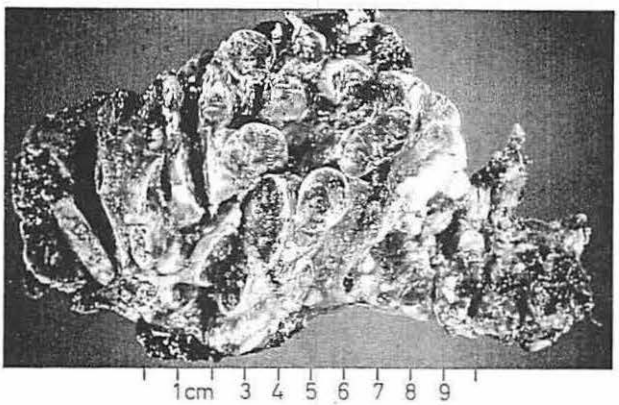

Fig. 1 Case 2. Gross surgical specimen, showing involvement of multiple lymph nodes by tumor.

On referral to Memorial Hospital in July 1967, oral, nasopharyngeal, and laryngeal examination did not reveal any abnormalities. A 6 × 10 × 10 cm, multinodular mobile mass of matted lymph nodes almost filled the left side of the neck. No evidence of deep invasion or neurological dysfunction was present. No hepatomegaly, splenomegaly, or other peripheral lymphadenopathy was noted, and the remainder of the physical examination was unremarkable. Laboratory study showed a normal complete blood count. Bone marrow examination was normal, with 2.5 percent plasma cells. Urin-

analysis was unremarkable. The blood urea nitrogen and fasting blood sugar determinations, and the serum calcium, phosphorus, and alkaline phosphatase levels were within normal limits. Serum protein electrophoresis (paper) showed the gamma globulin level to be 1.78 gm/100 ml. Urine examination for Bence Jones protein was negative, and immunoelectrophoresis of both serum and urine failed to show any abnormal proteins. Radiographic examination of the chest and skeleton showed no significant abnormalities or evidence of multiple myeloma.

In September, 1967 the patient underwent left radical neck dissection, with complete removal of the bulky involved lymph nodes (Fig. 1). Pathologic study of the specimen confirmed the diagnosis of plasmacytoma, involving multiple nodes at all levels in the neck. The normal architecture of the nodes was not recognized. There was no demarcation of cortical and medullary portions (Fig. 2). Occasionally, remnants of small lymphoid follicules were seen (Fig. 3). Well differentiated plasma cells and plasmablasts replaced the usual elements of lymph nodes (Fig. 4). Mitotic cells were extremely scanty. A few giant cells with two or more nuclei were observed (Fig. 5). Stains for amyloid were negative. The patient made an uneventful postoperative recovery. Serum protein electrophoresis done three weeks postoperatively showed a decrease in gamma globulin to 1.13 gm/100 ml. There was no evidence of recurrence of disease ten months after operation and 1 1/2 years after the left cervical mass was first noted.

Comments

Localized plasma cell tumors, or plasmacytomas, are most frequently a manifestation of multiple myeloma. Since plasma cells are generally considered to arise from the reticulo-endothelial system, either directly or through an intermediate lymphocytic phase, it is not surprising that plasmacytomas are encountered in a variety of extramedullary locations. Extraskeletal involvement in multiple myeloma is frequent, in the series of *Churg* and *Gordon* (6) there being involvement of the liver, spleen, or lymph nodes in 73 percent of thirty consecutive autopsied cases. Striking lymph node enlargement is unusual, however, and occured in only two of ninety-seven cases reported by *Snapper* et al. (7).

The histologic features of primary plasmacytoma of lymph nodes are less well known than those of the usual extraskeletal plasmacytoma. In view of our limited experience with this disease, rather than make unwarranted morphologic description, we would like to call attention to the conditions which require differentiation from primary plasmacytoma of lymph nodes. These are benign plasma cell hyperplasia, plasma cell granuloma and multiple myeloma.

The differentiation between benign plasma cell hyperplasia and plasmacytoma of lymph nodes depends upon preservation of lymphoid architecture. In plasma cell hyperplasia, the microscopic architecture of lymph nodes is maintained with good separation of cortical and medullary portions; solitary, well differentiated plasmacytes are diffusely present among the usual cellular elements of normal lymph nodes. There can be from slight to severe degree of follicular hyperplasia in the involved lymph node.

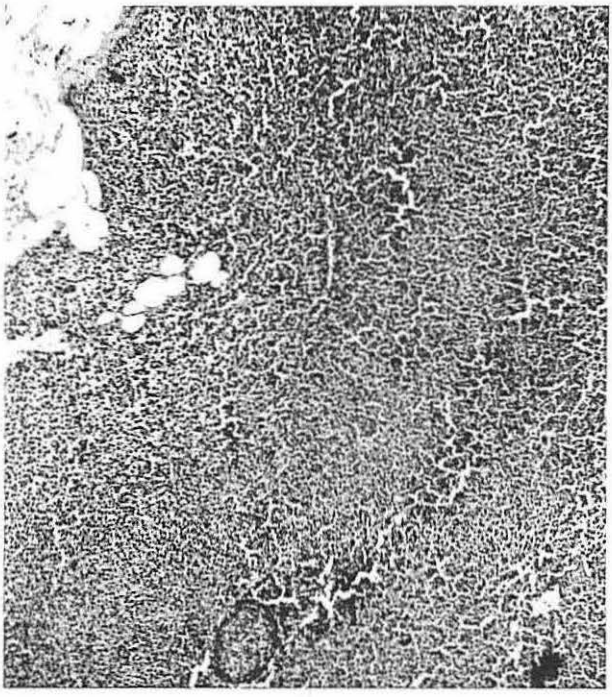

Fig. 2 Lymph node showing plasma cell infiltrate below an intact capsule (H. & E. X63).

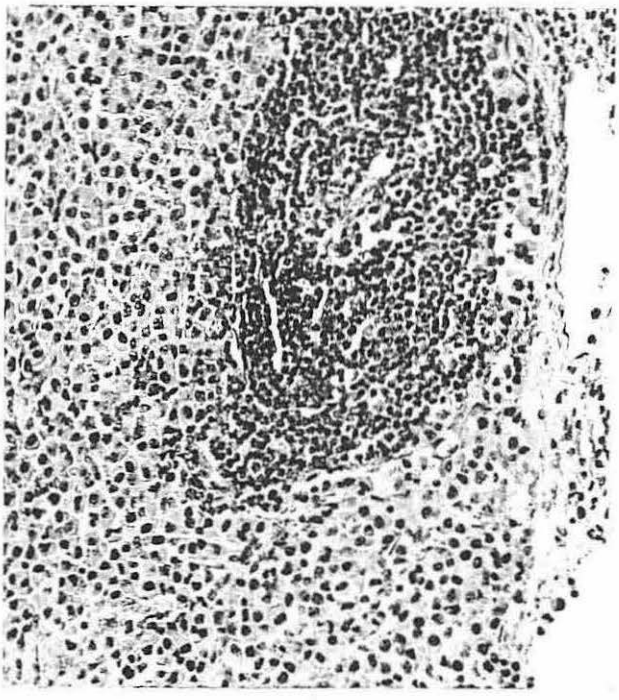

Fig. 3 Remnants of a cortical lymphoid follicle surrounded by well differentiated plasma cells (H. & E. X250).

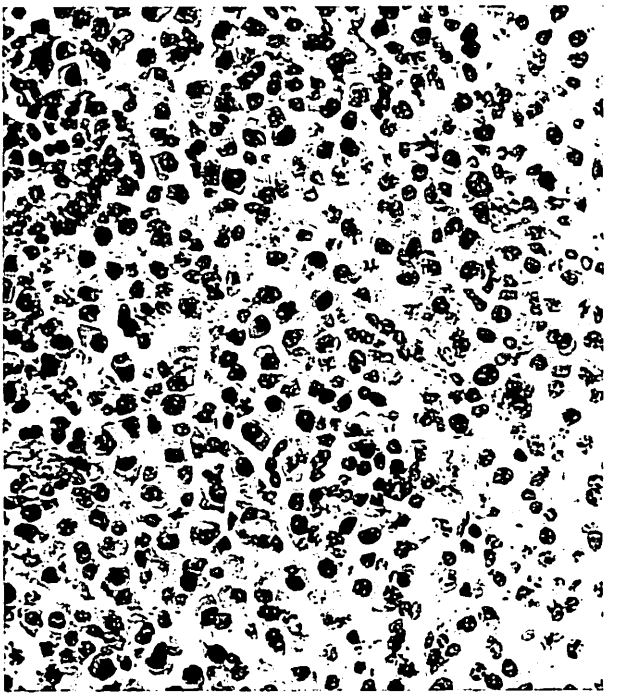

Fig. 4 High power photomicrograph showing monomorphic cellular morphology of plasma cells (H. & E. X420).

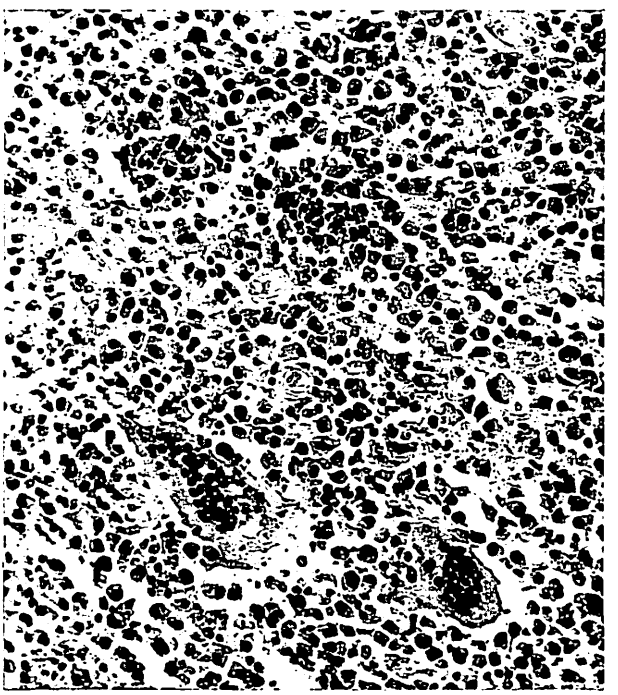

Fig. 5 Multinucleated giant cells with the characteristic plasma cells. (H. & E. X250).

The normal architecture of lymph nodes in primary plasmacytoma is not preserved. There is no demarcation of cortical and medullary portions of the lymph nodes. Well differentiated and anaplastic plasma cells partially or completely replace the usual cell population of the node. Occasionally, remnants of small atrophic lymphoid follicules can be recognized.

Plasma cell granuloma can be easily confused with plasmacytoma of lymph nodes. However, the presence of Russell bodies and large numbers of polymorphonuclear leukocytes and lymphocytes is in favor of a benign granulomatous process.

In primary plasmacytoma of lymph nodes, there is a strikingly monomorphic cell population with a diffuse uniformity in size and shape of cells in the entire lymph node. Of note, plasma cells are conspicuously absent in the pericapsular fat.

Although an apparently solitary extramedullary plasmacytoma can be the first presenting sign of a systemic neoplastic process, we believe our cases had been followed long enough to rule out systemic neoplastic disease. However, it is true that on morphologic ground alone, there is no way to be certain whether a lymph node involvement is a metastatic disease or a disease arising primarily in the lymph nodes.

Almost all patients with multiple myeloma have elevated serum levels of abnormal immunoglobulins of a monoclonal type which arise from the abnormal plasma cells, and may be detected by paper electrophoresis or immunoelectrophoresis of the serum or urine, or as Bence Jones protein in the urine. In our patient # 2 the gamma globulin level fell after resection of the tumor. Since there was no monoclonal peak, we would agree with *Suissa* et al. (4), that the elevations in gamma globulin reflect protein secretion from excessive plasma cell proliferation. The protein abnormalities would be expected to regress after removal of the source. Similar decreases in serum globulins were observed after treatment in the cases reported by *Nelson* and *Lyons* (3) and *Lane* (8).

The term "solitary" plasmacytoma is applicable only in those instances where multiple myeloma has been excluded by radiographic, hematologic, histologic, or chemical studies. Since the tumor usually represents the first manifestation of multiple myeloma and the time from the appearance of the apparently solitary plasmacytoma and evidence of disseminated disease that establishes the diagnosis of multiple myeloma may be months or years, continued observation over a reasonably long period (at least one year) and repeated laboratory studies are necessary before concluding that the process is not disseminated. Although the bone marrow in about 80 percent of cases of multiple myeloma has a diagnostic or suspicious cell pattern (9), and almost 90 percent of patients have serum protein abnormalities (10), either or both of these studies may sometimes be normal, and early bony lesions of multiple myeloma may escape radiologic detection. Since the plasma protein abnormalities may exist for months or even years before any clinical disease is evident, electrophoretic studies are especially important in these patients. The normal immunoelectrophoresis of serum and urine in patient # 2 would favor a benign process; he is the first reported patient to have this study done.

In a series of 128 patients with exramedullary plasmacytomas collected from the literature by *Hellwig* (11) in 1943, only one had disease confined to the lymph nodes, and was previously reported by *Jackson,* et al (1). Excluding plasmacytomas of the

conjunctivae, which are usually benign and are a different entity, the upper respiratory tract is the most common site of extra-medullary plasmacytoma. *Stout* and *Kenney* (12) reported 104 cases af these tumors arising in the upper respiratory passages. *Ewing* and *Foote* (13) presented twenty-seven patients from this institution with plasmacytomas of the mouth and upper airway. Only seven of these patients had disease limited to the soft tissues and three of the seven ultimately showed signs of disease elsewhere.

Table 1 Reported cases of solitary plasmacytoma of lymph nodes.

Author	Age	Sex	Site	Treatment/Recurrence	Serum electrophoresis	Bence Jones proteinuria	Known interval free of systemic disease after diagnosis
Jackson et al. (1)	67	♀	Neck	Surgery/none	not done	not done	3 years
Andersen (2)	52	♀	Submax.	Radiotherapy/decrease in size Surgery/none	not done	absent	3 1/2 years
Nelson & Lyons (3)	32	♂	Axilla	Surgery/recurred locally Surgery/recurred locally and ipsilateral supraclavicular area Radiotherapy/slight decrease in size Surgery/no recurrence	small γ globulin peak; disappeared after surgery	absent	17 years
Suissa et al. (4)	66	♂	Neck	Surgery/recurrence Surgery/no follow up	normal	absent	13 months
Gaston et al. (case 1)	72	♂	Neck	Surgery/none	not done	absent	2 1/2 years
Gaston et al. (case 2)	67	♂	Neck	Surgery/none	slight increase in γ globulin; disappeared after surgery*	absent	1 1/2 years

* Serum and urine immunoelectrophoreses negative.

There have been only four reported cases of solitary plasmacytoma to lymph nodes. We have excluded cases in which there was plasmacytosis of the bone marrow (14) or which later proved to be multiple myeloma. *Jackson* et al (1) cite the case of a sixty-seven year old woman with a discrete plasmacytoma in the left side of her neck. Three years after surgical removal she had no recurrence or extension of disease. *Andersen* (2) reported an isolated plasmacytoma of the left submaxillary region in a fifty-two year old woman. The patient had no evidence of disease in the 3-1/2 years after treatment. *Nelson* and *Lyons* (3) reported a forty-one year old man with a right axillary

mass that had recurred locally over a twenty-six year period of observation since the mass first appeared. This patient is interesting because a preoperative gamma globulin peak on electrophoresis decreased following surgical extirpation of the lesion. This patient was living and well twenty-six years after the onset of disease. *Suissa* et al. (4) reported a sixty-six year old man who had an apparently solitary cervical plasmacytoma surgically resected. There was no dysproteinemia, skeletal change, or bone marrow abnormality. These patients are summarized in Table 1.

Although it is difficult to determine the best method of treatment from so few cases, in five patients treated by surgical resection of the primary lesion, three (1; present cases) had no known recurrence. In two patients in whom primary resection did not result in cure, one was free of disease after later operative procedures (3) and another had no follow up given (4). The one reported patient who was given radiotherapy as primary treatment (2) had decrease in size of the primary lesion, which was later excised surgically without recurrence. In another case, given radiotherapy as secondary treatment (3), there was slight decrease in size of the tumor; later surgery was curative. *Rowlands* and *Shaw* (14) treated a patient with radiotherapy, with regression of enlarged lymph nodes, but since this patient had increased plasmacytes and plasma cell precursors in his bone marrow as well as elevated globulin levels in the blood, his case is not included in the table.

Ewing and *Foote* (13) reported a number of patients with plasmacytomas of the mouth and upper air passages. Of seven patients with disease limited to the soft tissues, two of three managed surgically were alive and without evidence of disease 4-1/2 years after surgery, while the other patient was dead of multiple myeloma four years after surgery. Of three patients who were treated with irradiation, one died of cancer of the stomach 3-1/2 years later, one had residual disease 6 month after treatment, and a third was lost to follow up. One patient treated with both surgery and radiotherapy was living and well 2-1/2 years later. *Ewing* and *Foote* were unable to correlate the histologic picture with the subsequent clinical course in twenty four cases of plasmacytoma of the mouth and upper air passages, and they concurred with the analysis of *Hellwig* (11), "From a prognostic standpoint the localization and gross appearance seem to be more reliable criteria than the histologic structure." Apparently histologically similar plasmacytomas in different patients have been observed to remain localized over long periods of time or to later develop into multiple myeloma. *Carson* et al (15), *Simon* and *Eidlow* (5), and *Osserman* (16) have emphasized that solitary plasmacytomas would usually later become generalized and would demonstrate the clinical manifestations of multiple myeloma. Nevertheless, the beneficial results of surgery in the patients reported in Table 1, including our two cases suggest that in a patient with solitary plasmacytoma of lymph nodes, without evidence of multiple myeloma, an aggressive surgical approach should be utilized.

Summary and Conclusions

Plasmacytoma, when encountered as an apparently isolated tumor of the lymph nodes, may remain localized and apparently benign, or may be an early manifestation of multiple myeloma. In the absence of other evidence of multiple myeloma, such as an abnormal bone marrow, skeletal lesions, or chemical or immunological evidence of

abnormal protein production, apparently localized plasmacytomas of lymph nodes should be treated by surgical resection if possible, utilizing radiotherapy if surgical removal cannot be accomplished. However, the patient must be suspect for the development of multiple myeloma and continual and prolonged observation is mandatory.

Acknowledgements

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The Structure of Normal Large Lymphatics: How This Determines their Permeabilities and their Ability to Transport Lymph

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It is well known that the structures of small lymphatics are very similar to those of small blood vessels (reviewed – 3, 4, 12). There are some differences, however, in that the lymphatics are more fragile, with tenous basement membranes, and endothelial intercellular junctions which sometimes lack zonulae adhaerentes and usually lack zonulae occludentes. (The zonulae are regions where the plasma membranes of two